BRITISH MEDICAL JOURNAL

SATURDAY 1 JULY 1967

P25569

105

CUIL-H06821-105-P25569

Leading Articles

Psychological Factors in Ulcerative Colitis (p. 1). **Hospital Junior Staff** (p. 2). **Segregation of Tuberculous Patients** (p. 3). **Oedema in Pregnancy** (p. 3). **Investigating Hypertension** (p. 4). **Mediastinal Emphysema** (p. 5). **Frozen Poultry and Staphylococcal Food-poisoning** (p. 6).

Papers and Originals

Neonatal Hirschsprung's Disease G. C. FRASER AND A. W. WILKINSON ... 7

Overinflation of the Lungs in Coal Miners COLIN OGILVIE, KEITH BROWN, AND W. E. KEARNS 10

Psychiatric Study of a Consecutive Series of 34 Patients with Ulcerative Colitis FRED FELDMAN, DAVID CANTOR, SIDNEY SOLL, AND WILLIAM BACHRACH ... 14

Pernicious Anaemia among Asians in Singapore F. J. JAYARATNAM; CHENG SIANG, SEAH; J. L. DA COSTA; KHENG-KHOO, TAN; AND W. O'BRIEN 18

Effects of Rabies Vaccine in Man J. C. M. SHARP AND SHEILA MCDONALD 20

Thymectomy in Subacute Sclerosing Leucoencephalitis O. KOLÁŘ, M. OBRUČNÍK, L. BĚHOUNKOVÁ, J. MUSIL, AND V. PĚNIČKOVÁ 22

Renal Colic JAMES A. RHIND 24

Asymmetrical Rheumatoid Arthritis after Poliomyelitis E. N. GLICK ... 26

Adverse Reactions from the Illicit Use of Lysergide THOMAS H. BEWLEY 28

Preliminary Communications

Trephine Biopsy for Diffuse Lung Lesions S. J. STEEL AND D. P. WINSTANLEY 30

Medical Memoranda

Agranulocytosis Coincident with Amodiaquine Therapy KATHLEEN BOOTH, K. LARKIN, AND I. MADDOCKS 32

Sudden Onset of Psychosis in Association with Vitamin-B$_{12}$ Deficiency ROSALINDE SMITH AND R. A. M. OLIVER 34

Current Practice

Clinician's Approach to Respiratory Viruses NEVILLE C. OSWALD 35

Today's Drugs
Aerosols in Asthma and Vaccines 37

Any Questions? 37

New Appliances
Inexpensive Heat-exchanger System for the Rygg Bag Oxygenator 38

Obituary Notices

J. St. George Wilson, M.C., F.R.C.S., F.R.C.O.G. 54
E. H. T. Cummings, C.B.E., M.D., D.P.H. 54
F. G. L. Barnes, M.B., D.P.M. 55
R. S. Reid, M.B.E., M.B. 55
R. B. McColl, M.C., M.B. 55

Book Reviews

Book Reviews 39

Middle Articles

Is There an Alternative?
Local Government Reform and the Health Services
ELIZABETH BURNEY ... 41

Conferences and Meetings
Thoracic Medicine 43

Tomorrow's Buildings
New Teaching Hospital at Oxford 44

Without Prejudice 45

News and Notes

Epidemiology 56
Parliament 57
Medical News 58

Correspondence

Casualty Department—or G.P. Service? *B. J. Preston*, F.R.C.S., *and others* 46
Endotracheal Tubes. *W. F. O'M. Doherty*, F.F.A. R.C.S. 46
Heavy Uterine Bleeding. *J. M. Gate*, F.R.C.S.ED. 47
Prevention of Rh Haemolytic Disease. *B. E. Gilliver*, M.B. 47
Unusual Bone Abnormality in Congenital Rubella. *W. C. Marshall*, M.B., *and others* 47
West Indian "Stomach." *N. V. Edwards*, M.B. 47
"Izeised" English. *J. R. Belcher*, F.R.C.S., *and L. H. Capel*, M.D. 48
Pericarditis in the Tropics. *R. H. Llerandi*, M.D. 48
Infant-scalp Vein Needles. *H. F. Nagamia*, F.R.C.S.ED. 48
Cephaloridine in Acute Pulmonary Infections. *A. Pines*, M.D. 48
Banning of Heroin. *B. H. P. Heber*, M.B. 48
Drug Addiction. *J. Twomey*, D.P.H. ...48
Tremulous Iris. *M. C. Carey*, M.B., *and O. P. N. A. FitzGerald*, M.D. 49
Inflatable Splints. *W. J. Gardner*, M.D.; *Heather Ashton*, M.R.C.P. 49
Frozen Sections. *T. J. Deeley*, M.B., F.F.R., *and J. I. Burn*, F.R.C.S. 50
Colistin in Purulent Bronchial Infections. *N. P. Halliday*, M.B. 50
Crush Injuries of the Chest. *W. Bargh*, F.F.A. R.C.S., *and others* 50
Accident Services. *A. Ward Gardner*, M.D., D.I.H. 51
Unexpected Foreign Body. *G. B. Stein*, M.B. 51
Intrauterine Contraceptive Devices. *Kathleen M. Frith*, M.R.C.O.G.; *J. S. Brown*, M.B. ... 51
Hypophysitis and Hypopituitarism. *P. B. S. Fowler*, F.R.C.P. 51
"Cruachan." *A. B. Stewart*, M.D. 51
A Matter of Principle. *J. M. London*, M.B. 52
B.M.A. Action. *R. S. Cormack*, F.F.A. R.C.S. 52
Recognizing Experience. *R. H. T. Ward*, M.B. 52
Is There a Shortage? *R. J. Evans*, M.D. ... 52
Merit Awards to Hospital Staff. *C. Remington-Hobbs*, F.R.C.S.ED. 52
New Constitution. *C. C. Lutton*, M.B. ... 53
Invasion of Privacy. *J. G. Tees*, M.R.C.S. ... 53
General Practice. *C. D. Strang*, M.B. ... 53
Ice-cream Van Accidents. *M. Briggs*, M.B., *and J. M. Potter*, F.R.C.S. 53
"Intimations of Immortality?" *C. M. Fleming*, F.R.C.P. 53

SUPPLEMENT

- **Annual Conference of Representatives of Local Medical Committees (continued)**, p. 1
- **Supplementary Annual Report of Council, 1966–7**, p. 13
- **A.R.M., 1967, Supplementary Agenda**, p. 13

No. 5556 **Brit. med. J., 1967, Vol. 3, 1–60** Weekly. Price 5s.

BRITISH MEDICAL ASSOCIATION, TAVISTOCK SQUARE, LONDON W.C.1 TEL: 01-387 4499

British Medical Association

annual exhibition 10-14 July 1967

In conjunction with the 135th Annual Meeting at the University of Bristol Union there will be an Exhibition of pharmaceutical products, medical and surgical apparatus, allied services and medical publications.

All members of the medical profession are invited to visit this Exhibition.

Monday, Tuesday, Wednesday and Thursday, 9.0 a.m. till 6.0 p.m.
Friday, 9.0 a.m. till 2.30 p.m.

THE WORLD HEALTH ORGANIZATION

requires from time to time

SPECIALISTS FOR TEACHING ASSIGNMENTS AND ADVISORY WORK IN:

- Preventive and Social Medicine
- Anatomy
- Biochemistry
- Physiology
- Pharmacology
- Microbiology (Parasitology—Bacteriology)
- Immunology
- Pathology
- Internal Medicine
- Psychiatry
- Paediatrics
- Obstetrics
- Epidemiology and Statistics

QUALIFICATIONS: Medical or science degree—minimum of 3 years' experience. For teaching assignments, preferably 3 years' experience in senior academic positions, e.g. Senior Lecturer, Reader, Associate Professor.

LANGUAGES: English or/and French.

Salary: According to grading of post—US $10,800–US $16,000 per annum (net of income tax).

Allowances: (applicable on appointments of at least one year) According to Staff Rules: post adjustment, dependants, assignment, education grant for children, health insurance for staff and dependants.

DUTY STATION: In the following regions: Africa, South East Asia, Western Pacific and Eastern Mediterranean countries.

DURATION OF ASSIGNMENT: Short-term contract of a few months' duration and long-term two years' or more renewable.

All applications should be sent to: **World Health Organization (VN/MS), Avenue Appia, Geneva.** Only candidates under consideration will receive a reply.

For BURNS · WOUNDS · ULCERS

NU-SAN GAUZE is an absorbent, non-greasy dressing, non-adherent to raw wound surfaces, easy to apply and remove.

MY-SAN is a more recent development being closely woven and, because of its special process of manufacture, is even less adherent, making it the dressing of choice for burns, donor sites and septic wounds, as well as for profusely discharging, infected ulcers.

Write for samples and leaflets to **NU-SAN LIMITED**
289 ILKESTON ROAD, NOTTINGHAM. Telephone: 72676
U.K. Distributors; Martindale Samoore Ltd. Welbeck Street, London, W.2

SLADE STRETCH THEMSELVES to make your cash go further

We have been appointed the official agents for the **7th World Assembly of the Israeli Medical Association** being held in Israel from 1st to the 10th August

Example Tour.
Hilton Hotel, Tel Aviv, 14-days ½ board
£159 Send for full details and syllabus.

SLADE TRAVEL AGENCY LTD.
397 HENDON WAY, HENDON
CENTRAL, LONDON, N.W.4.
Tel.: HENdon 0114

BRITISH MEDICAL JOURNAL

SATURDAY 8 JULY 1967

Leading Articles

Post-concussional Syndrome (p. 61). **Asbestosis** (p. 62). **Status Epilepticus: a Medical Emergency** (p. 63). **Safer Dental Anaesthesia** (p. 64). **A Year's Cancer Research** (p. 65). **Intestinal Necrosis due to Digitalis** (p. 66). **Therapeutic Misadventure** (p. 66).

Papers and Originals

Post-concussional Sequelae ALEX. R. TAYLOR 67
Prolapse of the Posterior Leaflet of the Mitral Valve: A Clinical, Familial, and Cineangiographic Study MARY STANNARD, J. G. SLOMAN, W. S. C. HARE, AND A. J. GOBLE 71
Carbenicillin: A New Semisynthetic Penicillin Active against Pseudomonas pyocyanea E. T. KNUDSEN, G. N. ROLINSON, AND R. SUTHERLAND ... 75
Prophylaxis and Therapy for Pseudomonas aeruginosa Infection with Carbenicillin and with Gentamicin R. J. JONES AND E. J. L. LOWBURY 78
Observations on Urinary White Cell Excretion Before and After Surgery R. M. LINDSAY, B. LUNAN, J. MCGEACHIE, AND A. L. LINTON 83
Use of Diazepam in Treatment of Severe Convulsive Status Epilepticus MAURICE J. PARSONAGE AND JOHN W. NORRIS 85
Intermittent Haemodialysis: Insertion and Care of the Silastic-Teflon Cannula G. J. A. CLUNIE, A. M. MARTIN, AND B. NOLAN 88
Prevention of Urinary Infection by Means of Closed Drainage into a Sterile Plastic Bag W. A. GILLESPIE, G. G. LENNON, K. B. LINTON, AND G. AUDREY BHIPPEN 90

Medical Memoranda

Methaqualone Addiction and Delirium Tremens ROBIN B. LOCKHART EWART AND ROBIN G. PRIEST 92
Thrombocytopenic Purpura in Patient with Autoimmune Haemolytic Anaemia, Successfully Treated with Mercaptopurine M. H. N. TATTERSALL ... 93

Current Practice

Today's Drugs
Radioiodine Therapy of Thyrotoxicosis 95
Any Questions? 96
New Appliances:
Suction Holder for Insertion and Removal of Contact Lenses under Visual Guidance 106

Obituary Notices

Sir Claude Frankau, C.B.E., D.S.O., F.R.C.S. 116
Lieutenant-Colonel S. R. Prall, M.D., I.M.S. (RET.) 116
T. Price, M.CH. 116
Ll. Rhys-Jones, M.R.C.S. 117
J. R. B. Russell, M.B 117
Janie H. McIlroy, M.B., D.P.H. ... 117
W. H. Parkinson, M.B. 117
D. B. Stephen, M.B. 117

Book Reviews 98

Middle Articles

Medical Education
Need for Integrated Training Schemes P. W. R. M. ALBERTI 101
Contemporary Themes
Memorandum on the Management of Accidents in Childhood 103
Research in Progress
M.R.C. Rheumatism Research Unit 105
Without Prejudice 107

News and Notes

Epidemiology 118
Parliament 119
Medico-Legal 120
Medical News 120

Correspondence

Common Market—a Challenge, Not a Danger. *S. R. Scagliola*, M.D. 108
Enzyme Activity and Cervical Carcinoma. *Charles P. Douglas*, F.R.C.O.G., *and Jean Ginsburg*, D.M. 108
Haematomas of the Abdominal Wall. *A. L. d'Abreu*, F.R.C.S., *and W. Gissane*, F.R.C.S.; *P. L. Berger*, F.R.C.S. 108
Experiments on Man. *B. W. Roper*, M.R.C.P. 109
Ophthalmic Graves's Disease. *P. Turner*, M.D., *and J. M. Sneddon*, B.SC. 109
Drugs and Driving. *J. C. Barker*, M.D. ... 109
Choledochoduodenostomy. *W. M. Capper*, F.R.C.S., *and J. E. Trapnell*, F.R.C.S.; *A. E. Stevens*, F.R.C.S., *and A. G. Johnson*, F.R.C.S. 109
Swiss-type Agammaglobulinaemia and Achondroplasia. *J. A. Davis*, M.R.C.P. ... 110
Treatment of Drug Addiction. *C. L. Brewer*, M.B. 110
Lyell's Toxic Epidermal Necrolysis. *J. G. Holmes*, M.D., *and others*; *A. Holzel*, M.D. 110
Health Week in Rural Practice. *P. A. Graham*, F.R.C.S. 110
"Swallowed" Endotracheal Tube. *J. S. Crawford*, F.F.A. R.C.S.; *R. A. Binning*, F.F.A. R.C.S. 111
Renal Potassium Wasting in Hypercalcaemia. *C. Romano*, M.D., *and others* 111
Autotransfusion. *D. P. C. Chan*, F.R.C.S.ED.; *D. Bull*, L.R.C.P.ED., *and M. Doreen Bull*, D.T.M.&H. 112
Successful Treatment of Cyanide Poisoning. *A. T. Proudfoot*, M.R.C.P.ED., *and S. S. Brown*, PH.D. 112
Folate Deficiency in the Elderly. *S. Varadi*, M.D., F.C.PATH., *and A. Elwis*, F.I.M.L.T. 112
Problems of Antenatal Care in the Tropics. *R. R. Trussell*, F.R.C.O.G. 113
Suppository Treatment of Haemorrhoids. *V. Goldman*, F.F.A. R.C.S. 113
Muscle Stiffness and Vitamin C. *J. L. Corbett*, M.B., *and A. Barr*, PH.D. ... 113
Neuro-anatomy. *J. Z. Young*, F.R.S. ... 113
Phenylketonuria. *Sir Alan Moncrieff*, F.R.C.O.G., *and others* 113
Principle of Merit Awards. *W. B. S. Crawford*, F.R.C.S.ED.; *J. L. Riley*, M.B.; *B. E. Cooke*, M.R.C.S. 114
Public Health Dispute. *E. D. Irvine*, M.D. 114
Disincentive to Acquisition of Special Skills. *Una M. P. Kroll*, M.B. 114
Democratic Efficiency at the A.R.M. *B. Williams*, F.R.C.O.G. 114
Health Centres. *H. Cairns*, M.R.C.S.; *D. S. Ractliffe*, M.B. 115
East Yorkshire's Memorandum. *R. L. Luffingham*, M.B., *and S. T. Lunt*, M.B. 115
Medical Practice Freedom Fund. *P. G. Jones*, M.B. 115

SUPPLEMENT

- **Proceedings of Council, p. 15**
- **General Medical Services Committee, p. 18**
- **Central Consultants and Specialists Committee, p. 21**

No. 5557 **Brit. med. J., 1967, Vol. 3, 61-122** **Weekly. Price 5s.**
BRITISH MEDICAL ASSOCIATION, TAVISTOCK SQUARE, LONDON W.C.1 TEL: 01-387 4499

Obstetrics
in General Practice

Published July 1966

This book is made up of a series of articles printed in the " Current Practice " section of the BRITISH MEDICAL JOURNAL. It is designed to give a lucid and practical account of obstetrics as it is carried out in the patient's home or in a maternity unit, with special emphasis on the role of the general practitioner and his relationship to the consultant obstetrician and the hospital. The principal authors are consultant obstetricians, but to ensure that the general practitioner's own view and special experience should be represented the consultant contributors were asked to prepare their articles in collaboration with general practitioners. The book as a whole is a product of such co-operative effort. It will prove a useful guide to this important branch of medical practice.

Demy Octavo *187 pages*

***Price 30s. net** (+ 2s. 6d. postage)*

(Canada $5.00 + 50c. postage)

Copies can be ordered through leading booksellers throughout the world or direct from The Publishing Manager, BRITISH MEDICAL JOURNAL, Tavistock Square, London, W.C.1

BRITISH MEDICAL JOURNAL

SATURDAY 15 JULY 1967

Leading Articles

Unity and Service (p. 123). Phenylketonuria (p. 124). Bristol A.R.M. (p. 125). Chemical Treatment of Skin Cancer (p. 125). Needs of Pre-school Children (p. 126) Safety of Drugs (p. 127). Bed Rest and Lumbar Disc Protrusions (p. 127). Tinea in Hospitals (p. 128). But eastward, look, the land is bright (p. 128).

Papers and Originals

One Profession, One Purpose ROBERT V. COOKE 129

Dietetic Treatment of Phenylketonuria: a Follow-up Study BARBARA CLAYTON, ALAN MONCRIEFF, AND G. E. ROBERTS 133

Studies in the Epidemiology of Tinea Pedis. VIII: Fungal Infection in a Long-stay Hospital MARY P. ENGLISH, R. R. WETHERED, AND ETHEL H. L. DUNCAN 136

Effects of Prompt Squatting on the Systolic Murmur in Idiopathic Hypertrophic Obstructive Cardiomyopathy M. NELLEN, M. S. GOTSMAN, L. VOGELPOEL, W. BECK, AND V. SCHRIRE 140

Reduction of Clotting in Scribner Shunts by Long-term Anticoagulation A. J. WING, J. R. CURTIS, AND H. E. DE WARDENER 143

Diagnostic Paracentesis in the Acute Abdomen W. N. W. BAKER, D. B. MACKIE, AND J. F. NEWCOMBE 146

Treatment of Stress Incontinence by Maximum Perineal Electrical Stimulation THOMAS MOORE AND PHILIP F. SCHOFIELD 150

Hepatocellular Damage with Ethacrynic Acid K. K. DATEY, S. N. DESHMUKH, C. P. DALVI, AND N. M. PURANDARE 152

Preliminary Communications

Sugar Consumption in Acne Vulgaris and Seborrhoeic Dermatitis D. G. G. BETT, JILL MORLAND, AND JOHN YUDKIN. With an Appendix by JOHN YUDKIN 153

Medical Memoranda

Hepatitis with Biliverdinaemia in Association with Indomethacin Therapy FREDERICK F. FENECH, WILLIAM H. BANNISTER, AND J. L. GRECH 155

Mycobacterium Battey Infection Resembling Tuberculosis B. R. ADELS AND P. J. N. COX 157

Current Practice

Today's Drugs
- Fenfluramine 159

Preparations and Appliances
- Apparatus for Automatic Preparation and Scanning in Cervical Cytology 160

Any Questions? 161

Obituary Notices

Sir Alexander Macgregor, K.B.E., F.R.C.P. GLASG., D.P.H. 181

Somerville Hastings, F.R.C.S. 182

Lieutenant-Colonel W. C. Gray, M.B., F.R.C.S.ED., I.M.S.(RET.) 182

Sir Claude Frankau, C.B.E., D.S.O., F.R.C.S. 182

Book Reviews 163

Middle Articles

Is There an Alternative?
- Prospects for Private Health Insurance ARTHUR SELDON 166

Self-help in the Hospitals
- St. Christopher's Hospice ... 169
- Radio Communication and the Emergency Department M. H. HALL AND R. S. GARDEN 170

Without Prejudice 172

News and Notes 183

Correspondence

Nature of the Scrapie Virus. *D. H. Adams,* D.SC., *and E. A. Caspary,* M.SC. ... 173

Future of Mental Hospitals. *A. A. Baker,* M.D., D.P.M. 173

Trismus Following Inferior Dental Nerve Block. *H. C. Killey,* M.R.C.S., F.D.S., *and L. W. Kay,* M.R.C.S., M.D.S. 173

Guanoxan. *Susan G. Cotton,* M.R.C.P., *and E. Montuschi,* M.D. 174

Lead Absorption in Children. *Sir Alan Moncrieff,* F.R.C.P., *and others* 174

The Scabies Epidemic. *Major T. C. Hindson,* M.R.C.P., D.T.M.&H.; *R. W. Smith,* M.B.; *L. J. Bacon,* M.D., D.P.H. ... 174

Problems of Antenatal Care in the Tropics. *V. J. Hartfield,* M.R.C.O.G. 175

Treatment of Choriocarcinoma. *W. W. Park,* M.D. 175

Varicose Veins, Oral Contraceptives, and Thromboembolism. *H. O. Jones,* F.R.C.S., *and J. C. F. Townsend,* F.R.C.S. ... 175

Lyell's Toxic Epidermal Necrolysis. *Major W. S. Jamieson,* M.R.C.P.GLAS., *and Major I. Capperauld,* F.R.C.S.ED.; *Wing Commander D. J. Stoker,* M.R.C.P. 176

Heavy Uterine Bleeding. *J. J. Taylor,* M.C.PATH. 176

"Swallowed" Endotracheal Tube. *M. G. Prinn,* F.R.C.S. 176

Enuresis and Psychiatry. *I. G. Wickes,* M.D. 176

Ophthalmic Graves's Disease. *D. K. Ray,* M.B. 177

Carbenoxolone Sodium. *N. Mackay,* M.R.C.P., *and C. D. Forbes,* M.R.C.P. ... 177

Cervical Smears. *M. B. Carson,* M.B. ... 177

Live Donors for Renal Transplantation. *Mary G. McGeown,* M.D., *and J. A. Kennedy,* F.R.C.S.ED. 177

Radioactive Corpses. *K. H. Clarke,* M.SC. 178

Health of Students and Soldiers. *Colonel H. G. Skinner,* D.P.H. 178

Smoking and Atherosclerosis. *S. Szanto,* M.D. 178

"Escape from Sanity." *R. G. Murray,* D.P.H. 179

Research in General Practice. *L. P. Martin,* M.B. 179

Coroners' Jurisdiction. *H. H. Pilling,* M.B. 179

Maximal Midexpiratory Flow Time. *J. J. Segall,* M.B., *and Beatrice A. Butterworth,* M.R.C.P. 179

Fees for Health Certificates. *A. S. Playfair,* M.R.C.S., *and W. M. B. Strangeways,* M.B. 180

Appointments Systems in General Practice. *A. Smith,* M.B.; *C. Taylor,* M.B. ... 180

SUPPLEMENT

- **Annual Representative Meeting, Bristol, 1967, p. 25**
- **Central Consultants and Specialists Committee, p. 66**

No. 5558 **Brit. med. J., 1967, Vol. 3, 123–186** **Weekly. Price 5s.**

BRITISH MEDICAL ASSOCIATION, TAVISTOCK SQUARE, LONDON W.C.1 TEL: 01-387 4499

Opportunities in BRITISH MEDICINE

The Board will comprise:

Dr. R. H. Barrett,
OBE, MRCS, LRCP, DTM & H DPH,
Principal Medical Officer,
Ministry of Health, London.

Professor A. G. W. Whitfield,
PhD, MD, FRCP,
Director of the Board of Graduate Medical Studies,
University of Birmingham.

Dr. A. Talbot Rogers,
CBE, MB, BS, FRCGP
Principal Medical Officer,
Ministry of Health, London.

Dr. Stephen Whittaker,
MA, MD, FRCP,
Consultant Physician and Chairman of the Consultant Services Committee,
Birmingham Regional Hospital Board.

Dr. Christie Gordon,
MB, ChB, MRCP, DPH, Dr.PH (*Johns Hopkins*),
Senior Administrative Medical Officer,
Birmingham Regional Hospital Board.

AN INTERVIEW BOARD sponsored by the Ministry of Health will visit various centres in the

UNITED STATES AND CANADA

during October, 1967, and will be interested to meet British doctors considering a return to medical work in the United Kingdom.

There are career opportunities in most branches of medicine, including administration in the National Health Service.

Payment of fares to the United Kingdom (including family) can be authorised for selected applicants.

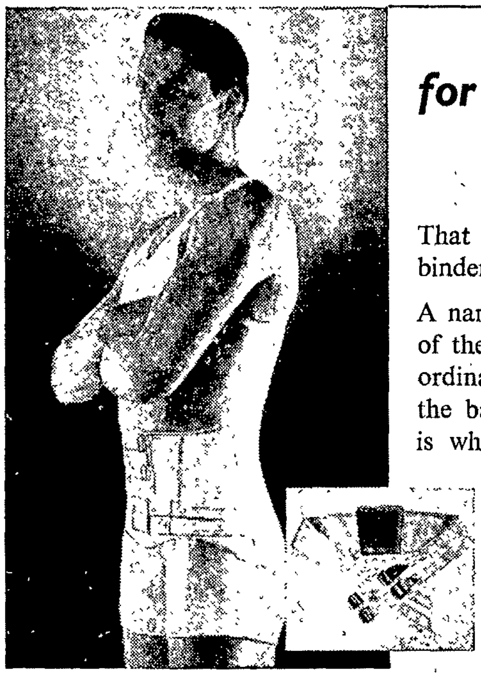
Doctors wishing to avail themselves of these facilities should write to:

Dr. R. H. Barrett, Ministry of Health,
Alexander Fleming House,
LONDON, SE1, ENGLAND,

stating their special interests and work in which they would like to engage in the United Kingdom.

Enquiries will be treated in confidence.

Interviews will be arranged at the centres to be visited by the Board.



for Sacro-iliac strain a narrow belt alone is not enough . . .

That is why Spencer Designers incorporate an easily adjustable pelvic binder (see inset below) inside each Spencer created for Sacro-iliac strain.

A narrow belt alone will not provide adequate continuous immobilization of the sacro-iliac joints, because such a belt will *not* stay in place. With ordinary body movements, any narrow belt alone will ride up and dig in at the back, thus causing faulty posture that increases the disability. That is why every Spencer Sacro-iliac Support is a "belt within a support", designed to the necessary heights and lengths to bridge the lumbar curve and correlate abdominal and back support. Thus improvement in posture—essential to relief in sacro-iliac strain—is attained and maintained.

Every Spencer—for abdomen, back, breasts—is individually designed, cut and made for each patient.

For further information and brochure on Spencer Supports write to:

SPENCER (BANBURY) LTD
Consulting Manufacturers of
SURGICAL AND ORTHOPAEDIC SUPPORTS
Spencer House · Banbury · Oxfordshire · Tel. 2265

BRANCH OFFICES:

LONDON: 2, South Audley Street, W.1. Tel. GROsvenor 4292.
LIVERPOOL: 79, Church Street, 1. Tel: ROYal 4021.
LEEDS: Victoria Buildings, Park Cross Street, 1. (Opposite Town Hall Steps.) Tel. Leeds 3-3082.
BRISTOL: 18, Whiteladies Road, 8. (Opposite Broadcasting House). Tel.: Bristol 36410.
GLASGOW: 86, St. Vincent Street, C.2. Tel: CENtral 3232.
EDINBURGH: 125A, Princes Street, 2. Tel: CALedonian 6162.

BRITISH MEDICAL JOURNAL

SATURDAY 22 JULY 1967

Leading Articles

Children of Short Stature (p. 187). Fulminating Ulcerative Colitis (p. 188). Carcinogenic Hazard (p. 189). Haematology Automated (p. 190). Hereditary Malignant Melanoma (p. 191). Contaminated Cylinders of Nitrous Oxide (p. 191). B.M.A. at Bristol (p. 192).

Papers and Originals

Early Surgery in the Management of Severe Ulcerative Colitis J. C. GOLIGHER, F. T. DE DOMBAL, N. G. GRAHAM, AND G. WATKINSON ... 193
Acute Metabolic Response to Human Growth Hormone in Different Types of Dwarfism K. E. W. MELVIN, A. D. WRIGHT, M. HARTOG, A. C. ANTCLIFF, A. M. COPESTAKE, AND T. RUSSELL FRASER 196
Chronic Intestinal Ischaemia J. KENNEDY WATT, W. C. WATSON, AND S. HAASE 199
Controlled Trials of a Sulphonamide Given Weekly to Prevent Exacerbations of Chronic Bronchitis A. PINES 202
Comparison of Methods of Expressing the Results of Augmented Histamine Tests R. J. ABERNETHY, R. M. ROSS, A. G. COX, A. W. KAY, AND I. E. GILLESPIE 205
Late Changes in Peripheral Blood after Thorotrast Administration A. O. LANGLANDS AND E. R. D. WILLIAMSON 206
Association between Digital Ischaemia and Malignant Disease P. R. HAWLEY, A. W. JOHNSTON, AND J. T. RANKIN 208
Solar Retinopathy A. E. A. RIDGWAY 212
Effect of Oral Contraceptives on Erythrocyte Sedimentation Rate in Healthy Young Women J. Ll. BURTON 214
Treatment of Radiation Sickness with Pyridoxine Hydrochloride in Outpatients of a Radiotherapy Unit H. MATTIE, E. W. EMERY, I. D. HILL, AND D. R. LAURENCE 215

Medical Memoranda

Case of Englemann's Disease P. D. GULATI, O. P. BHARDWAJ, AND P. B. VYAS 217
Phenindione-induced Neuropathy T. N. MEHROTRA 218

Current Practice

Medicine Today
Recognition of Heart Failure 219
Today's Drugs
Hazards of Drug-Prescribing in Pregnancy 220
Any Questions? 223

Book Reviews

... ... 224

Obituary Notices

D. Ioan-Jones, F.R.C.S. 246
W. Briggs, F.R.C.S. 246
Brigadier R. V. Franklin, O.B.E., M.B., A.M.S.(RET.) 247
H. L. Gulati, M.R.C.S., D.O.M.S. ... 247
Colonel P. J. Ryan, M.C., M.B., A.M.S. (RET.) 247
C. J. Lewis, M.D., D.P.H. 248
J. Stirling, M.D. 248
T. E. James, M.R.C.S. 248
A. H. Ferguson, B.M. 248

Middle Articles

B.M.A. Annual Scientific Meeting, Bristol, 10–14 July 227
Without Prejudice 237

News and Notes

Epidemiology 249
Parliament 250
Medical News 251

SUPPLEMENT

- Annual Representative Meeting, Bristol, 1967 (Concluded), p. 69
- Proceedings of Council, p. 98
- Adjourned Annual General Meeting, p. 98

Correspondence

Ophthalmic Graves's Disease. *R. Hall,* M.R.C.P. 238
Mental Health Services for Children. *B. Barnett,* D.P.M. 238
Carcinogenic Properties of Ortho-dianisidine. *Omer Karrar,* B.A., *and D. J. A. Jenkins,* B.A. 238
Local Government Reform and the Health Services. *P. O. Nicholas,* D.P.H. ... 239
Idiopathic Haemochromatosis. *L. W. Powell,* M.R.A.C.P. 239
Pressurized Aerosols in Asthma. *Judith M. Atkinson,* B.SC., *and M. J. Rand,* PH.D.; *G. F. Edwards,* M.R.C.P. 239
Nebulizers. *I. S. Bruce,* F.F.A. R.C.S. ... 240
Typhoid Fever—30 Years On. *J. C. M. Sharp,* D.P.H. 240
Human Vibriosis. *Rachel G. Evans,* M.R.C.P., D.C.H., *and J. V. Dadswell,* M.B., M.C.PATH. 240
Integrated Training Schemes. *M. Horowitz,* F.R.C.S.; *J. E. Woodyard,* F.R.C.S. .. 240
Oculogyric Crises Due to Phenothiazines. *J. R. Harries,* M.D. 241
National Kidney Centre. *S. Shaldon,* M.D. 241
Psychological Factors and Ulcerative Colitis. *D. D. Cowen,* M.B. 241
Unexpected Foreign Body. *V. T. Powell,* F.R.C.S.ED. 241
"Swallowed" Endotracheal Tube. *J. V. I. Young,* F.F.A. R.C.S. 242
Urinary Infection Presenting with Jaundice. *T. Heim,* M.D., *and G. Karoliny,* M.D. .. 242
Drug Treatment Centres. *M. M. Glatt,* M.D., D.P.M. 242
Liquor Bilirubin Levels. *G. W. Pennington,* M.D., M.C.PATH. 242
Ehlers–Danlos Syndrome. *A. P. Barabas,* F.R.C.S. 242
Infant-scalp Vein Needles. *M. L. Snaith,* M.B. 243
Diet and Diverticulitis. *G. D. Campbell,* F.R.C.P.ED. 243
I.V.P. in Renal Colic. *D. J. Mitchell,* F.F.R. R.C.S.I. 243
Chloroquine. *H. de Glanville,* D.T.M.&H. 243
Appointments Systems. *A. J. Hawes,* M.B. 243
Diabetes in the Tropics. *A. F. Tuboku-Metzger,* F.R.C.P.GLASG. 243
Portable Pharmacy. *G. S. W. Evans,* M.D. 244
Blood Pressure Monitoring. *Amy M. Fleming,* F.R.C.O.G. 244
Muscle Stiffness and Vitamin C. *I. H. Syed,* D.T.M.&H. 244
Folate Deficiency in the Elderly. *J. D. B. Andrews,* M.D., D.P.H. 244
Sliding Board for Severely Disabled Patients. *Mary J. Seiffert,* M.C.S.P. 244
Ventriculo-atrial Shunt for Hydrocephalus. *V. C. Talwalker,* F.R.C.S. 244
Annual Representative Meeting. *J. D. Shapland,* M.B. 245
Casualty Department—or G.P. Service? *R. S. Murley,* F.R.C.S. 245
Psychological Medicine Group Conference. *J. C. Barker,* M.D., D.P.M. 245
Merit Awards in General Practice. *S. H. F. Howard,* M.R.C.S. 245

No. 5559 **Brit. med. J., 1967, Vol. 3, 187–254** **Weekly. Price 5s.**

BRITISH MEDICAL ASSOCIATION, TAVISTOCK SQUARE, LONDON W.C.1 TEL: 01-387 4499

Three Impressive Books from Saunders

Beeson and McDermott: (Cecil-Loeb)

TEXTBOOK OF MEDICINE (New 12th edition)

The publication of this *New* (12*th*) *Edition* precisely 40 years after the first edition indicates how this book through the years has met the exacting demands of the medical profession . . . presenting a contemporary, authoritative and precise picture of virtually every known disease entity. The scope of medicine it embraces today is reflected in the fact that three separate Forewords are utilized in this revision.

Edited by Paul B. Beeson, M.D., *University of Oford,* and Walsh McDermott, M.D., *Cornell University Medical College. With the assistance of* 170 *eminent authorities.*

1,738 pages. Illustrated.

Single Volume **£7 3s. 6d.** Two-Volume Set **£8 11s. 6d.** Also available in a De Luxe Two-Volume Set **£10 10s.**

Sodeman and Sodeman:

PATHOLOGIC PHYSIOLOGY:

Mechanisms of Disease

(New 4th edition)

This book is designed to bridge the gap between the standard texts on physiology and textbooks of medicine. It presents a modern clinical picture of disease as resulting from physiological disturbance or dysfunction. Its twenty-eight distinguished contributors represent a vast storehouse of experienced, up-to-date, medical knowledge.

Edited by William A. Sodeman, M.D., Sc.D., F.A.C.P., *Jefferson Medical College;* and William A. Sodeman, Jr., M.D., *University of Michigan Medical School. With* 28 *contributors.*

1,051 pages. Illustrated. **£6 13s. 0d.**

Robbins: PATHOLOGY

(New 4th edition)

The new edition of *Pathology* will give you the clearest possible portrait of the dynamics of diseases as they are understood today. Dr. Robbins has almost completely rewritten his popular text to give you deeper insight into diseases from their origins to their most advanced stages.

By Stanley L. Robbins, M.D., *Professor and Chairman, Department of Pathology, Boston University School of Medicine, Boston, Mass.*

1,434 pages. Illustrated.

Single Volume **£7 3s. 6d.**
Two-volume Set **£8 15s. 0d.**

W. B. Saunders Company *12 Dyott Street, London, W.C.1*

CHILD CARE

Published 1 January, 1967

This book is the second to be published from a series of articles that have appeared in the "Current Practice" section of the *British Medical Journal*. It gives practical up-to-date advice on problems faced by general practitioners. The articles that make up the book cover the period from infancy to adolescence, and in their scope cover child-care in the broadest sense, with sections on normal development, adoption, puberty, and behaviour disorders as well as the diagnosis and management of childhood diseases. The authors are consultant paediatricians or leading authorities in their fields, but the emphasis throughout has been on a practical approach. It is hoped that the book will be a useful guide for all family doctors.

Demy Octavo *350 pages*

Price 30s. (U.S.A. $4.50) net

Postage 2s. 6d. (U.S.A. 50c.) extra

ORDER NOW

'CHILD CARE' can be ordered direct from the Publishing Manager, BRITISH MEDICAL JOURNAL, B.M.A. House, Tavistock Square, London W.C.1, *or through any leading bookseller throughout the world.*

SECOND CLASS POSTAGE PAID AT NEW YORK, N.Y.

BRITISH MEDICAL JOURNAL

SATURDAY 29 JULY 1967

Leading Articles

Changed Character of Osteomyelitis (p. 255). Thyrocalcitonin (p. 256). Problems of Transplantation (p. 257). A Disease of Skin and Bowel (p. 258). A Case for Cannabis? (p. 258). Respiratory Burns (p. 259). Sjögren's Syndrome (p. 260).

Papers and Originals

Psychiatric Sequelae of Subarachnoid Haemorrhage P. B. STOREY ... 261
Psychiatric Aspects of Pernicious Anaemia: A Prospective Controlled Investigation RALPH SHULMAN ... 266
Stenosis and Occlusion of Vessels in Cerebral Infarction
S. K. BATTACHARJI, E. C. HUTCHINSON, AND A. J. MCCALL ... 270
Mechanism of Bronchoconstriction Caused by Cigarette Smoking
G. M. STERLING ... 275
Is the Woulfe Bottle an Efficient Humidifier for Oxygen?
BERNARD J. FREEDMAN ... 277
Heparin as an Analgesic in Myocardial Infarction: A Double-blind Trial
C. J. BULPITT ... 279
Calcium Infusion Test in Osteomalacia: An Appraisal J. V. LEVER, C. R. PATERSON, AND D. B. MORGAN ... 281
Renal Papillary Necrosis in Sickle-cell Haemoglobinopathy
O. O. AKINKUGBE ... 283

Preliminary Communications

A Serological Method for Demonstrating Recent Infection by Rubella Virus
J. E. BANATVALA, JENNIFER M. BEST, ELIZABETH A. KENNEDY, ELIZABETH E. SMITH, AND MARJORIE E. SPENCE ... 285

Medical Memoranda

Guillain–Barré Syndrome Associated with Chronic Lymphatic Leukaemia
R. L. POWLES AND J. S. MALPAS ... 286
Gas in the Portal Vein in Association with a Pelvic Abscess
N. G. GRAHAM ... 288

Current Practice

Any Questions? ... 289
New Appliances
New Urinary Diversion Appliance ... 297

Book Reviews

Book Reviews ... 290

Clinicopathological Conference

A Case of Diarrhoea and Goitre 293

News and Notes

Epidemiology ... 315
Parliament ... 316
Medical News ... 317

Middle Articles

Hospital Topics
Organization of a Coronary Care Unit in a General Hospital B. L. PENTECOST, N. MAYNE, AND PATRICIA LAMB ... 298
B.M.A. Annual Scientific Meeting, Bristol, 10–14 July (concluded) ... 300
Without Prejudice ... 304

Obituary Notices

Sir Eardley Holland, M.D., F.R.C.P., F.R.C.S., F.R.C.O.G. ... 313
Lady Forber, M.D. ... 314
E. Neumark, M.D., M.C.PATH. ... 314
Sir Claude Frankau, C.B.E., D.S.O., F.R.C.S. 314

Correspondence

Post-concussional Sequelae. *J. Schorstein,* F.R.C.S. ... 305
Hetacillin and Ampicillin. *M. Ridley,* M.C.PATH. ... 305
Investigating Hypertension. *Wing Commander P. W. Robertson,* F.R.C.P. ... 306
Accident Service. *J. C. Scott,* F.R.C.S. ... 306
Coroner's Verdict and Industrial Compensation. *H. C. Lewinsohn,* M.B. ... 306
Avoidable Hazards. *J. E. deB. Norman,* F.D.S. R.C.S. ... 307
Chloasma and the "Pill." *R. Carruthers,* M.B. ... 307
Antinuclear Factors. *N. R. Rowell,* M.R.C.P., *and J. Swanson Beck,* F.R.C.P.ED. ... 307
Combined Antifungal and Antibiotic Therapy. *P. J. Kozinn,* F.A.A.P. *and Claire L. Taschdjian,* M.S.ED. ... 307
Protective Helmets and Traumatic Epilepsy. *W. B. Jennett,* F.R.C.S. ... 308
Enuresis and Psychiatry. *R. A. B. Rorie,* M.D., D.P.M. ... 308
Unusual Examples of Adnexal Torsion. *B. S. Cox,* F.R.C.S. ... 308
Down's Syndrome in India. *S. Ghosh,* D.T.M.&H. ... 309
Tolerance to Mandrax. *S. S. Brown,* PH.D., *and others* ... 309
Common Market—a Challenge, not a Danger. *E. Montuschi,* M.D. ... 309
Treatment of Choriocarcinoma. *K. D. Bagshawe,* M.D. ... 309
Trephine Biopsy of the Lung. *A. L. Jacobs,* F.R.C.P. ... 310
Scopolamine with Morphine. *G. F. Blane,* PH.D. ... 310
Infant-scalp-vein Needles. *A. D. Holliday-Rhodes,* M.B. ... 310
Is Anaesthetist Dentist's Agent? *A. M. Danziger,* D.A. ... 310
Cardiac Catheter Introducer. *W. G. Smith,* M.D. ... 311
Amitriptyline and Heart Block. *R. B. W. Smith,* M.R.A.C.P., *and Barbara J. Rusbatch,* M.B. ... 311
Cervical Smears. *Katalin E. Schopflin,* L.R.C.P.; *R. D. Last,* B.M. ... 311
Experiments on Man. *B. W. Roper,* M.R.C.P. ... 311
Appointment Systems in General Practice. *S. L. H. Smith,* B.M. ... 312
Repeat Prescription Cards. *J. S. K. Stevenson,* M.B. ... 312
Merit Awards to Hospital Staff. *H. Jacobs,* D.P.M. ... 312
Form E.C. 73. *A. B. Leys,* M.B. ... 312
Opportunities in British Medicine. *P. D. Robertson,* M.R.C.P.ED. ... 312

SUPPLEMENT

● **Overseas Conference of B.M.A.,** p. 101
● **General Medical Council,** p. 104

No. 5560 Brit. med. J., 1967, Vol. 3, 255–320 Weekly. Price 5s.
BRITISH MEDICAL ASSOCIATION, TAVISTOCK SQUARE, LONDON W.C.1 TEL: 01-387 4499

Treatment of common skin diseases

Published July 1967

Patients with skin diseases take up a large part of the time of busy general practitioners and the number of preparations available for the treatment of these disorders is rising each year. Treatment of Common Skin Diseases is a collection of articles, specially written for the *British Medical Journal,* designed to give practical advice on the management of these diseases and the selection of remedies. The articles are easy to read and give full details of dosage and administration of drugs, advice on diet, and answers to the questions asked by patients and their relatives.

Demy Octavo 116 *pages*

Price 10s. (U.S.A. $1.50) including postage

Copies can be ordered through any leading bookseller or direct

From the British Medical Journal, B.M.A. House, Tavistock Square, London, W.C.1.

BRITISH MEDICAL JOURNAL

SATURDAY 5 AUGUST 1967

Leading Articles

Chest Pain after Infarction (p. 321). Risky Grandmothers in Rh Disease (p. 322). Disorders of Defaecation in Children (p. 323). Musculo-skeletal Disorders after Renal Transplantation (p. 323). Dangers of Squint (p. 324). Fall-out and Strontium (p. 325). Coin-operated Vending Machines (p. 325). One Step Nearer? (p. 326). Elusive Popliteal Pulse (p. 326).

Papers and Originals

Personality Traits Associated with Different Chest Pains after Myocardial Infarction R. R. H. LOVELL AND A. VERGHESE 327

Comparison between Three Radioisotope Methods for Measuring Iron Absorption J. A. LUNN, JOHN RICHMOND, J. D. SIMPSON, JOAN D. LEASK, AND PETER TOTHILL 331

Epidemiological Aspects of Squint A. M. ADELSTEIN AND JOHN SCULLY 334

Progestin Therapy of Breast Cancer: Comparison of Agents BASIL A. STOLL 338

Heart Block and Coronary Artery Disease M. J. DAVIES, D. REDWOOD, AND A. HARRIS 342

Dip-Slide: An Aid to Quantitative Urine Culture in General Practice DENNIS GUTTMANN AND G. R. E. NAYLOR 343

Sodium Uptake in Peritoneal Dialysis J. D. SWALES 345

Thalassaemia and Hydrops Foetalis—Family Studies DAVID TODD, MICHAEL LAI, AND CAROLINA A. BRAGA 347

Preliminary Communications

Virus Antibodies in Subacute Sclerosing Panencephalitis: a Study of 22 Patients NIGEL J. LEGG 350

Medical Memoranda

Diffuse Systemic Sclerosis with Abnormal Liver and Gall Bladder P. W. MONCKTON COPEMAN AND W. E. MEDD 353

Current Practice

Any Questions? 355

Book Reviews 356

Obituary Notices

H. Stokes, O.B.E., M.D., F.R.C.S.I. ... 375
S. W. Maslen-Jones, M.S., F.R.C.S., F.R.C.O.G. 375
W. Dunlop, O.B.E., M.B., D.T.M.&H. ... 375
H. J. Gibson, M.D., D.P.H. 376
M. C. Macqueen, M.B., F.F.A. R.C.S. ... 376
J. H. Mellotte, M.B. 376
C. de W. Kitcat, M.R.C.S. 377
J. T. Anderson, M.B., D.T.M.&H. ... 377
I. Davies, L.R.C.P.&S.ED., D.M.R.E. ... 377
C. E. Harrison, M.B. 377
Z. Green, L.R.C.P.&S.I. 378
Sir Eardley Holland, M.D., F.R.C.P., F.R.C.S., F.R.C.O.G. 378
Sir Alexander Macgregor, K.B.E., F.R.C.P. GLASG., D.P.H. 378
Sir Claude Frankau, C.B.E., D.S.O., F.R.C.S. 378

Middle Articles

Pathology in Britain in the First Half of the Twentieth Century, with a Glance Forward C. H. BROWNING 359

Conferences and Meetings
Disorders of Protein Metabolism: Conference at R.C.P. London 362
Centenary Annual Meeting of Canadian Medical Association 364

Research in Progress
M.R.C. Annual Report ... 366

News and Notes

Epidemiology 379
Medico-Legal 380
Parliament 380
Medical News 381

Correspondence

Snakebite Poisoning. *H. A. Reid*, O.B.E., F.R.C.P.ED. 367
Undesirable Effects of Marijuana. *P. J. Dally*, F.R.C.P., D.P.M. 367
Disturbed Geriatric Patients. *H. M. Davies*, D.P.H. 367
Hetacillin and Ampicillin. *R. E. Weissgerber*, M.D. 367
Treatment of Mendelson's Syndrome. *G. Taylor*, F.F.A. R.C.S. 368
What is Psychosomatic Disease? *J. W. Todd*, M.D. 368
Fulminating Ulcerative Colitis. *T. A. Boxall*, F.R.C.S. 368
Abdominal Decompression and Foetal Blood Gases. *J. W. Newman*, M.R.C.O.G. *and E. C. Wood*, F.R.C.S. 368
Lyell's Toxic Epidermal Necrolysis. *K. B. Shilkin*, M.B. 369
Warning of Massive Pulmonary Embolism. *W. G. Smith*, M.D. 370
"Swallowed" Endotracheal Tube. *H. E. Pooler*, F.F.A. R.C.S.; *C. J. M. Dawkins*, M.D. 370
Intrauterine Contraceptive Devices. *Hilary F. H. Hill*, M.R.C.P.ED., *and Sara R. Abels*, M.B. 370
Hazard from Nylon. *G. G. Noott*, L.R.C.P.I.&L.M., L.R.C.S.I.&L.M. 370
Nalidixic Acid and Intracranial Hypertension. *O. D. Fisher*, M.D. 370
Disposable Drainage Bag for Peritoneal Dialysis. *G. Douglas*, M.B., *and others* 371
Fenfluramine. *A. Bois* 371
Screening for Cervical Cancer. *Nora H. Spens*, M.B. 371
Coroners' Jurisdiction. *H. A. Kidd*, F.R.C.S.ED. 372
Aversion Therapy of Homosexuals. *I. Bieber*, M.D. 372
Self-expulsion of a Nasal Polypus. *B. Green*, M.R.C.S. 372
Muscle Stiffness and Vitamin C. *N. T. Pollitt*, M.B.; *P. T. Lascelles*, M.D., *and D. Donaldson*, M.R.C.P. 372
Difficult Knee-jerks. *C. B. Franklin*, D.C.H. 373
The Wheel Turns. *C. W. A. Emery*, M.B. 373
Gluten-free Diets. *J. Wright*, F.P.S. ... 373
Carcinogenicity of Tobacco and Tobacco Smoke. *M. Glass*, M.B. 373
Unexpected Foreign Bodies. *J. W. S. Harvey*, M.R.C.S., F.D.S. R.C.S. 373
Policlinic: Medical Teaching at the Bedside. *G. C. Moss*, F.R.A.C.P. 373
Local Government Reform and the Health Services. *P. Sylvester*, D.P.H. 374
Annual Representative Meeting. *E. N. Callum*, F.R.C.S.ED. 374
Degrees of Seniority. *N. V. Williams*, D.P.H. 374
B.M.A. as a Negotiating Body. *J. D. Sinson*, M.B. 374
Radio Communication and the G.P. *K. A. Harden*, M.B. 374

SUPPLEMENT

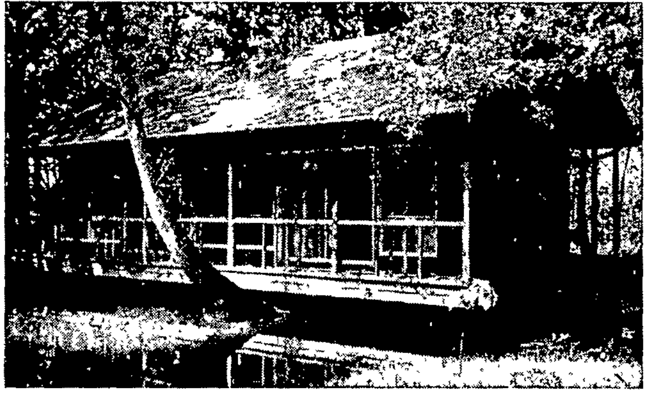
- **General Medical Services Committee (Scotland), p. 109**
- **Telephones for Hospital Staff, p. 110**

No. 5561 **Brit. med. J., 1967, Vol. 3, 321–382** **Weekly. Price 5s.**

BRITISH MEDICAL ASSOCIATION, TAVISTOCK SQUARE, LONDON W.C.1 TEL: 01-387 4499

Plan to have a Colt home

For the sheer beauty of rich red cedar. For design that you will love to live with. For workmanship you cannot fault. And for freedom from building delays, because you can have a Colt home built immediately... Anywhere and for no more than an ordinary home. Send 2/- for 48-page colour brochure and book of plans.



Come and browse around our show houses. Open weekdays from 9.30 am — 4.15 pm. Saturdays by appointment.

COLT CEDAR HOUSES
W. H. COLT, SON & COMPANY LIMITED
Bethersden, Nr. Ashford 68 Kent. Tel.: 456

Colt

For BURNS · WOUNDS · ULCERS

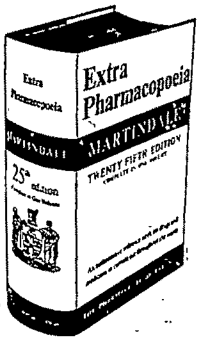
MY-SAN NU-SAN

NU-SAN GAUZE is an absorbent, non-greasy dressing, non-adherent to raw wound surfaces, easy to apply and remove.

MY-SAN is a more recent development being closely woven and, because of its special process of manufacture, is even less adherent, making it the dressing of choice for burns, donor sites and septic wounds, as well as for profusely discharging, infected ulcers.

Write for samples and leaflets to **NU-SAN LIMITED**
289 ILKESTON ROAD, NOTTINGHAM. Telephone: 72673
U.K. Distributors: Martindale Samoore Ltd. Welbeck Street, London, W.1

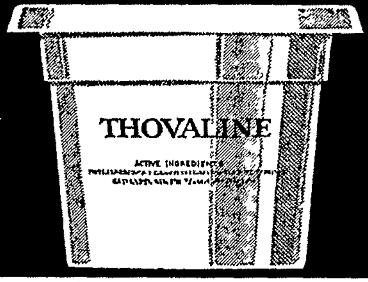
IF YOU NEED TO KNOW ABOUT DRUGS YOU NEED MARTINDALE



Martindale's Extra Pharmacopoeia, 25th edition, is the world's most comprehensive guide to drugs and medicines in current use. 1¾ million words. 150s. (+ 4s. 6d. p/p.)

THE PHARMACEUTICAL PRESS
17 Bloomsbury Square, London, W.C.1

This is THOVALINE for nappy rash



NEW

Spray on Thovaline for burns. Now available in aerosol pack.

Extensively used in Hospitals throughout the country.

ACTIVE INGREDIENTS
Talc B.P.C. 7.4%; Kaolin (light) B.P. 3.5%; Zinc Oxide B.P. 21.8%; Cod Liver Oil B.P. 2.15%; Wool Fat B.P. 1.075%.

Write to-day to THOVALINE, Dept. A7, Ilon Laboratories (Hamilton) Ltd.., Hamilton, Scotland, for full information.

Obstetrics in General Practice

Published July 1966

This book is made up of a series of articles printed in the "Current Practice" section of the BRITISH MEDICAL JOURNAL. It is designed to give a lucid and practical account of obstetrics as it is carried out in the patient's home or in a maternity unit, with special emphasis on the role of the general practitioner and his relationship to the consultant obstetrician and the hospital. The principal authors are consultant obstetricians, but to ensure that the general practitioner's own view and special experience should be represented the consultant contributors were asked to prepare their articles in collaboration with general practitioners. The book as a whole is a product of such co-operative effort. It forms a useful guide to this important branch of medical practice.

Demy Octavo 187 *Pages*

Price 30s. (Can. $5.00) net

postage 2s. 6d. (Can. 50c) extra

ORDER NOW

The Publishing Manager
BRITISH MEDICAL JOURNAL Tavistock Square, London W.C.1.

BRITISH MEDICAL JOURNAL

SATURDAY 12 AUGUST 1967

Leading Articles

Future of General Practice (p. 383). Penicillin Encephalopathy (p. 384). Rheumatic Fever in Scotland (p. 384). Experiments on Man (p. 385). New Light on Leprosy (p. 386). Psychogenic Vomiting (p. 386). Ruptured Chordae Tendineae (p. 387). Hirsuties (p. 387). Blood Changes in Manned Space Flights (p. 388).

Papers and Originals

Autistic Conditions in Early Childhood: A Survey in Middlesex J. K. WING, N. O'CONNOR, AND V. LOTTER 389
Evolution of the Ventilatory Capacity in Chronic Bronchitis PETER HOWARD 392
Management of Incoordinate Uterine Action under Continuous Epidural Analgesia DONALD D. MOIR AND JAMES WILLOCKS 396
Value of Rectal Biopsy in Paediatric Neurology: Report of 165 Biopsies E. M. BRETT AND C. L. BERRY 400
Effect of Total Dose Infusion of Iron-dextran on Iron, Folate, and Vitamin B$_{12}$ Nutrition in Postpartum Anaemia J. METZ, T. EDELSTEIN, M. DIVARIS, AND S. S. ZAIL 403
Influenza in the West of Scotland, 1966 J. C. TAYLOR, CONSTANCE A. C. ROSS, AND E. J. STOTT 406
Comparison of Duration of Activity of Corticotrophin-Gelatin and Corticotrophin-Carboxymethylcellulose M. FRIEDMAN 409
Cystic Adventitial Disease of the Popliteal Artery G. J. T. LEWIS, D. M. DOUGLAS, W. REID, AND J. KENNEDY WATT. With an Addendum by G. LEAF 411

Medical Memoranda

Chronic Thyrotoxic Myopathy with Involvement of Respiratory and Bulbar Muscles D. GAAN 415

Current Practice

Growing Points
Autoimmune Disease—I
G. L. ASHERSON 417
Today's Drugs
Prevention of Motion Sickness 421
Any Questions? 422

Book Reviews 423

Obituary Notices

Colonel C. H. Reinhold, M.C., F.R.C.S.ED., I.M.S.(RET.) 440
S. C. Ghosh, M.B., F.R.C.S. 440
C. E. Cobb, M.B., D.T.M. 440
S. C. Barnes, M.B. 440
J. L. Brown, M.B. 441
H. F. G. Hensel, M.R.C.S. 441
A. H. Shelswell, V.R.D., M.R.C.S. ... 441
W. Lumley, T.D., L.R.C.P.&S.I. 441

Middle Articles

Contemporary Themes
Relevance of American Experience of Narcotic Addiction to the British Scene
GRIFFITH EDWARDS ... 425
Medical Ethics
Supervision of the Ethics of Clinical Investigations in Institutions: Report of R.C.P. Committee ... 429
Computers in Medicine
Bibliography on Cannabis: a Medlars Search 430
New Appliances
Miniature Electric Drill ... 431

News and Notes

Epidemiology 442
Medico-Legal 443
Medical News 443

Correspondence

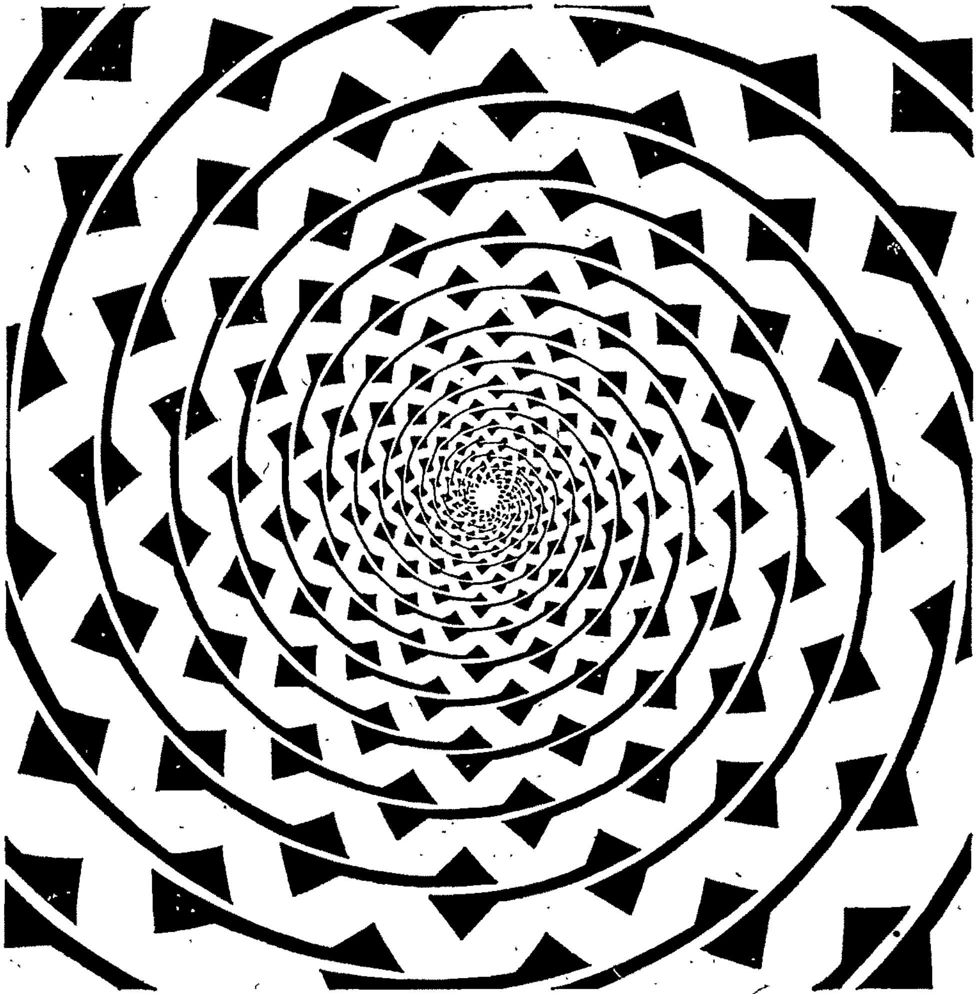
Changed Character of Osteomyelitis. *H. L.-C. Wood*, F.R.C.S., *and others* ... 432
Thyrocalcitonin. *J. H. Burn*, M.D., F.R.S.; *Iain MacIntyre*, M.C.PATH. 432
On Withholding Antibiotics. *A. S. Russell*, M.B. 432
Clinician's Approach to Respiratory Viruses. *M. H. Hambling*, M.D., M.C.PATH.; *T. H. Flewett*, M.D., *and others* 432
Ten-year Recovery from Chronic Lymphocytic Leukaemia—Twelve Years Later. *M. Schott*, M.D. 433
Amoebic Pericarditis. *S. J. Powell*, F.R.C.P.ED., *and others* 433
Management of Breast Cancer. *G. W. Watson*, F.R.C.S.ED., *and R. L. Turner*, M.D. 433
Wassermann Reaction and Vaccination. *D. J. M. Wright*, M.B. 434
Diet and Diverticulitis. *N. S. Painter*, F.R.C.S. 434
Treatment of Radiation Sickness. *B. A. Stoll*, F.F.R. 434
A Case for Cannabis? *D. Stafford-Clark*, F.R.C.P.; *N. Capener*, F.R.C.S. 435
Disinfectants and Plastic Mop Heads. *D. A. Leigh*, M.B., *and Christine Whittaker*, B.SC. 435
Potentiation of Anticoagulants. *J. D. Eddy*, M.B., *and J. Mackinnon*, M.D. 435
Safer Dental Anaesthesia. *M. W. P. Hudson*, F.F.A. R.C.S.; *S. L. Drummond-Jackson*, L.D.S. R.C.S. 436
Aversion Therapy of Homosexuals. *B. Kalcev*, M.D. 436
Results of Augmented Histamine Tests. *J. H. Baron*, D.M. 436
Folate Deficiency in the Elderly. *A. J. Gardner*, M.B. 436
Dietetic Treatment of Phenylketonuria. *B. E. Deere*, D.P.H. 437
Cardiac Resuscitation. *J. D. Barrett*, M.R.C.S. 437
Dopa and Parkinsonism. *J. A. G. Watt*, D.P.M. 437
Infectivity of Scabies. *R. W. Carslaw*, F.R.C.P.GLASG. 437
Compulsory Treatment of Addicts. *N. C. Lendon*, M.D. 438
Regurgitation during Induction. *D. D. Davies*, F.F.A. R.C.S. 438
Mortality of the Ambulance Ride. *C. H. Cullen*, F.R.C.S., *and others* 438
Oculogyric Crises Due to Phenothiazines. *J. McIvor*, M.B., F.D.S.; *Mary R. Medhurst*, M.B. 438
Cervical Cytology. *J. A. U. Morgan*, M.R.C.P.; *H. C. McLaren*, F.R.C.O.G. ... 439
Another Hardship of Hospital Junior Staff. *I. M. Cosgrove*, M.B. 439
Without Prejudice. *T. V. Tattersall*, M.B.; *G. Worrall* 439

SUPPLEMENT

- **General Medical Services Committee, p. 111**
- **Negotiating Machinery for Hospital Doctors, p. 117**

No. 5562 **Brit. med. J., 1967, Vol. 3, 383–444** **Weekly. Price 5s.**
BRITISH MEDICAL ASSOCIATION, TAVISTOCK SQUARE, LONDON W.C.1 TEL: 01-387 4499

A spiral or concentric circles?



clinical studies show pain relief is no illusion with

PONSTAN

Ponstan* (mefenamic acid, Parke-Davis) has superior analgesic, anti-inflammatory and antipyretic properties . . . is effective in a wide variety of conditions including chronic rheumatic disorders, acute pain of most aetiologies and pyrexial conditions . . . is well tolerated with an impressive absence of serious toxic effects . . . is less liable to cause gastro-intestinal haemorrhage than acetylsalicylic acid. Ponstan is available in Kapseals* of 250 mg. in containers of 12, 100 and 500, and as a suspension containing 50 mg. mefenamic acid per 5 ml. in bottles of 60 ml.

Ann.phys.Med., 8:26, 1965; Practitioner, 194:817, 1965; J.New Drugs, 4:333, 1964; The Medical Annual (Bristol) 1965.

PARKE-DAVIS Parke, Davis & Company, Hounslow, Middlesex. Telephone: Hounslow 2361 *Trade mark

SECOND CLASS POSTAGE PAID AT NEW YORK, N.Y.

BRITISH MEDICAL JOURNAL

SATURDAY 19 AUGUST 1967

Leading Articles

Accuracy of Mortality Statistics (p. 445). Anaemia in Kwashiorkor (p. 446). Thymic Function and Disease Processes (p. 447). Tests for Pregnancy (p. 448). Mao's Medicine (p. 449). Studies of Platelets (p. 449). Appointment in Surrey (p. 450).

Papers and Originals

Observations on the Aetiology and Treatment of Anaemia in Kwashiorkor E. B. ADAMS, J. N. SCRAGG, B. T. NAIDOO, S. K. LILJESTRAND, AND V. I. COCKRAM ... 451
The Liver after Kwashiorkor G. C. COOK AND M. S. R. HUTT ... 454
Small Intestine in Psoriasis SAM SHUSTER, A. J. WATSON, AND JANET MARKS ... 458
Rhinovirus Infection in Acute Exacerbations of Chronic Bronchitis: A Controlled Prospective Study A. C. STENHOUSE ... 461
Mycological and Clinical Evaluation of Griseofulvin for Chronic Onychomycosis R. R. DAVIES, J. D. EVERALL, AND ELIZABETH HAMILTON 464
Importance of Dietary Calcium in the Definition of Hypercalciuria M. PEACOCK, A. HODGKINSON, AND B. E. C. NORDIN ... 469
Renal Function after Leptospirosis B. SIMPSON, A. T. COOK, A. H. DIMOND, M. BROWN, AND R. N. T. THIN ... 472
Effect of Medical and Surgical Vagotomy on Intrinsic Factor Secretion J. F. ADAMS, A. G. COX, ELIZABETH H. KENNEDY, AND J. THOMPSON ... 473

Medical Memoranda

Hydatidiform Mole and Coexistent Foetus, both with Triploid Chromosome Constitution N. A. BEISCHER, D. W. FORTUNE, AND M. G. FITZGERALD 476

Current Practice

Growing Points
Autoimmune Disease—II G. L. ASHERSON ... 479
Any Questions? ... 483

Middle Articles

Medical History
International Congress of Medicine 1867 and Some of the Personalities Involved • W. H. MCMENEMEY ... 487
Is There an Alternative?
Yearly or Quinquennial Grants? A. MCWILLIAM ... 489
Conferences and Meetings
Dialysis and Transplantation 491
New Appliances
Modified Brown Clamp for Atraumatic Vascular Occlusion 492

Book Reviews ... 484

Obituary Notices

T. J. Hennelly, M.D., D.P.M. ... 501
P. W. Hampton, M.D. ... 501
J. Broadfoot, M.D., D.P.H. ... 501
H. Simmons, M.R.C.S. ... 501

News and Notes

Epidemiology ... 502
Motoring ... 503
Medico-Legal ... 504
Medical News ... 504

SUPPLEMENT

• **Negotiations with N.H.S. Hospital Doctors and Dentists: Joint Second Report, p. 119**

Correspondence

The "Pill" and Deep Venous Thrombosis. *K. Hæger and others* ... 493
Overinflation of the Lungs of Coal Miners. *G. B. Field*, M.R.A.C.P., *and J. E. Cotes*, D.M.; *Israel Rappaport*, M.D. ... 493
Tests for Lead Poisoning. *M. K. Williams*, B.M., D.I.H. ... 494
Treatment of Radiation Sickness. *E. V. Hulse*, M.D. ... 494
Carcinogenic Properties of Ortho-dianisidine. *H. Lehmann*, F.R.C.P. ... 494
Trismus Following Inferior Dental Nerve Block. *J. W. S. Harvey*, M.R.C.S., F.D.S. R.C.S. ... 494
Investigating Hypertension. *M. J. Chamberlain*, M.R.C.P., *and J. A. Gleeson*, M.R.C.P. ... 495
Elusive Popliteal Pulse. *F. A. R. Stammers*, F.R.C.S.; *Winifred L. Turner*, M.B.; *A. T. Carty*, M.R.C.P.I. ... 495
Chemical Treatment of Skin Cancer. *G. M. King*, M.D. ... 495
Two Types of Breast Cancer? *G. Hems*, PH.D. ... 496
Digital Ischaemia and Malignant Disease. *E. N. Wardle*, M.R.C.P.; *D. N. Golding*, M.D. ... 496
Undesirable Effects of Marijuana. *E. G. Wilkins*, M.D. ... 496
Dopa and Parkinsonism. *G. C. Cotzias*, M.D. ... 497
Guillain-Barré Syndrome with Leukaemia. *D. S. Ractliffe*, M.B. ... 497
Changed Character of Osteomyelitis. *J. H. Bulmer*, F.R.C.S.; *T. J. Fairbank*, F.R.C.S.; *D. R. Richard*, F.R.C.S. ... 497
Recognition of Heart Failure. *P. H. M. Carson*, M.R.C.P. ... 497
Cardiac Arrest in Asthma. *Mary A. Millar*, M.R.C.P.GLASG., *and T. Semple*, M.D. ... 498
Pressurized Aerosols in Asthma. *E. C. Bloch*, F.F.A. R.C.S. ... 498
Stress Incontinence Treated by Electrical Stimulation. *S. A. Vincent*, F.R.C.S. ... 498
Enuresis and Psychiatry. *P. A. Barker*, M.R.C.P.ED., D.P.M. ... 498
Coroners' Jurisdiction. *J. E. Miller*, L.R.C.P.ED. ... 499
Asbestosis. *L. B. Bourne*, D.I.H. ... 499
Psychological Factors and Ulcerative Colitis. *H. Gainsborough*, F.R.C.P. ... 499
Pericarditis in the Tropics. *K. S. Somers*, M.B. ... 499
Sugar Consumption and Acne. *S. Bourne*, M.R.C.P. ... 500
Sliding Board for Severely Disabled Patients. *R. E. Jowett*, F.R.C.S. ... 500
Is Anaesthetist Dentist's Agent? *R. I. Dixon*, D.A. ... 500
Opportunities in British Medicine. *D. C. Prior*, L.M.S.S.A. ... 500
Seniority Allowance. *A. M. Poornan*, M.B. 500
Seniority from 1913? *E. C. White*, M.B. ... 500

No. 5563 **Brit. med. J., 1967, Vol. 3, 445–506** **Weekly. Price 5s.**

BRITISH MEDICAL ASSOCIATION, TAVISTOCK SQUARE, LONDON W.C.1 TEL: 01-387 4499

Obstetrics in General Practice

Published July 1966

This book is made up of a series of articles printed in the " Current Practice " section of the BRITISH MEDICAL JOURNAL. It is designed to give a lucid and practical account of obstetrics as it is carried out in the patient's home or in a maternity unit, with special emphasis on the role of the general practitioner and his relationship to the consultant obstetrician and the hospital. The principal authors are consultant obstetricians, but to ensure that the general practitioner's own view and special experience should be represented the consultant contributors were asked to prepare their articles in collaboration with general practitioners. The book as a whole is a product of such co-operative effort. It will prove a useful guide to this important branch of medical practice.

Demy Octavo *187 pages*

***Price 30s. net** (+ 2s. 6d. postage)*

(Canada $5.00 + 50c. postage)

Copies can be ordered through leading booksellers throughout the world or direct from The Publishing Manager, BRITISH MEDICAL JOURNAL, Tavistock Square, London, W.C.1

BRITISH MEDICAL JOURNAL

SATURDAY 26 AUGUST 1967

Leading Articles

Rise in Industrial Accidents (p. 507). Early Discharge of Maternity Patients (p. 508). Activation Analysis (p. 509). Architectural Aids for Disabled (p. 510). Allergic Gastroenteropathy (p. 510). Oxygen Therapy Equipment (p. 511). Children in Care (p. 512). Sentence Without Trial (p. 512).

Papers and Originals

Renal Function after Acute Tubular Necrosis J. D. BRIGGS, A. C. KENNEDY, L. N. YOUNG, R. G. LUKE, AND MARY GRAY 513

Paediatric Aspects of the Early Discharge of Maternity Patients M. W. ARTHURTON AND F. N. BAMFORD 517

Obstetric Aspects of the Early Discharge of Maternity Patients G. A. CRAIG AND J. M. B. MUIRHEAD 520

Urinary Steroid Assays and Response to Endocrine Ablation B. S. THOMAS, R. D. BULBROOK, AND J. L. HAYWARD 523

Effect of Cyclandelate on Mental Function and Cerebral Blood Flow in Elderly Patients J. A. C. BALL AND A. R. TAYLOR 525

Glossopharyngeal and Vagal Neuralgia JAGDISH C. CHAWLA AND MURRAY A. FALCONER 529

Haemoglobin F Hull (γ121 Glutamic Acid→Lysine), Homologous with Haemoglobins O Arab and O Indonesia L. S. SACKER, D. BEALE, A. J. BLACK, R. G. HUNTSMAN, H. LEHMANN, AND P. A. LORKIN 531

Paraplegia Caused by Spinal Metastasis from Thyroid Cancer K. E. HALNAN AND P. H. ROBERTS 534

Medical Memoranda

Need for Clarity in Infant Feeding Instructions H. SIMPSON AND J. O'DUFFY 536

Anaemia Due to Blood Loss from the Telangiectases of Scleroderma JOHN M. HOLT AND RALPH WRIGHT 537

Current Practice

Transport of Invalids by Air K. G. BERGIN 539

Any Questions? 543

Clinicopathological Conference

A Case of Hypertension, Anuria, and Uraemia 544

Obituary Notices

Leon Gillis, M.B.E., M.CH.ORTH., F.R.C.S., F.R.C.S.ED., D.L.O. 562

Colonel E. E. S. Wheatley, C.B.E., M.R.C.S. 562

J. Caldwell, M.D. 562

G. R. Cubitt, T.D., M.B. 563

G. R. Malkin, M.R.C.S. 563

S. W. Maslen-Jones, M.S., F.R.C.S., F.R.C.O.G. 563

Book Reviews 548

Middle Articles

Outside Europe

Medicine in Burma Today A. W. WOODRUFF 551

Conferences and Meetings

Otolaryngology Conference ... 555

New Appliances

A Means of Speaking for Patients with Cuffed Tracheostomy Tubes ... 547

Approved Names 554

News and Notes

Epidemiology 564

Medical News 565

Correspondence

Restrictions on Doctor in South Africa. *Lord Adrian*, O.M., M.D., F.R.S., *and others* 556

A Case for Cannabis? *Elizabeth Tylden*, M.B.; *D. Wild*, D.P.H. 556

Dangers of the Woulfe Bottle. *W. M. Edgar*, M.D. 557

Friction is the Rub. *J. V. S. A. Davies*, F.R.C.P. 557

Investigating Hypertension. *R. W. D. Turner*, F.R.C.P. 557

Diabetic Lipaemia. *T. Hargreaves*, M.D. ... 557

Carcinogenic Properties of Ortho-dianisidine. *R. A. M. Case*, M.D. 557

Transplacental Transmission of Herpes Simplex. *L. Cederqvist*, M.D., *and others* 558

Snakebite Poisoning. *C. Gardner-Thorpe*, M.B. 558

Ehlers-Danlos Syndrome. *R. M. Bannerman*, D.M., *and others* 558

Warning of Massive Pulmonary Embolism. *D. Negus*, F.R.C.S. 559

Chemical Treatment of Skin Cancer. *F. J. C. Roe*, D.M. 559

Hazard from Nylon. *E. N. Callum*, F.R.C.S.ED. 559

Treatment of Mendelson's Syndrome. *Margaret J. Watt*, F.F.A. R.C.S. 559

Stewart–Morel Syndrome. *I. P. Rowlands*, M.R.C.P., *and B. C. Das*, M.B. 559

Hypogammaglobulinaemia in Adults. *K. M. Citron*, M.D. 560

Cardiac Resuscitation. *W. E. Hadden*, D.P.H. 560

Insulinotropic Action of Secretin. *J. Dupré*, M.D., *and others* 560

Mortality of the Ambulance Ride. *F. G. St. Clair Strange*, F.R.C.S. 560

Fulminating Ulcerative Colitis. *D. M. Sinclair*, F.R.C.S.GLASG. 561

Casualty Department—or G.P. Service? *J. H. Jennings*, M.B. 561

Health of Students and Soldiers. *Colonel F. G. Neild*, D.P.H. 561

Consultants' Views of G.P. *C. W. Flemming*, F.R.C.S. 561

Radio Communication and the G.P. *R. A. Briggs*, M.B., *and others* 561

B.M.A. Department of Audio-visual Communication. *T. A. Quilliam*, PH.D., D.L.O. 561

SUPPLEMENT

- **Security of Tenure of Consultant Appointment, p. 123**
- **Public Health Service Dispute, p. 124**

No. 5564 **Brit. med. J., 1967, Vol. 3, 507–566** **Weekly. Price 5s.**

BRITISH MEDICAL ASSOCIATION, TAVISTOCK SQUARE, LONDON W.C.1 TEL: 01-387 4499

The problem of the dirty mouth

Even in 1967 the dangers, and the unpleasantness, of the dirty mouth are still present in the post-operative period, as well as in many fevers; the geriatric patient being especially prone to them. Careful attention to oral hygiene will usually, of course, keep the patient comfortable and prevent complications. Such attention, however, is very time-consuming to the nurse; and it is not often realised that for most patients it can be replaced or supplemented by the use of chewing gum.

The regular use of chewing gum, by stimulating salivary flow, keeps the mouth clean in the most natural way possible. The patient is in a sense providing his own nursing care with the minimum of energy expenditure by himself.

Child patients, of course, need no encouragement to chew gum. The older patient may need encouraging—but not once he has appreciated the very obvious cleansing and refreshing effect that chewing gum has upon the mouth. Chewing gum is also of value to patients who are forbidden to smoke.

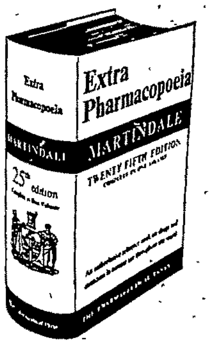
*

THE WRIGLEY COMPANY LIMITED,
WEMBLEY, MIDDLESEX
Manufacturers of Pure Chewing Gum

IF YOU NEED TO KNOW ABOUT DRUGS, YOU NEED
MARTINDALE

Martindale is the world's most up-to-date drug reference book, a unique appraisal of virtually every drug and medicine in use today. Ask your pharmacist to show you *his* copy. Five minutes' browsing will convince you: if you need to know about drugs, you need Martindale. You can order it from any bookseller, or direct from the publishers.

Martindale's Extra Pharmacopoeia
25th edition, complete in one vol.
1840 pages. 150s. (+4s. 6d. p.p.)
THE PHARMACEUTICAL PRESS
17 Bloomsbury Sq., London, W.C.1
Illustrated prospectus free on request



Books on every subject, including Medicine, Art, Education, Philosophy, Music, Commerce, Law, Religion.

The World's Greatest Bookshop

W. & G. FOYLE LTD.
119-125 CHARING CROSS RD., LONDON WC2
Open 9—6 *inc. Sats.* (*Thur.* 9—7)

ADVERTISEMENTS

PHARMACEUTICAL PRODUCTS

Readers are reminded that prescribers' literature and clinical information are always available from advertisers on request.

BRITISH MEDICAL JOURNAL

SATURDAY 2 SEPTEMBER 1967

Leading Articles

Place of the Mentally Retarded (p. 567). Training for Obstetrics and Gynaecology (p. 568). Antibodies in Schizophrenics (p. 569). Progress with Air Pollution (p. 570). S.T.P. (p. 570). Healing Processes in Wounds (p. 571). Diet and Alcohol in Gout (p. 572).

Papers and Originals

Institutional Care of the Mentally Subnormal THOMAS McKEOWN AND IAN LECK ... 573

Clinical Application of Demand Pacemakers EDGAR SOWTON ... 576

Diagnosis of Phenylketonuria (Phenylalanine Hydroxylase Deficiency, Temporary and Permanent) J. B. P. STEPHENSON AND M. S. McBEAN 579

Phenylketonuria: A Reassessment of Mass Infant Screening by Napkin Test J. B. P. STEPHENSON AND M. S. McBEAN ... 582

Detection of Incompetent Perforating Veins by Venography at Operation JULIAN TOWNSEND, HUGH JONES, AND J. EDMUND WILLIAMS ... 583

Acute Myocardial Infarction in Pregnancy E. FLETCHER, E. W. KNOX, AND P. MORTON ... 586

Oil Mist Hazard and Piped Air Supplies JOHN A. BUSHMAN AND PETER A. CLARK ... 588

Bronchial Carcinoma with Hypercalcaemia Simulating Cerebral Metastases N. J. STRICKLAND, A. M. BOLD, AND W. E. MEDD ... 590

Choice of Method for Administration of Oxygen I. D. GREEN ... 593

Preliminary Communications

Phagocytosis by Polymorphonuclear Leucocytes from Patients with Renal Failure T. D. BROGAN ... 596

Medical Memoranda

Subcutaneous Atrophy after Local Corticosteroid Injection ANN BEARDWELL ... 600

Suicidal Chlorate Poisoning Treated with Peritoneal Dialysis R. K. KNIGHT, J. R. TROUNCE, AND J. S. CAMERON ... 601

Current Practice

Forensic Medicine and Toxicology
- Drug Addiction THOMAS H. BEWLEY ... 603

Any Questions? ... 605

Obituary Notices

Gregory Pincus, D.SC. ... 621
E. B. Verney, F.R.C.P., F.R.S. ... 621
Gaetano Martino, M.D. ... 622
J. B. S. Guy, C.B.E., T.D., D.L., M.B. ... 622
W. H. Harwood-Yarred, M.B. ... 623
A. Greenhalgh, M.B. ... 623
F. D. C. Ford, B.M. ... 623
W. E. H. Banks, M.B. ... 623

Book Reviews

Book Reviews ... 606

Middle Articles

Hospital Topics
- Clinical Virology: A Year's Experience J. E. BANATVALA, ELIZABETH A. KENNEDY, AND JENNIFER M. BEST ... 609

Computers in Medicine
- Notification of Death Occurring after Discharge from Hospital M. R. HUBBARD AND E. D. ACHESON ... 612

Correspondence

Yearly or Quinquennial Grants? *H. B. May*, F.R.C.P. ... 614

Disturbed Geriatric Patients. *M. R. P. Hall*, M.R.C.P., *and others* ... 614

Propranolol in Myxoedema. *R. Greene*, F.R.C.P. ... 614

Carcinogenicity of Tobacco and Tobacco Smoke. *H. D. Beckett*, D.P.M.; *F. J. C. Roe*, D.M., *and A. L. Levene*, F.R.C.S. ... 614

Carcinogenic Properties of Ortho-dianisidine. *G. Discombe*, F.C.PATH. ... 615

Lead Absorption in Children. *N. S. Gordon*, F.R.C.P.ED., *and others* ... 615

Dermatitis from Occlusion Plasters. *N. Cridland*, D.M. ... 616

Experiments on Man. *M. H. Pappworth*, M.D. ... 616

Digital Ischaemia and Malignant Disease. *E. B. Jarrett*, F.R.C.P. ... 616

Safer Dental Anaesthesia. *J. G. Bourne*, F.F.A. R.C.S.; *M. P. Coplans*, F.F.A. R.C.S. 616

Holiday Camps for the Disabled. *Sir Treffry Thompson*, D.M. ... 617

Mental Illness in Foreign Nationals. *H. R. George*, D.P.M. ... 618

"Swallowed" Endotracheal Tube. *E. S. Mucklow*, M.R.C.P.ED., D.C.H. ... 618

What is Psychosomatic Disease? *D. Stafford-Clark*, F.R.C.P.; *B. Inglis*, PH.D. 618

Court Lees School. *J. H. Lankester*, M.B. 619

Coroners' Jurisdiction. *I. M. Jones*, M.B. .. 619

"Long-acting" Corticotrophin. *M. J. Flynn*, M.B. ... 619

Disinfectants and Plastic Mop Heads. *L. Steingold*, M.B., *and others* ... 620

Opportunities in British Medicine. *J. W. Davidson*, M.R.C.P.GLASG. ... 620

Impression of General Practice. *A. R. H. Williamson*, M.R.C.S., *and others* ... 620

News and Notes

Medico-Legal ... 624
Epidemiology ... 624
Medical News ... 625

SUPPLEMENT

- **Medical Registration, p. 125**
- **Compulsory Attachment Scheme, p. 126**
- **B.M.A. Planning Unit, p. 126**

No. 5565 **Brit. med. J., 1967, Vol. 3, 567–626** **Weekly. Price 5s.**

BRITISH MEDICAL ASSOCIATION, TAVISTOCK SQUARE, LONDON W.C.1 TEL: 01-387 4499

Indispensables

Certain things are *basic* . . . The books, for instance. You may not take them down every day, but you *know* them. Sound, fundamental.

You know Aspellin, too. A really effective, economical treatment for rheumatic conditions and muscular trauma—a spirit-based liniment containing Acid Acetylsalicylic to relieve symptomatic pain *rapidly*, and Methyl Salicylate, with Menthol and Camphor, to reduce inflammation and muscle tension.

Rheumatism sufferers can only obtain Aspellin if you prescribe it. Aspellin is *only* obtainable on prescription. Cost: 10½d. per oz.

ASPELLIN—*indicated in the treatment of acute rheumatic conditions, sciatica, lumbago, fibrositis, muscular trauma.*

Professional literature and samples from: Radiol Chemicals Ltd., Stepfield, Witham, Essex. Tel. Witham 2538

Books on every subject, including Medicine, Art, Education, Philosophy, Music, Commerce, Law, Religion.

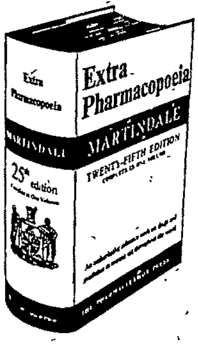
The World's Greatest Bookshop

W. & G. FOYLE LTD.

119-125 CHARING CROSS RD., LONDON WC2

Open 9—6 *inc. Sats.* (*Thur.* 9—7)

HAVE YOU SEEN THE NEW MARTINDALE?



Martindale's Extra Pharmacopoeia 25th edition, is the world's most comprehensive guide to drugs and medicines in current use. Ask your pharmacist to show you *his* copy. Five minutes' browsing will convince you: if you need to know about drugs, you need Martindale. 1½ million words. 150s. (+ 4s. 6d. p./p.).

THE PHARMACEUTICAL PRESS
17 Bloomsbury Square, London, W.C.1

A MONEY SAVING OFFER

Attention is drawn to the following special discounts offered by

FRED SNELLGROVE LTD.

Furnishers, Jewellers and General Salesmen

Watches	Less 22½%
Diamond Rings	Less 20%
Cutlery, Fountain Pens, Lighters	Less 20%
Signet Rings, Wedding Rings	Less 20%
Tape Recorders	Less 20%
*Furniture (most makes)	Less 20%
Carpets	Less 20%
Perambulators, Cribs, etc.	Less 20%
Jewellery	Less 15%
Brush Sets, Cut Glass, Musical Boxes	Less 15%
Clocks, Barometers, Binoculars	Less 15%
Electric Razors	Less 15%
Radio Sets and Record Players	Less 15%
Typewriters (portable)	Less 15%
Refrigerators, Spin Dryers, Washing Machines, Electric Blankets, Food Mixers, Electric Fires	Less 12½%
Oil Heaters, Lawn Mowers, Garden Tools	Less 12½%

ALL DISCOUNTS QUOTED ARE OFF THE FULL RETAIL PRICE INCLUDING PURCHASE TAX

* Extra discount on furniture orders over £100

We give a note of introduction to Wholesalers' showrooms where these may be viewed as in a retail shop, which in most cases means a saving of 17½ to 20% on normal retail prices. In the event of a customer knowing what is required we will endeavour to obtain and supply if he will advise to the make and model.
On acceptance of an order we require a deposit of 10%, the balance to be paid immediately after delivery.
We cover a very wide range of goods and welcome all enquiries.

Delivery can be arranged anywhere in U.K.

FRED SNELLGROVE LIMITED
(Wholesale and Contract Dept.)
37 Woodgrange Road, Forest Gate, E.7
Telephone: 01-534-8401 *and* 8402
Bankers: *Westminster Bank Ltd. (Walworth Road Branch, London, S.E.17)*
Closed 1 p.m. Thursdays

BRITISH MEDICAL JOURNAL

SATURDAY 9 SEPTEMBER 1967

Leading Articles

Which Pill? (p. 627). Management of the Idiopathic Respiratory Distress Syndrome (p. 628). Single-dose Treatment of Pyelonephritis (p. 629). Chlorpromazine Melanosis (p. 630). Closure of Kidney Centre (p. 631). Role of the Married Nurse (p. 632). Allergy to Seminal Fluid (p. 632).

Papers and Originals

Gammaglobulin in Prevention of Rubella and Congenital Defect: A Study of 30,000 Pregnancies J. C. McDONALD, CATHERINE S. PECKHAM, AND JUDITH MUNK 633
Incidence of Rubella Antibodies among Pregnant Women in Six Areas: Prophylactic Effect of Two Doses of Gammaglobulin REPORT TO THE PUBLIC HEALTH LABORATORY SERVICE RUBELLA WORKING PARTY 638
Comparison of Intragastric and Intravenous Routes of Glucose/Bicarbonate Administration in Respiratory Distress Syndrome J. M. ABRAHAM AND R. J. K. BROWN 640
Formed Visual Hallucinations: A Symptom of Cranial Arteritis C. T. HART 643
Effect of an Oral Contraceptive Immediately Post Partum on Initiation of Lactation TEIT KÆRN 644
Idiopathic Gangrene in African Children A. G. G. TURPIE, C. D. FORBES, AND G. P. McNICOL 646
Single-dose Treatment of Acute Urinary Tract Infection: a Controlled Trial R. N. GRÜNEBERG AND W. BRUMFITT 649
Controlled Trial of Methandienone in Treatment of Diabetic Retinopathy P. R. HUNTER, SUSAN G. COTTON, J. H. KELSEY, AND ARNOLD BLOOM ... 651

Preliminary Communications

Fibrinolytic Activity in the Clinical Crisis of Sickle-cell Anaemia A. MAHMOOD, DORIS M. MACINTOSH, AND A. G. SHAPER 653

Medical Memoranda

Embolism from Mural Thrombus in the Thoracic Aorta D. O. OLIVER ... 655
Chronic Milk-alkali Syndrome after Prolonged Excessive Intake of Antacid Tablets A. J. CAMERON AND M. P. SPENCE 656
Pernicious Anaemia and Intestinal Malabsorption: Spinal Cord Degeneration Developing during Vitamin B12 Treatment C. G. RILEY 657
Irreducible Posterior Dislocation of the Elbow A. DEVADOSS 659
Human Infection with a Tapeworm, Bertiella sp., Probably of African Origin C. D. THOMPSON, C. H. JELLARD, AND J. J. C. BUCKLEY 659
Self-poisoning with Digoxin: Successful Treatment with Atropine F. NAVAB AND M. HONEY 660
Self-poisoning with Digitalis Glycosides JAMES BUCHANAN 661

Current Practice

Imipramine and Amitriptyline Poisoning in Children C. M. STEEL, J. O'DUFFY, AND S. S. BROWN 663
Any Questions? 668

Book Reviews 669

Middle Articles

Hythe Medical Centre—an Appraisal G. H. WARRICK ... 672
Hospital Admissions among Students GRAHAM GRANT ... 674
New Appliances 676

Obituary Notices 684

Correspondence

Medicine in Burma. *Sir George R. McRobert,* F.R.C.P.; *J. H. Middlemiss,* M.D., F.F.R.; *H. A. Constable,* M.R.C.S. 677
Penicillin Encephalopathy. *H. G. Smith,* M.D. 677
Treatment of Staphylococcal Endocarditis. *S. W. B. Newsom,* M.B., M.C.PATH. ... 678
Mortality of the Ambulance Ride. *J. R. Glover,* M.B.; *C. B. Heald,* F.R.C.P.; *J. Horton,* M.B. 678
Problems of Accident and Emergency Services. *C. R. G. Howard,* M.B. 678
Mercury Perchloride in Surgery of Bowel Cancer. *H. Brendan Devlin,* F.R.C.S. ... 679
Elusive Popliteal Pulse. *F. E. Weale,* F.R.C.S. 679
Nalidixic Acid and Intracranial Hypertension. *S. A. Stephen,* M.R.C.P.ED. ... 679
Achondroplasia and Leukaemia. *J. F. Fraumeni, jun.,* M.D., *and Miriam D. Manning,* M.D. 680
Smallpox Revaccination. *Elizabeth L. M. Perkins,* M.B. 680
Changed Character of Osteomyelitis. *N. H. Harris,* F.R.C.S. 680
National Kidney Centre. *M. Medway* ... 680
Amphetamine. *T. G. Reah,* M.D. 681
The "Pill" and Deep-venous Thrombosis. *R. J. Hetherington,* M.B. 681
Surgery in Acquired Cardiac Disease. *J. F. Goodwin,* F.R.C.P. 681
Protective Helmets and Traumatic Epilepsy. *R. H. P. Fernandez,* M.D. 681
Recognizing Early Myxoedema. *A. U. MacKinnon,* M.D. 682
Investigating Hypertension. *Wing Commander P. W. Robertson,* F.R.C.P. ... 682
Progestin Therapy of Breast Cancer. *B. Jolles,* M.D. 682
G.P.s and Health Centres. *I. Gordon,* M.D., D.P.H., *and A. Shaw,* D.P.H. 683
Importance of Medical Administrators. *N. V. Williams,* D.P.H. 683
Opportunities in British Medicine. *F. W. B. Breakey,* M.B. 683

News and Notes

Epidemiology 687
Medical News 687

SUPPLEMENT

- **Was it a Drug? p. 127**
- **B.M.A. Career Service, p. 128**

No. 5566 Brit. med. J. 1967, Vol. 3, 627–688 Weekly. Price 5s.
BRITISH MEDICAL ASSOCIATION, TAVISTOCK SQUARE, LONDON W.C.1 TEL: 01-387 4499

Two numbers just published

Tissue and Organ Transplantation

The Proceedings of a Symposium organised by the College of Pathologists

Genetic background and transplantation antigens • Action of lymphocytes in transplantation • The role of the macrophage in transplantation immunity • Humoral and cell-mediated effector mechanisms in tissue transplantation • Immunological tolerance • The response of draining lymph nodes to immunological stimulation in intact and thymectomized animals • Immunological properties of antilymphocytic serum • Immunosuppressive agents and allogeneic transplantation • Immunosuppressive action of ribonucleases • The relevance of leucocyte antigens for allogeneic renal transplantation • The transplantation of cartilage • Rejection in treated renal allografts • Grafts of haemopoietic tissue: the nature of haemopoietic stem cells • Bone transplantation.

PRICE 30s. (U.S.A. $4.50) including postage

The Thyroid Gland

The Proceedings of a Symposium organised by the Association of Clinical Pathologists

The structure of the thyroid gland • The biosynthesis of thyroid hormones • The action of thyroid hormones • The control of thyroid secretion • The radioimmunoassay of thyroid-stimulating hormone in human blood • Carriage of circulating thyroid hormones and the estimation of total plasma hormone levels • The estimation of thyroid hormone binding by plasma proteins and of unbound levels of thyroxinein plasma • The value of inorganic iodine studies in the clinical assessment of thyroid disease • Stimulation and suppression tests of thyroid function • Tests based on the peripheral action of thyroid hormone • Aetiology of hyperthyroidism • The diagnosis of hyperthyroidism • Hypothyroidism • Hypothyroidism due to congenital dyshormonogenesis • Thyroid autoimmune disease • Extrathyroidal thyroglobulin • Medullary carcinoma of the thyroid • Thyrocalcitonin.

PRICE 30s. (U.S.A. $4.50) including postage

These publications can be ordered now from

The Subscription Manager, JOURNAL OF CLINICAL PATHOLOGY
B.M.A. House, Tavistock Square, London W.C.1, *or through any leading bookseller*

BRITISH MEDICAL JOURNAL

SATURDAY 16 SEPTEMBER 1967

Leading Articles

Control of Drugs (p. 689). Poisoning from Paraquat (p. 690). Allergic Alveolitis (p. 691). Doctors for Industry (p. 692). Treatment of Addicts (p. 692). Australian Doctors in Vietnam (p. 693). Disc Protrusion and the Bladder (p. 693). Hypotonia and Obesity Syndrome (p. 694). Guide to Hospitals (p. 694).

Papers and Originals

Obstetric Complications and School Performance D. J. P. BARKER AND J. H. EDWARDS 695
Paraproteins, Benign or Malignant? J. R. HOBBS 699
Lymphocyte Transformation and Chromosome Studies in Hodgkin's Disease SYLVIA D. LAWLER, C. R. PENTYCROSS, AND B. R. REEVES 704
Mushroom-worker's Lung ALEX SAKULA 708
Dietary Iron and Haematological Status in Normal Subjects R. H. DAVIS, A. JACOBS, AND ROSA RIVLIN 711
Acro-osteolysis Occurring in Men Engaged in the Polymerization of Vinyl Chloride D. KENWIN HARRIS AND W. G. F. ADAMS 712
Sickle-cell Haemoglobin O Disease in a Sudanese Family S. A. IBRAHIM AND DAOUD MUSTAFA 715

Preliminary Communications

Intestinal Spirochaetosis W. A. HARLAND AND F. D. LEE 718

Medical Memoranda

Volvulus of the Small Intestine after Herniorrhaphy C. J. C. RENTON AND N. H. VELLANI 719
Relation of Pregnancy Toxaemia to Trophoblastic Tumours DEREK LLEWELLYN-JONES 720
Death from Paraquat after Subcutaneous Injection C. H. ALMOG AND E. TAL 721
Insulin Allergy Treated by Low-dosage Hydrocortisone ROY COCKEL AND SHEILA MANN 722
"Railroading" in Retinal Vessels P. J. TOMLIN 722
Haemoperitoneum after Traumatic Avulsion of Uterine Fibroid C. W. VENABLES AND I. L. CRAFT 124

Current Practice

Medicine Today
One or Two Fits 725
Any Questions? 726

Book Reviews 727

Middle Articles

Collection of Unwanted Drugs from Private Homes
W. A. NICHOLSON ... 730
New Appliances
Roto-rest 731
Proposed Legislation on Drugs ... 734

Obituary Notices

J. A. Hadfield, M.B. 742
B. T. Squires, O.B.E., D.M. 742
J. D. B. MacDougall, M.D., F.R.C.S.ED. 742
J. B. Davey, M.B., D.T.M. 743
K. A. W. Law, M.B.E., M.B., B.S. ... 743
G. Jamieson, M.B. 743
D. Skinner, M.B. 744
J. M. Davidson, M.B. 744
Janet W. Hepburn, M.B., D.P.H. ... 744
B. E. A. Harley, M.R.C.S., D.O. .. 744
Terence East, D.M., F.R.C.P. 744

News and Notes

Epidemiology 745
Medico-Legal 746
Medical News 746

Correspondence

Consultants' Views of General Practitioners. *B. D. M. Williams,* B.M.; *W. B. S. Crawford,* F.R.C.S.ED. 735
Place of the Mentally Retarded. *R. Payne,* D.P.M.; *D. A. A. Primrose,* M.D. 735
S.T.P. and the Law. *C. R. B. Joyce,* PH.D. 735
Experiments on Man. *C. Fletcher,* C.B.E., F.R.C.P. 736
Training for Obstetrics and Gynaecology. *C. H. G. Macafee,* F.R.C.O.G. 736
Summer and Death from Neuroblastoma. *R. W. Miller,* M.D., *and Judith A. Hill* ... 736
Speed Control. *W. Gissane,* F.R.C.S. ... 736
Hetacillin and Ampicillin. *B. Sjöberg,* PH.D., D.SC. 737
Hypernatraemic Dehydration. *T. H. Hughes-Davies,* B.M. 737
Overinflation of the Lungs of Coal Miners. *C. M. Ogilvie,* M.D., *and others* ... 737
Oxygen Therapy Equipment. *Mary Catterall,* M.B., *and G. Kazantzis,* F.R.C.S. 738
Advertising Arthritis. *K. E. Britton,* M.R.C.P., *and Heather C. Suckling,* M.B. 738
Oculogyric Crises Due to Phenothiazines. *J. E. Freeman,* M.R.C.P., *and others* ... 738
Multiple Sclerosis in South Africa. *J. F. Kurtzke,* F.A.C.P. 739
Early Discharge of Maternity Patients. *S. E. Browne,* M.B.; *R. S. Saxton,* M.B. 739
Chest Pain After Infarction. *J. Calvo Melendro* 739
Changed Character of Osteomyelitis. *R. L. Huckstep,* F.R.C.S. 739
Ruptured Chordae Tendineae. *R. S. O. Rees,* M.R.C.P. 739
Drugs and Driving. *J. Allan* 739
Recognition of Heart Failure. *S. H. Nicolaides,* M.R.C.P.ED. 740
Stress Incontinence Treated by Electrical Stimulation. *T. Moore,* F.R.C.S. ... 740
Trephine Biopsy of the Lung. *S. J. E. Steel,* M.D., *and D. P. Winstanley,* M.R.C.P. 740
Healing Processes in Wounds. *L. A. Rauscher,* M.R.C.S. 740
Mandrax and Porphyria. *C. M. Van Rooyen,* M.B. 740
Side-effect of Antidepressant Drugs. *Surgeon Captain G. G. Wallis,* M.D., D.P.M. 740
Reprints: Who Should Pay? *D. Murray-Bruce,* M.B. 740
Smallpox Revaccination. *T. McL. Galloway,* F.R.C.P.ED. 740
B.M.A. as a Negotiating Body. *J. H. Briggs,* M.R.C.P. 741
Sales Promotion. *J. R. Caldwell,* M.B. ... 741
Junior Staff Representation. *J. H. Wetherill,* M.R.C.P. 741
Special Service for Doctors. *The Reverend J. R. W. Stott* 741

SUPPLEMENT

- **Vocational Training for General Practice, p. 129**

No. 5567 **Brit. med. J., 1967, Vol. 3, 689–748** **Weekly. Price 5s.**
BRITISH MEDICAL ASSOCIATION, TAVISTOCK SQUARE, LONDON W.C.1 TEL: 01-387 4499

Treatment of common skin diseases

Published July 1967

Patients with skin diseases take up a large part of the time of busy general practitioners and the number of preparations available for the treatment of these disorders is rising each year. Treatment of Common Skin Diseases is a collection of articles, specially written for the *British Medical Journal,* designed to give practical advice on the management of these diseases and the selection of remedies. The articles are easy to read and give full details of dosage and administration of drugs, advice on diet, and answers to the questions asked by patients and their relatives.

Demy Octavo 116 *pages*

Price 10s. (U.S.A. $1.50) including postage

Copies can be ordered through any leading bookseller or direct

From the British Medical Journal, B.M.A. House, Tavistock Square, London, W.C.1.

BRITISH MEDICAL JOURNAL

SATURDAY 23 SEPTEMBER 1967

Leading Articles

World Medical Assembly (p. 749). Epidemiological Studies of Leukaemia (p. 750). Diverticular Disease of the Colon (p. 751). New Respiratory Virus (p. 752). Overwhelming Infection after Splenectomy (p. 752). Obstetric Forceps or Vacuum Extractor? (p. 753). Menace of Smoking (p. 753). Good General Practice (p. 754).

Papers and Originals

Childhood Leukaemia in Greater London: a Search for Evidence of Clustering MORWENNA M. TILL, R. M. HARDISTY, M. C. PIKE, AND RICHARD DOLL ... 755
Leukaemia in Lewisham (1957–63) S. P. LOCK AND MAXINE MERRINGTON 759
Transit Times of Food in Patients with Diverticulosis or Irritable Colon Syndrome and Normal Subjects O. N. MANOUSOS, S. C. TRUELOVE, AND K. LUMSDEN ... 760
Prevalence of Colonic Diverticulosis in General Population of Oxford Area O. N. MANOUSOS, S. C. TRUELOVE, AND K. LUMSDEN ... 762
Electric Fire Burn ANDREW GUNN ... 764
Effects of a "New" Human Respiratory Virus in Volunteers A. F. BRADBURNE, M. L. BYNOE, AND D. A. J. TYRRELL ... 767
Acute Exudative Arthritis in Leprosy—Rheumatoid-Arthritis-like Syndrome in Association with Erythema Nodosum Leprosum A. B. A. KARAT, S. KARAT, C. K. JOB, AND M. A. FURNESS ... 770
Infectious Hepatitis in Leicester 1963–6 C. BURNS ... 773
Natural History of Refsum's Syndrome in a Gloucestershire Family A. M. G. CAMPBELL AND E. R. WILLIAMS ... 777

Medical Memoranda

Perforated Duodenal Ulcer Presenting as Acute Respiratory Failure A. CUSCHIERI AND K. F. EDWARDSON ... 779
Lupus-like Syndrome Induced by Procainamide D. G. MCDEVITT AND J. F. T. GLASGOW ... 780
Hypoparathyroidism and Malabsorption R. I. RUSSELL ... 781
Schizophrenia in a Male Pseudohermaphrodite K. L. K. TRICK ... 783
Haemorrhage from Base of Tongue J. H. WETHERILL AND A. G. GANDHI 784

Current Practice

Today's Drugs
Tolnaftate ... 785
Any Questions? ... 786
New Appliances
Apparatus for Warming Blood for Transfusions ... 787

Middle Articles

Orthopaedic Care of Children with Myelomeningocele E. H. STRACH ... 791
Twenty-first World Medical Assembly STANLEY S. B. GILDER ... 795

Book Reviews ... 788

Obituary Notices

H. A. Magnus, M.D., F.R.C.P., F.C.PATH. 803
Ewen Cameron, M.D., F.R.C.P.(C.), D.P.M. 803
R. Vaughan Hudson, F.R.C.S. ... 804
Isabel M. S. Reid, M.B. ... 804
F. R. Brown, O.B.E., F.R.C.S.ED. ... 804
A. M. Hendry, M.B., F.R.C.S.ED. ... 805
J. G. Stevens, M.R.C.S. ... 805
Terence East, D.M., F.R.C.P. ... 805

News and Notes

Epidemiology ... 806
Medical News ... 807

Correspondence

Mortality of the Ambulance Ride. *A. B. Stewart*, M.D.; *K. J. Gurling*, M.D. ... 797
Thyrocalcitonin. *A. M. Parfitt*, M.R.C.P. ... 797
Place of the Mentally Retarded. *M. E. Y. York-Moore*, D.P.M.; *R. Beaver*, D.P.H. ... 797
S.T.P. and Alcohol. *A. S. Paterson*, F.R.C.P.ED. ... 798
Sodium Uptake in Peritoneal Dialysis. *M. V. Moriarty*, M.R.C.P. ... 798
Peripheral Gangrene in Infancy and Childhood. *Dr. J. W. Koten* ... 798
Activation Analysis. *W. D. Alexander*, F.R.C.P.ED., *and others* ... 799
Hypercalcaemia and Malignant Tumours. *W. M. Keynes*, F.R.C.S. ... 799
Dietary Calcium and Hypercalciuria. *Squadron Leader M. J. Phillips*, M.B., M.C.PATH., *and Wing Commander J. N. C. Cooke*, F.R.C.P. ... 799
Oxygen Therapy. *G. J. Addis*, M.R.C.P. GLASG.; *J. M. Collis*, F.F.A. R.C.S., *and D. W. Bethune*, F.F.A. R.C.S. ... 800
Calcium Infusion Test. *K. A. Kehayoglou*, M.D., *and C. D. Holdsworth*, M.D. ... 800
Haematomas of the Abdominal Wall. *H. FitzGibbon*, F.A.C.O.G. ... 800
Diet and Diverticulitis. *S. N. Salem*, D.PHIL., M.R.C.P.ED. ... 800
Dose of Metaraminol. *A. B. Rees* ... 801
Progestin Therapy of Breast Cancer. *B. A. Stoll*, F.F.R. ... 801
Sodium Chlorate Poisoning. *A. C. Kennedy*, M.D., F.R.C.P.ED., *and R. G. Luke*, M.R.C.P. 801
Disturbed Geriatric Patients. *M. R. P. Hall*, M.R.C.P., *and others* ... 801
Early Discharge of Maternity Patients. *F. D. McEwan*, D.P.H. ... 801
Future of General Practice. *B. Barnett*, L.R.C.P., D.P.M. ... 802
Computer Control. *A. Donaldson*, D.P.H. 802
Night Visits. *J. D. Wigdahl*, B.M. ... 802

SUPPLEMENT

- **G.M.S. Committee: Vocational Training for General Practice,** p. 131
- **Was it a Drug?** p. 137

No. 5568 Brit. med. J., 1967, Vol. 3, 749–808 Weekly. Price 5s.
BRITISH MEDICAL ASSOCIATION, TAVISTOCK SQUARE, LONDON W.C.1 TEL: 01-387 4499

Three Unique Anticholinergics

with exceptional therapeutic characteristics

PIPTAL

(Pipenzolate methobromide)

For Peptic Ulcer

Piptal decreases acid secretion, suppresses abnormal gastric motility and relieves the pain of peptic ulcer.
It is unusually well-tolerated, even when administered over long periods.

DACTIL

(Piperidolate hydrochloride)

For Gastro-duodenal Spasm

Dactil selectively relieves pain due to upper gastro-intestinal spasm usually within ten minutes. Indications include abdominal cramps as in gastro-duodenal spasm, as well as biliary spasm, hiatus hernia, cardiospasm, pylorospasm, post-gastrectomy syndrome and regional ileitis.

CANTIL

(Mepenzolate bromide)

For the Colon

Cantil effectively relieves pain due to colonic spasm in irritable colon, spastic colitis and diverticulitis. It counteracts colonic hypermotility in acute and chronic non-specific diarrhoeas, mucous colitis and ulcerative colitis.

SIDE EFFECTS have only rarely been observed. The selective actions of all three products —*fully supported by extensive clinical trials*—have been found to provide a high degree of therapeutic efficacy with almost complete freedom from the side effects commonly attributable to anticholinergic drugs.

CONTRA-INDICATIONS—Piptal, Dactil and Cantil are contra-indicated in glaucoma and should be used with caution in prostatic hypertrophy.

Full information available on request

M.C.P. Pure Drugs Limited

ALPERTON, WEMBLEY, MIDDLESEX. Tel: 01-902 1191

SECOND CLASS POSTAGE PAID AT NEW YORK, N.Y.

BRITISH MEDICAL JOURNAL

SATURDAY 30 SEPTEMBER 1967

Leading Articles

Alcohol and the Law (p. 809). Aspirin and Gastric Bleeding (p. 810). Operations on the Gall Bladder (p. 811). Nonbacterial Vegetations on the Heart Valves (p. 812). Acute Necrotizing Encephalitis (p. 812). Increase in Stabbing (p. 813). Senescence (p. 814). Vital Decision (p. 814).

Papers and Originals

Facial Paralysis HENRY MILLER ... 815
Observations on Interpretation of Blood Alcohol Levels Derived from Analysis of Urine J. P. PAYNE, D. V. FOSTER, D. W. HILL, AND D. G. L. WOOD ... 819
Splenectomy in "Big Spleen Disease" P. J. S. HAMILTON, JOHN RICHMOND, G. W. K. DONALDSON, ROGER WILLIAMS, M. S. R. HUTT, AND V. LUGUMBA ... 823
Splenectomy in Tropical Splenomegaly D. S. PRYOR ... 825
Joint Haemorrhage in Haemophilia: Is Full Advantage Taken of Plasma Therapy? ANITA M. ALI, R. H. GANDY, MARGARET I. BRITTEN, AND KATHARINE M. DORMANDY ... 828
Trial of Gastric Cooling for Haematemesis J. B. MCFARLAND AND J. G. GOW ... 831
Lactobacillus casei C.S.F. Folate Activity D. G. WELLS AND H. J. CASEY 834
Gritti–Stokes Amputation in Atherosclerosis: a Review of 237 Cases PETER MARTIN, STUART RENWICK, AND E. MAELOR THOMAS ... 837

Medical Memoranda

Familial Myasthenia Gravis C. B. C. WARRIER AND T. D. G. PILLAI ... 839
Self-inflicted Oleogranuloma of Breast R. B. CROSBIE AND H. D. KAUFMAN ... 840
Oldest Pituitary Dwarf? H. L. CAPLAN AND F. I. R. MARTIN ... 842
Adenomyoma of Stomach JAMES G. MCNULTY ... 843
Spontaneous Rupture of Uterus at 22 Weeks' Pregnancy D. E. R. BATEMAN ... 844
Diaphysial Aclasia with Compression of the Spinal Cord P. J. STILES ... 844

Current Practice

Today's Drugs
Immunization Schedules ... 846
Any Questions? ... 847
New Appliances
Substitute for Gauze Swabs during Surgery ... 852

Clinicopathological Conference

A Case of Polycythaemia with Aortic Stenosis ... 848

Book Reviews ... 853

Obituary Notices ... 869

Middle Articles

General Practice Observed
Study of the Demand for Urgent Treatment in General Practice J. A. FORBES, L. M. M. MUTCH, G. T. SMITH, AND A. J. TULLOCH ... 856
Hospital Topics
Neasden Memorandum on Resuscitation ... 858
Conferences and Meetings
Laboratory Screening Procedures ... 859

News and Notes

Epidemiology ... 872
Medical News ... 873

Correspondence

Psychotropic Drugs. *W. W. Sargant,* F.R.C.P., D.P.M. ... 861
Alcohol and Driving. *M. E. Glanvill,* M.R.C.S., *and A. J. Ferris,* B.M. ... 861
Cardiac Resuscitation. *M. Aminoff,* M.B., *and others* ... 861
Lithotomy Position for Forceps. *A. H. Morley,* M.B. ... 862
Safer Dental Anaesthesia. *A. M. Danziger,* D.A. ... 862
Phenylketonuria: a Reassessment of Screening by Napkin Test. *L. I. Woolf,* PH.D. ... 862
Respiratory Distress Syndrome. *Margaret E. R. Stoneman,* M.D., *and Rosalind M. Owens,* B.SC.; *M. McL. Reid,* M.B. ... 862
Problem of Unused Drugs. *J. C. Gunn,* M.B.; *F. J. G. Lishman,* M.D., D.P.H. ... 863
Penicillin Encephalopathy. *G. T. Stewart,* M.D. ... 863
Visual Hallucinations in Cranial Arteritis. *M. J. Gilkes,* F.R.C.S. ... 863
Prophylaxis in Haemophilic Arthropathy. *J. B. King,* M.B. ... 864
Early Discharge of Maternity Patients. *A. F. Clift,* F.R.C.O.G. ... 864
Thrombosis and the "Pill." *S. Rivlin,* M.R.C.S.; *P. Ghosh,* M.R.C.P., *and others* 864
Human Infection with Porcine *Ascaris. R. F. Phillipson,* PH.D., *and J. W. Race,* M.B. ... 865
Chromosomes in Hodgkin's Disease. *Sylvia D. Lawler,* M.D., *and others* ... 865
Medicine in Burma. *A. W. Woodruff,* F.R.C.P. ... 865
Anxiety State after "Sex Education." *Louise F. W. Eickhoff,* M.D., D.P.M. ... 865
Occupation, Chemicals, and Cancer. *R. E. Eckardt,* M.D. ... 866
Second British Academic Conference in Otolaryngology. *L. F. W. Salmon,* F.R.C.S. ... 866
Delayed Death in Imipramine Poisoning. *A. B. Masters,* D.P.M. ... 866
Oculogyric Crises after Phenothiazines. *E. C. B. S. Keat,* M.D., *and P. J. Toghill,* M.R.C.P. ... 867
Case of Diarrhoea and Goitre. *I. Kennedy,* F.R.C.S.ED. ... 867
Mercury Perchloride in Surgery. *J. C. Gingell,* F.R.C.S., *and others* ... 867
Diagnostic Paracentesis. *T. O. Mulligan,* F.R.C.S.ED. ... 867
Headlight Glare. *S. J. Lines,* M.B. ... 867
Doctoring the Unattractive Areas. *G. M. Jones,* M.R.C.S. ... 868
Consultants' Views of General Practitioners. *G. N. Cash,* M.B. ... 868
Financing the Health Service. *A. Youatt,* D.S.C., M.R.C.S. ... 868
Sales Promotion. *W. H. Sims,* F.PH.S. .. 868

SUPPLEMENT

- **Hospital Junior Staffs Group Council,** p. 139
- **Organization Committee,** p. 141
- **Police Tests in Hospital,** p. 142

No. 5569 Brit. med. J., 1967, Vol. 3, 809–874 Weekly. Price 5s.
BRITISH MEDICAL ASSOCIATION, TAVISTOCK SQUARE, LONDON W.C.1 TEL: 01-387 4499

Special Allowances in General Practice

1. A £400 a year special allowance

is made to principals providing full general medical services in areas which, for three years or more, have been continuously designated by the Medical Practices Committee as needing more doctors. These areas are:

Bedfordshire: Luton.
Buckinghamshire: Cippenham; Slough; Taplow and Burnham
Cambridgeshire: Wisbech.
Cheshire: Crewe and Haslington.
Cumberland: Carlisle.
Derbyshire: Chesterfield; Heanor; Swadlincote.
Durham: Billingham; Darlington; Easington, Houghton-le-Spring; Seaham; Sedgefield; Stanley; Stockton-on-Tees with Norton-on-Tees; Sunderland; Washington; West Hartlepool.
Essex: Basildon; Benfleet; Southend; Wickford.
Hampshire: Bishopstoke; Chandler's Ford; Eastleigh; Fair Oak.
Hertfordshire: Hertford; Potters Bar; Stevenage,
Kent: Dartford; Gravesend; Northfleet; Rochester.
Lancashire: Accrington; Ashton-under-Lyne; Blackburn; Bootle; Chorley; Denton; Droylesden and Audenshaw; Failsworth; Great Harwood; Haydock; Irlam; Leigh; Manchester; Middleton; Oldham; Preston; Rochdale; St. Helens; Widnes; Worsley.
Leicestershire: Leicester.
Lincolnshire (Holland): Spalding.
Lincolnshire (Kesteven): Grantham.
Lincolnshire (Lindsey): Cleethorpes; Scunthorpe.
Greater London: Canning Town; Custom House; Dagenham; Silvertown; East Ham; Feltham; Hayes and Harlington; Hornchurch.
Northamptonshire: Kettering.
Nottinghamshire: Hucknall; Nottingham; Sutton-in-Ashfield; Worksop.
Salop: Wellington.
Staffordshire: Brierley Hill; Cannock; Coseley; Darlaston; Newcastle-under-Lyme; Rowley Regis; Rugely; Sedgley; Stoke-on-Trent; Stone; Tamworth; Tipton; Walsall; Wednesbury; West Bromwich; Wolverhampton.
Warwickshire: Birmingham; Coventry; Kingsbury/Polesworth; Nuneaton; Rugby.
Worcestershire: Dudley.
Yorkshire (East Riding): Kingston upon Hull.
Yorkshire (North Riding): Middlesbrough.
Yorkshire (West Riding): Barnsley; Bentley with Arksey; Bradford; Castleford Borough; Dewsbury; Hatfield and Stainforth; Hemsworth; Leeds; Maltby; Morley; Rotherham; Royston; Sheffield; Stockbridge; Worsborough.

2. An initial practice allowance

is also payable to a doctor who is
(a) setting up a new single-handed practice,
(b) filling a vacancy in a small single-handed practice,
(c) joining, as an additional partner, an existing practice which has a very large list.

This applies in *all areas* classified by the Medical Practices Committee as 'designated' and not only in those quoted above.

Full details of the circumstances in which these allowances are payable, the extent of the income guaranteed by them, and the latest list of designated areas may be obtained from the Ministry of Health. If you are interested, please write for these details to:

DR. A. B. STEWART, Ministry of Health (Room B 306)
Alexander Fleming House, Elephant & Castle, London, S.E.1.

BRITISH MEDICAL JOURNAL

LONDON SATURDAY 1 JULY 1967

Pointers

Hirschsprung's Disease: Mr. G. C. Fraser and Mr. A. W. Wilkinson emphasize high mortality in the neonate and the necessity for relieving obstruction on diagnosis (p. 7).

Dyspnoea in Coal Miners: Study of aetiology, by Dr. C. Ogilvie and colleagues (p. 10).

Enigma of Ulcerative Colitis: Dr. Fred Feldman and colleagues, from Los Angeles, question whether this is a psychosomatic disease (p. 14). Leader this page.

Pernicious Anaemia in Asians: Dr. F. J. Jayaratnam and colleagues report this condition for the first time from Singapore (p. 18).

Rabies: Complications of immunization are sufficiently serious for Drs. J. C. M. Sharp and Sheila McDonald to suggest stringent regulations about human access to animals in quarantine (p. 20).

Subacute Sclerosing Leucoencephalitis: Dr. O. Kolář and colleagues from Czechoslovakia obtained improvement from thymectomy in one case (p. 22).

I.V.P. in Renal Colic: Calculi were the cause in most cases investigated by Mr. J. A. Rhind (p. 24).

Rheumatoid Arthritis in Polio Patients: Dr. E. N. Glick found sparing effect in limbs of paralysed side (p. 26).

L.S.D.: Dr. T. H. Bewley reports six adverse reactions (2 fatal) from use of drug obtained illicitly (p. 28).

Lung Biopsy: Description of large trephine for use in diffuse lesions (p. 30).

Case Reports: Agranulocytosis coincident with amodiaquine therapy (p. 32). Onset of psychosis in association with vitamin-B_{12} deficiency (p. 34).

Respiratory Viruses: Dr. Neville C. Oswald discusses the clinician's approach in his Current Practice article (p. 35).

Is there an Alternative? Miss Elizabeth Burney discusses the health services in the light of local government reform (p. 41).

Oxford: Plans for new teaching centre (p. 44).

Pertinax: Without Prejudice (p. 45).

Local Medical Committees: Annual Conference of Representatives (*Supplement*, p. 1).

Annual Meeting
Bristol
6-14 July 1967

Psychological Factors in Ulcerative Colitis

For many years it has been widely accepted that psychological factors are prominent in ulcerative colitis. Some physicians indeed go so far as to regard ulcerative colitis as a psychosomatic disease in the strict sense of this term—namely, as an illness in which the organic lesions are the consequence of emotional disturbances.

An extensive literature exists on the psychological aspects of the disease. Perhaps the outstanding pioneer was C. D. Murray,[1] who in 1930 investigated twelve patients from the psychological viewpoint. He found "a well-marked time-relationship between the outbreak of an emotional disturbance and the onset of the symptoms." Mental conflicts concerned with marriage were the most common source of anxiety, and he judged that the patients faced their problems in an inadequate and infantile manner. E. Wittkower[2] made personality studies of 40 unselected patients with ulcerative colitis and found that psychological abnormalities and disorders far beyond the range of individual differences in the normal population existed before the onset of the colitis in the majority. Furthermore, in 28 of the 40 patients "a clear-cut emotional trauma, serious enough to be regarded as a precipitating agent, immediately preceded the onset of the colitis."

The psychosomatic hypothesis was fully reviewed by G. L. Engel[3-5] in articles dealing with 39 of his own patients and the published reports on 700 others. He found that four factors emerged "with impressive consistency": defects in personality long preceding the colitis; dependent and restricted relationship with other people; psychopathology in the mothers; and failure to achieve full heterosexual development.

Some physicians[6 7] have been so impressed by the importance of psychological factors in ulcerative colitis that they have regarded psychotherapy as the mainstay of treatment. Some objective evidence that psychotherapy can be beneficial comes from W. J. Grace, R. H. Pinsky, and H. G. Wolff.[8] They compared two matched groups of 34 patients in the first of which the management was by one physician (W. J. G.) with the emphasis on superficial psychotherapy aimed at relieving stress, whereas the second group was managed by various physicians who relied on diet, medication, and antibiotics. The psychotherapeutic group fared better than the control group, but even so the results do not appear impressive.

While many of the psychiatric studies of ulcerative colitis have been on individuals or on small groups of patients and are thus necessarily subjective and anecdotal, some workers have attempted to provide objective evidence. For example, L. Krasner[9] made use of a battery of intelligence and personality tests, including the Guilford–Martin factor inventory, to compare two groups of patients suffering from "psychosomatic diseases" (duodenal ulcer and ulcerative colitis) with a control group

© *British Medical Journal*, 1967. All reproduction rights reserved.

of patients who had never suffered from any of the diseases often considered to be psychosomatic. The group with ulcerative colitis did best in the intelligence test, but their results did not depart significantly from the normal distribution. Personality differences between the ulcerative colitis group and the control group were revealed by significant differences in scores on the Guilford–Martin factor inventory, the results tending to confirm previous descriptions of the ulcerative patients as being passive, insecure, shy, sensitive, and moody.

The article by Drs. F. Feldman, D. Cantor, S. Soll, and W. Bachrach which appears at page 14 of the *B.M.J.* this week must be one of the few psychiatric studies to discount the importance of psychological factors in the aetiology of ulcerative colitis. Its sharp disagreement with most of the conclusions reached by earlier authors is bound to excite controversy, which can hardly fail to be beneficial. The study consisted of a psychological evaluation of 34 patients with ulcerative colitis and a comparison with the general population and also with 74 patients admitted for other gastroenterological conditions. In essence, on the basis of scoring 65 variables, the subjects were placed in five categories of normality or abnormality. The great majority of the patients were classified as "normal" as regards personality and psychiatric illness. In only a small number was there an emotional precipitant closely preceding the first attack of ulcerative colitis. Seven of the patients had undergone extensive psychiatric treatment after the onset of ulcerative colitis. In three of these psychotherapy had helped the patient to adjust to his illness, but in none did it appear to have had any appreciable effect on the course of the disease.

Some support for the iconoclastic view of Feldman and his colleagues comes from the epidemiological study by E. D. Acheson and M. D. Nefzger[10] of ulcerative colitis in the United States Army. They were able to match each case with a control subject of the same rank, age, and sex, and it is interesting that they found no appreciable difference in intelligence, educational attainments, income before enlistment, or military conduct. M. Monk[11] made a study in Baltimore designed to uncover differences in social environment between patients with ulcerative colitis and the population from which they came. She found no differences in educational attainments, amount of life lived with parents or alone, degree of social contact with others before the onset of the illness, or the number of bereavements or marital disagreements in the month preceding the symptoms. However, she did show that the ulcerative colitis group were more likely to have fathers who had died during the patient's childhood. Does this positive finding support the view of J. W. Paulley[12] that "the disease is associated with a well-defined personality not uncommonly related to the unfortunate effect of overpossessive mothers"?

---

[1] Murray, C. D., *Amer. J. med. Sci.*, 1930, **180**, 239.
[2] Wittkower, E., *Brit. med. J.*, 1938, **2**, 1356.
[3] Engel, G. L., *Psychosomat. Med.*, 1954, **16**, 496.
[4] —— *Amer. J. Med.*, 1954, **16**, 416.
[5] —— ibid., 1955, **19**, 231.
[6] Groen, J., and Bastiaans, J., *Gastroenterology*, 1951, **17**, 344.
[7] Paulley, J. W., *Lancet*, 1956, **2**, 215.
[8] Grace, W. J., Pinsky, R. H., and Wolff, H. G., *Gastroenterology*, 1954, **26**, 462.
[9] Krasner, L., *J. abnorm. soc. Psych.*, 1953, **48**, 10.
[10] Acheson, E. D., and Nefzger, M. D., *Gastroenterology*, 1963, **44**, 7.
[11] Monk, M., Paper read at the First Internat. Congr. Soc. Psychiat., London, 1964.
[12] Paulley, J. W., *Gastroenterology*, 1963, **44**, 7.

Hospital Junior Staff

The wisdom of giving autonomous powers to sectional interests within the B.M.A., which exists to represent the medical profession as a whole, has often been questioned. The exercise of autonomy has on occasions seriously strained intraprofessional relations. Yet to those who possess it the advantages of autonomy have always seemed to outweigh its disadvantages, and under the new B.M.A. constitution, which the Annual Representative Meeting at Bristol next week is likely to approve, the autonomous powers of the committees representing the major branches of medical practice will be strengthened rather than weakened. It is therefore not surprising, nor unreasonable, that there should be renewed demands from hospital junior medical staff for the same rights of self-government as their seniors in established practice have.

However, the wish for autonomy is by no means universal among hospital junior doctors. Some think they would fare no better with it and perhaps less well. The Hospital Junior Staffs Group Council, which represents hospital junior doctors in the B.M.A., is against breaking away from the Central Consultants and Specialists Committee (or, as it will be named, the Committee for Hospital Medical Services), on which junior doctors will in future have twelve representatives instead of four. It is to be hoped, therefore, that the Junior Hospital Doctors' Association, the prime mover in the demand for autonomy, will not press the matter too hard. It would be a pity if this association went so far as to demand the right to negotiate separately on behalf of its members, as its chairman has stated[1] it will in the event of failing to get antonomous powers for hospital junior staff within the B.M.A. That would create an unfortunate division.

It is doubtful whether any organization could completely overcome the problems in representing the interests of a group of doctors so disparate as hospital junior staff. The personal and professional concerns of a middle-aged senior registrar experienced in a specialty and those of a newly fledged, provisionally registered houseman uncommitted for the future are far apart. But both rank as hospital junior staff—as do a British-born registrar intent on becoming a consultant and his colleague from the Commonwealth wanting postgraduate experience. It is difficult to make a convincing case for autonomy for what may be called the "junior" hospital junior staff, whose future may lie in any branch of medicine. Their membership of the hospital population is surely too transient to make it worth while for them to try to create the elaborate and expensive machinery needed for self-government. The more senior among the junior staff are in the main committed to a hospital career, and their interests are as much in what their terms of service are likely to be on promotion as in what they currently are. Their polarity must be towards the top of the ladder.

Last week the Council of the B.M.A. approved the Hospital Junior Staffs Group Council's proposals for reorganizing the constitution of the Group Council itself and of its constituent regional groups. The number of representatives from the regions on the Group Council are to be increased from 42 to 50. The total membership of the Group Council will be 60 instead of 48, and of the 60 only two will be appointed by the Central Consultants and Specialists Committee. Participation in the affairs of the Group is to be open to all hospital junior staff, whether members of the B.M.A. or not.

---

[1] Briggs, J. H., *World Medicine*, 1967, **2**, 15.
[2] *Brit. med. J. Suppl.*, 1967, **2**, 45.

The local organization is to be based on hospital meetings, and these will elect the regional committees. The larger regions will have bigger regional committees who, in turn, will appoint a larger number of representatives on the Group Council.

These new arrangements give ample scope for democracy to work. The Hospital Junior Staffs Group Council should be able in future fairly to claim that it represents all hospital junior doctors. Its executive committee is to appoint 12 members of the Central Committee for Hospital Medical Services, and this committee is in future to be responsible, through a Negotiating Subcommittee, for remuneration and all terms of service for all hospital doctors.[2] Three of the Central Committee's nine representatives on the Negotiating Subcommittee are to be hospital junior staff members.

Hospital junior doctors will not only have more opportunity to make their voice heard centrally and round the negotiating table but also more power, and therefore more responsibility, in shaping the future of the hospital services as a whole. It would surely be better for them first to try out their new power alongside their senior colleagues rather than independently of them and, sometimes needlessly, in opposition. The medical profession has enough to contend with without also having contention in its own ranks.

Segregation of Tuberculous Patients

Removal of patients with infectious pulmonary tuberculosis from their homes in an attempt to protect the family has been generally accepted as a sound preventive measure. This policy now needs reappraisal.

How effective and necessary is segregation of patients receiving modern chemotherapy, which rapidly reduces infectivity ? This question has been investigated in Madras by the Tuberculosis Chemotherapy Centre. It has reported a five-year controlled study of the attack rate of tuberculosis among close-family contacts of patients with newly diagnosed infectious pulmonary tuberculosis.[1] The contacts lived in poor, overcrowded conditions and all had been living, feeding, and cooking with the patients for at least three months before the diagnosis was made. None of the contacts were given B.C.G. vaccination or chemoprophylaxis. Attack rates were studied in family contacts whose only infectious member was initially the index case. A comparison was made between 272 "sanatorium" family contacts, whose index case was isolated in a sanatorium for one year, and 256 "home" contacts, who remained exposed to the index case during treatment at home. The study covered five years. Both home and sanatorium patients received isoniazid and sodium P.A.S. (sodium para-aminosalicylic acid) for one year. By the end of it in 86% of the home and 92% of the sanatorium patients the disease was bacteriologically quiescent.

During the five years' follow-up tuberculosis developed in 9% of the home and 14% of the sanatorium contacts, including 5% and 7% respectively in the first year. About one-third of the contacts were initially tuberculin-negative. Among these the attack rate of tuberculosis over the five years was 10% in the home series and 11% in the sanatorium series, including 8.1% and 8.0% respectively in the first year. The corresponding figures for the initially tuberculin-positive contacts were 9% and 16% over the five years and 3% and 7% in the first year. Thus the risk of developing tuberculosis was no greater for the home contacts than it was for the sanatorium contacts either over the whole five-year period or even in the first year.

The sanatorium contacts were exposed to the risk of infection from two sources—firstly, from the patient before the diagnosis of tuberculosis had been made, and, secondly, from other sources in the urban community in which the family lived. The home contacts were exposed to both these risks and in addition to that of continued contact with the patient during home treatment. Exposure to the patient during treatment at home was not an important risk, since the attack rate was similar in the tuberculin-negative contacts in the two groups, while in the tuberculin-positive contacts it was actually higher in the sanatorium group—apparently by chance. The main risk to the contacts seemed to be from exposure to the patient before diagnosis. The continued contact with the patient at home during treatment was little extra hazard.

This demonstration that well-organized domiciliary treatment is practicable, effective, and safe for family contacts is of great importance in developing countries with shortage of sanatorium beds.[2] [3] In Britain facilities for domiciliary treatment are good, yet many physicians admit almost all the sputum-positive patients to hospital for several months. This policy can hardly be justified on the grounds of risk to family contacts, for it proved to be unnecessary in the overcrowded conditions of Madras. The risk is likely to be even less in Britain, where patients can often be isolated in their own home. Moreover, B.C.G. vaccination and chemoprophylaxis are freely available for suitable contacts and are known to be effective in preventing tuberculosis.[4] [5] It is thus reasonable to conclude that, although there may be several good reasons for treating pulmonary tuberculosis in hospital, admission cannot be regarded as essential to prevent infection of the family contacts of co-operative patients from good homes, who can be given well-supervised domiciliary chemotherapy.

---

[1] Kamat, S. R., *et al.*, *Bull. Wld Hlth Org.*, 1966, **34**, 517.

[2] Fox, W., *Lancet*, 1962, **2**, 413 and 473.

[3] —— *Brit. med. J.*, 1964, **1**, 135.

[4] Medical Research Council, ibid., 1963, **1**, 973.

[5] Ferebee, S. H., and Mount, F. W., *Amer. Rev. resp. Dis.*, 1962, **85**, 490.

Oedema in Pregnancy

Many clinical interpretations have been put on oedema in pregnancy. The relationship of this physical sign to gain in weight and to pre-eclamptic toxaemia is not fully understood Nor is it clear to what extent oedema means an increase i the total amount of water in the body or a change i the distribution of water between plasma, tissue fluid, an intracellular fluid.

Since these matters have probably been oversimplified, recent study by A. M. Thomson, F. E. Hytten, and W. Billewicz[1] is of special interest. They examined the recor of 24,079 women living in Aberdeen who had given birth single, legitimate babies. From the records they were al to recognize women who had no oedema, those with oede of the legs only, and those with generalized oedema—that elsewhere than in the legs and ankles. They also classif the women as normotensive or hypertensive (diastolic press (of 90 mm. Hg or more), and as being pre-eclamptic when there was proteinuria in addition to hypertension.

In the normotensive women oedema, mainly of the legs, increased with age, being present in 14% of those under 20 years of age and in 29% of those over 30. Preliminary evidence suggested that women who had been oedematous in one pregnancy were twice as likely to develop oedema in a subsequent pregnancy as those who did not have this sign. Women too heavy for their height at 20 weeks of pregnancy were more likely to have oedema, usually of the generalized type, than those of average weight or less. If overweight women gained weight at the rate of 1.2 lb. (545 g.) or more per week from 30 to 36 weeks of pregnancy, there was a 42% chance that they would have generalized oedema and a 24% chance that they would develop oedema of the legs. When the rate of weight gain was less, so was the chance of developing oedema. It should be emphasized that these were the changes found in normotensive women.

When the blood pressure rose above 90 mm. Hg the incidence of oedema, particularly of the generalized form, rose too, and such generalized oedema was even more likely when there was proteinuria as well. Oedema of some kind was present in 35% of normotensive women, 65% of hypertensive, and 85% of those with pre-eclampsia as defined. It is perhaps worth noting the considerable numbers of women who did not have clinically recognizable oedema even when they had hypertension with or without proteinuria.

In general, women with oedema tended to have larger babies than those who did not have oedema, though the difference was only 0.17 lb. (77 g.). The prematurity rate was, on the average, less when there was oedema, especially of the legs, while the perinatal mortality rate was the same whether there was oedema or not. The conclusion the authors reach is that "Oedema, in the absence of other evidence of pre-eclampsia, is associated with a slight advantage in terms of birthweight and incidence of low birthweight, and is not associated with any disadvantage in terms of perinatal mortality. To that extent, it is possible to affirm that oedema in pregnancy is not necessarily harmful and unphysiological." This careful investigation therefore begins to put oedema in perspective.

Hytten, Thomson, and N. Taggart[2] investigated total body water in pregnancy. In 93 patients at least three readings of total body water were made in pregnancy and one 6 to 8 weeks after delivery, all the patients being clinically normal. The mean body water gained in pregnancy amounted to 8.5 kg. Between 10 and 38 weeks of pregnancy the gain in body water was 6.84 kg. in women with no oedema, 7.19 kg. in those with oedema of the legs, and 9.80 kg. in those with generalized oedema. It seems probable that those without oedema held between 1 and 2 litres of water in the extracellular spaces. The women with generalized oedema would appear to hold a further 3 litres somewhere which cannot be accounted for in the products of conception, the uterus, or elsewhere. Such women can be essentially normal, eing healthy themselves and having normal babies. If the weight of the total body water gained is deducted from the otal gain in weight, the "dry weight" gained can be stimated. When this is done it is found that overweight atients put on less "dry weight" than do those who are of average weight for height or underweight. This "dry weight" is probably mainly fat when it cannot be accounted for in other known factors of the total weight gain. The conclusion seems to be that those women who have large fat stores already do not store much extra in pregnancy, while those with small fat stores lay down some more fat.

Hytten and Thomson[3] measured total body water in six patients who developed pre-eclampsia as shown by a rise in blood pressure, proteinuria, and some oedema. The amount gained was within the limits found in normal women without pre-eclampsia, though the rate of gain of water in the last ten weeks of pregnancy was faster than in normal women with generalized oedema.

It is still not easy to assess the significance of oedema in the individual pregnant patient, but this work shows that age, oedema in a previous pregnancy, site of oedema, weight-for-height ratio, blood pressure, proteinuria, and rate of weight gain may all have to be taken into account. Oedema of itself would not seem to be invariably a bad prognostic sign and indeed might signify a slightly better prognosis for the baby when all other factors are considered. This work helps to clarify the relationship between oedema and increase in total body water in pregnancy, but the difference between normal and pre-eclamptic pregnancy in terms of water metabolism is still conjectural.

Thomson, A. M., Hytten, F. E., and Billewicz, W. Z., *J. Obstet. Gynaec. Brit. Cwlth*, 1967, 74, 1.

ytten, F. E., Thomson, A M., and Taggart, Nan, ibid., 1966, 73, 553.

—— ——, ibid., 1966, **73**, 714.

Investigating Hypertension

In general the significance of a patient's renal lesion to his hypertension is difficult to decide. For instance, renal-artery stenosis may occur with[1] or without[2] hypertension. Thus there is still no single reliable investigation for selecting those hypertensive patients with unilateral renal disease who may be expected to benefit from surgery.

The help of various complex inpatient investigations is sought before resorting to surgical operation. They include aortography, possibly with renal-function studies of each kidney, assay of pressor substances in systemic or renal circulation, angiotensin-infusion tests, studies of renal blood flow, and bilateral renal biopsy. These are formidable tests to put any patient through, and it is not easy to find agreement on which patients should be subjected to them. H. W. Smith[3] estimated the incidence of curable renal hypertension to be at most 2% of all hypertensive patients. This fairly gloomy picture is confirmed by M. J. Chamberlain and J. A. Gleeson,[4] who found that in a series of patients subjected to aortography the number permanently benefited by surgery was unduly small in relation to the morbidity of the investigation and later operation. But a higher proportion of cases of correctable renal hypertension has been reported by M. E. DeBakey and colleagues[5] and E. F. Poutasse.[6] A compromise figure, 5–10%, of renovascular hypertension has been proposed by M. H. Maxwell and G. B. Prozan,[7] who thought that the great majority of such patients could benefit from surgery. In Britain renal-artery stenosis has been reported in 10% of hypertensive patients at aortography,[8] and the surgical treatment of carefully selected patients has certainly been rewarding.[9 10]

Viewed against this background any advance in the accuracy of outpatient screening tests to select patients for more complex inpatient studies would be welcome. If the small number of potentially curable patients could be detected with some certainty at this stage many others might be spared fruitless further investigation. The standard intravenous pyelogram (I.V.P.) is not adequate to this end, failing to select about half of those with renovascular hypertension.[5 11] It gives excellent information about important correctable lesions like unilateral hydronephrosis, pyelonephritis, or tuberculosis, but these play only a small part in renal hypertension. In cases of unilateral renal ischaemia major structural changes in kidney or ureter may be evident. Attempts to improve the diagnostic value of the I.V.P. have been based on studies of asymmetric patterns in the excretion of contrast medium deriving from the selective sodium and water reabsorption in the ischaemic kidney.[12]

Films taken at minute intervals after the injection of contrast medium show up any delay in the appearance of contrast, and this technique has been of help in some hands.[13] However, when differences between the two sides are small, perhaps a minute or less, interpretation can be difficult.[14] Increased density of contrast medium due to marked reabsorption of water in the affected kidney can also cause confusion. To accentuate the asymmetry of contrast density K. Amplatz[15] proposed establishing an osmotic diuresis in the course of the I.V.P. by infusion of urea, thus allowing comparison between the rapid wash-out of contrast from the normal kidney with contrast retention in the ischaemic, oliguric kidney. The early reports of this technique of "radiological divided renal-function studies" suggested a much-improved detection rate of renovascular hypertension, with no false-negative results in the sense of failures to select patients improved by surgery, though "pseudo-positive" results to the test were reported.[16 17] M. H. Schreiber and colleagues[18] have recently laid down a range for the normal and shown that the test does not contribute to the diagnosis of bilateral renovascular disease. The whole place of "wash-out" pyelograms in this field has now been questioned by D. M. Witten and his colleagues,[19] who used mannitol infusion during the I.V.P. in preference to urea, to avoid the latter's potential hazards.

If the success rate of the intravenous pyelogram in the diagnosis of renovascular hypertension can be increased only from 50% to between 60% and 70% by these various refinements it is reasonable to look in other directions for a complementary outpatient screening test of individual renal function. After an uncertain start the hippuran radioisotope renogram has for some time been used with success.[20-22] The careful work of R. G. Luke and his colleagues[23] has now confirmed it as a simple, safe, and rapid investigation in the search for renovascular hypertension. Performed with care and used in conjunction with an initial I.V.P., the incidence of false-negative and false-positive assessments can be kept below 5%.[24] This is a fairly good rate of detection, and one that materially helps to prevent fruitless further investigation.

On present-day evidence the best way of selecting those hypertensive patients who may benefit from further inpatient investigation into a renal cause of their disease is to perform an intravenous pyelogram, supplemented by radiographs during the first five minutes of the examination, and to follow this with a radioisotope renogram.

---

[1] Lawrence, J. R., Doig, A., Knight, I. C. S., MacLaren, I. F., and Donald, K. W., *Lancet*, 1964, **1**, 62.

[2] Holley, K. E., Hunt, J. C., Brown, A. L., Kincaid, O. W., and Sheps, S. G., *Amer. J. Med.*, 1964, **37**, 14.

[3] Smith, H. W., *J. Urol. (Baltimore)*, 1956, **76**, 685.

[4] Chamberlain, M. J., and Gleeson, J. A., *Lancet*, 1965, **1**, 619.

[5] DeBakey, M. E., Morris, G. C., Morgen, R. O., Crawford, E. S., and Cooley, D. A., *Amer. J. Surg.*, 1964, **107**, 84.

[6] Poutasse, E. F., ibid., 1964, **107**, 97.

[7] Maxwell, M. H., and Prozan, G. B., *Progr. cardiovasc. Dis.*, 1962, **5**, 81.

[8] Sutton, D., Brunton, F. J., and Starer, F., *Clin. Radiol.*, 1961, **12**, 80.

[9] Brown, J. J., Owen, K., Peart, W. S., Robertson, J. I. S., and Sutton, D., *Brit. med. J.*, 1960, **2**, 327.

[10] Owen, K., *Brit. J. Urol.*, 1964, **36**, 7.

[11] Spencer, F. C., Stamey, T. A., Bahnson, H. T., and Cohen, A., *Ann. Surg.*, 1961, **154**, 674.

[12] Mueller, C. B., Surtshin, A., Carlin, M. R., and White, H. L., *Amer. J. Physiol.*, 1951, **165**, 411.

[13] Maxwell, M. H., Gonick, H. C., Wiita, R., and Kaufman, J. J., *New Engl. J. Med.*, 1964, **270**, 213.

[14] Fenton, S. S. A., Lyttle, J. A., and Pantridge, J. F., *Lancet*, 1966, **2**, 117.

[15] Amplatz, K., *Radiology*, 1962, **79**, 807.

[16] Stejskal, R. E., Staub, E. V., Loken, M. K., and Amplatz, K., *Amer. J. Roentgenol.*, 1964, **92**, 1397.

[17] Schreiber, M. H., Sarles, H. E., Herring, M. E., and Remmers, A. R., *New Engl. J. Med.*, 1964, **270**, 1223.

[18] Schreiber, M. H., Remmers, A. R., Sarles, H. E., and Smith, G. H., *Amer. J. Roentgenol.*, 1966, **98**, 88.

[19] Witten, D. M., Hunt, J. C., Sheps, S. G., Greene, L. F., and Utz, D. C., ibid., 1966, **98**, 114.

[20] Doig, A., Lawrence, J. R., Philp, T., Tothill, P., and Donald, K. W., *Brit. med. J.*, 1963, **1**, 500.

[21] Farmelant, M. H., Lipetz, C. A., Bikerman, V., and Burrows, B. A., *Amer. J. Surg.*, 1964, **107**, 50.

[22] Andrews, D., Parsons, V., and Roebuck, E. J., *Brit. J. Radiol.*, 1965, **38**, 527.

[23] Luke, R. G., Briggs, J. D., Kennedy, A. C., and Stirling, W. B., *Quart. J. Med.*, 1966, **35**, 237.

[24] Kennedy, A. C., Luke, R. G. Briggs, J. D., and Stirling, W. B., *Lancet*, 1965, **2**, 963.

Mediastinal Emphysema

Mediastinal emphysema has the distinction of being one of the very few conditions which enable the heart beats to be heard from the foot of the bed. With the stethoscope the "crunching" sound described by L. Hamman[1] is usually heard best down the left border of the heart; it varies in intensity and may be absent. If the sign is associated with subcutaneous emphysema of the neck or chest the diagnosis of mediastinal emphysema is virtually certain. The radiological appearances are characteristic, showing a small air space running parallel to the left, and sometimes the right, border of the heart. There may be an associated pneumothorax.

Air may enter the mediastinum by any of several routes. The commonest, as in so-called benign mediastinal emphysema, seems to be through the pulmonary alveoli, when a small rupture causes a pressure gradient between the alveoli and adjacent connective tissue.[2] The mechanism of such a gradient is obscure, but it seems at times to be precipitated by pulmonary emphysema, asthma, pneumonia, or childbirth. Once the air has entered the tissue it takes the line of least resistance and passes along the perivascular sheaths to the mediastinum and thence to the subcutaneous tissue. Ordinarily it does not extend far beyond the neck and in the benign form subsides within a few days. But occasionally the air spreads beyond the neck to the hand, arms, trunk, and even the legs, in which case there is a danger of suffocation. The other possible complication is the so-called "malignant" form of mediastinal emphysema, in which the pressure of air in the mediastinum becomes excessive and embarrasses the action of the heart. This can be fatal, especially if tension pneumothorax coexists.

---

[1] Hamman, L., *Trans. Ass. Amer. Phycns*, 1937, **52**, 311.

[2] Macklin, M. T., and Macklin, C. C., *Medicine (Baltimore)*, 1944, **23** 281.

[3] Gray, J. M., and Hanson, G. C., *Thorax*, 1966, **21**, 325.

Other modes of entry of air into the mediastinum include rupture of the trachea, bronchus, or oesophagus from any cause and penetrating wounds of the lung and mediastinal pleura. These are clearly formidable conditions and must always be considered in patients who develop mediastinal emphysema.

There are thus two different clinical problems. In the commoner, benign, form a patient may present with no more than a vague precordial ache,[3] possibly with Hamman's sign and some subcutaneous emphysema of the neck. A careful watch needs to be kept in case complications develop, but usually the prognosis is excellent. If the emphysema spreads or the patient becomes breathless or shows signs of collapse, immediate removal to hospital, preferably to a thoracic surgical unit, is essential. A radiograph of the chest will confirm the mediastinal emphysema; it will also show a pneumothorax and the extent of any preceding trauma. If oesophageal rupture is suspected, surgical treatment is imperative as soon as possible. The diagnosis may not be easy, but a rapidly developing state of shock, and upper abdominal rigidity in cases of perforation of the lower oesophagus, are suggestive and call for *x*-ray examination by Gastrografin swallow. Only slightly less urgent is oversuture of a rupture of the trachea or bronchus. Malignant mediastinal emphysema may be relieved by needling parallel to the deep surface of the sternum, but cervical mediastinotomy or even a sternal split may be necessary. Tension pneumothorax is best treated with a wide-bore intercostal tube. Extensive subcutaneous emphysema may be relieved by "milking" the air through small incisions in the skin.

Frozen Poultry and Staphylococcal Food-poisoning

Two recent reports from Australia[1] and the U.S.A.[2] have suggested that frozen poultry meat may be a common source of staphylococcal enterotoxin food-poisoning. No figures for the incidence of staphylococcal food-poisoning, either in relation to other causal agents or in relation to the various foods responsible for outbreaks, were given by Anderson. Nevertheless, C. Genigeorgis and W. W. Sadler[2] quote G. M. Dack[3] as saying that in the years 1956 to 1961 poultry meat was the third most frequent food (after meat and bakery products) implicated in outbreaks of staphylococcal enterotoxin food-poisoning.

Records of food-poisoning incidents in the United Kingdom are compiled by the Public Health Laboratory Service from reports received from public health and hospital laboratories, and from notifications sent by medical officers of health to the Ministry of Health. A report is published annually in the *Bulletin of the Ministry of Health and Public Health Laboratory Service*. A study of these statistics up to 1966 does not suggest that staphylococcal food-poisoning and poultry meat have often been associated in the past. Thus not more than one or two outbreaks have been recorded in any one year. The number of incidents of staphylococcal food-poisoning reported every year has varied between 74 and 143 during the last decade, while the foods usually concerned were cold meat, such as ham and tongue, and sweet dishes, such as cakes and trifles.

One explanation for these apparent differences may be that both the methods of manufacture for poultry products and the national feeding habits in Australia and the U.S.A. are different from those in Britain. Thus the manufacture and distribution of cooked and frozen poultry rolls made up of compressed meat in plastic wrapping is commoner in the U.S.A., and Australia—though these have recently been imported and produced in Britain, and this may increase the likelihood of staphylococcal food-poisoning from poultry meat. Any food handled after cooking and before freezing may be contaminated with staphylococci from the hands of the workers and from the processing equipment. Whether the food remains safe will depend on the time between cooking, handling, and freezing and on the actions of the caterer or householder responsible for the preparation of food for the table. To produce enough toxin to cause food-poisoning staphylococci must grow in food, and every hour that the latter is exposed to room temperature increases the risk considerably. Moreover, washing the hands before handling food is no safeguard against the removal of staphylococci, which are well known to stick closely to the hands within the skin and in crevices and to defy all efforts at removal.[4]

Another question that has to be answered is whether the prevalence of coagulase-positive staphylococci could be due to their frequent occurrence in the birds themselves or in poultry workers, who then contaminate the environment. The broiler trade is troubled by staphylococcal sepsis in poultry, but little is known of the epidemiology of this disease or of its relation to the staphylococci carried by the workers in the intensive poultry farms and factories.

The multiplication of staphylococci on chicken meat before cooking could give rise to enterotoxin in situations inside the bird where heat penetration is poor, so that the toxin or perhaps even the organism itself would not be destroyed during cooking. But despite the heat resistance of enterotoxin, and despite the prevalence of *Staphylococcus aureus* in the slaughter-houses,[5] there are no reports of staphylococcal food-poisoning from meat contaminated when raw and subsequently eaten shortly after cooking. The survival of coagulase-positive staphylococci in lightly cooked meat or poultry could result in multiplication during long, slow cooling periods, yet it is the survival of salmonellae—and more particularly *Clostridium welchii*—which has given rise to many reported outbreaks of food-poisoning. The spores of *Cl. welchii* readily survive cooking temperatures, and germinate into actively growing bacilli in slowly cooling masses of meat and poultry, particularly those of large bulk. Thus at present codes of practice for caterers and housewives are under consideration. What is also badly needed are codes of practice for means and materials to clean equipment and working surfaces soiled by raw food materials, which bring food-poisoning organisms into the kitchen.

---

[1] Anderson, K., *Med. J. Aust.*, 1966, **2**, 1223.

[2] Genigeorgis, C., and Sadler, W. W., *Poult. Sci.*, 1966, **45**, 973.

[3] Dack, G. M., in *International Symposium on Food Protection, Chemical and Biological Hazards in Foods*, ed. by J. C. Ayres *et al.*, 1962, p. 320. Iowa

[4] Brodie, J., *Scot. med. J.*, 1965, **10**, 115.

[5] Ludlam G. B., *Mth. Bull. Minist. Hlth Lab. Serv.*, 1952, **11**, 138.

Papers and Originals

Neonatal Hirschsprung's Disease

G. C. FRASER,* M.B., F.R.C.S., F.R.C.S.ED.; A. W. WILKINSON,† CH.M., F.R.C.S., F.R.C.S.ED.

Brit. med. J., 1967, 3, 7-10

During the 18 years since Swenson and Bill (1948) first showed that Hirschsprung's disease could be cured by resection of the abnormally innervated distal segment of rectum and colon the clinical status of the disease has been transformed. Though the early onset of the clinical disturbance in Hirschsprung's disease has been repeatedly emphasized, the diagnosis was seldom made or the disease treated in the early days or weeks of life (Forshall, 1964). It seems likely that formerly many of the babies born with this disease died undiagnosed within a few weeks or months of birth. Bodian *et al.* (1949) and Eek and Knutrud (1962) estimated that the mortality in the first year was 50%. Most of these children probably died of gastroenteritis superimposed on the intestinal obstruction caused by the unrecognized aganglionosis.

Hirschsprung's disease has long been associated clinically with the picture of a young child with chronic or occasionally intermittent but severe constipation, accompanied by progressive distension of the abdomen and a striking failure to thrive. In the few survivors this led eventually to the classical form of the disease still described in many textbooks—a child with wasted limbs and a wizened face looking anxiously over the top of a huge belly packed with hard masses of faeces. Such children were often the survivors of regimens of repeated bowel washouts and constant purgation, and were poor subjects for radical surgical treatment.

The aganglionosis of Hirschsprung's disease affects the developing lower bowel at a very early stage (Bodian and Carter, 1963). That some degree of intestinal obstruction has been present for weeks before birth is indicated by the hypertrophy of the intestinal muscle of the transitional segment and the most distal part of the normally innervated segment. This hypertrophy may be readily seen at operation just after birth. With few exceptions the clinical features on which a diagnosis of Hirschsprung's disease can be made are evident within a day or two of birth (Forshall, 1964). One consequence of the increased interest in neonatal disorders during the past 10 years has been the recognition that Hirschsprung's disease is much commoner than had been suspected.

This report is based on a review of 54 babies (44 boys, 10 girls) who were admitted to the Hospital for Sick Children between 1 January 1958 and 31 December 1965, and who were under the age of 1 month on admission. The diagnosis of Hirschsprung's disease has been confirmed by histological evidence in every case. Only 36 patients survived their initial admission, a mortality of 33%. The birth weight was known in 53 patients (Fig. 1), of whom 22 weighed more than 3.5 kg. (7¾ lb.), and 6 (27%) of these died, whereas 11 died of the 31 who weighed less than 3.5 kg. (7¾ lb.) and 8 of the 12 who weighed less than 3 kg. (6½ lb.). Age on admission varied from a few hours to 28 days, but this did not seem to have any relation to mortality, because the average age on admission of babies who died was 12 days and of the survivors 10 days.

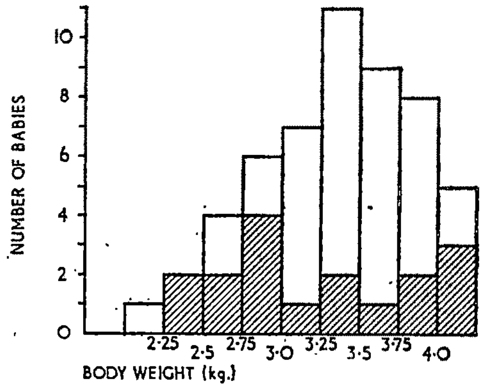


FIG. 1.—Birth weight in 53 cases. Cross-hatched squares indicate patients who died.

The lesions extended proximal to the pelvic colon ("long segment") in 12 babies, of whom 8 (66%) died, whereas of the 42 patients in whom only a short segment was involved 10 (24%) died.

Clinical Features

When Forshall (1964) reviewed a group of children of al ages with Hirschsprung's disease she found that four mai clinical features were common in the neonatal period—vomiting, abnormality of bowel habit, abdominal distension, an reluctance to feed. In addition to these features the genera appearance also may be characteristic. The face is thinne than normal and wrinkled; the skin looks dull and grey an feels limp even when the baby is only 2 or 3 days old an vomiting has not been so severe as to cause dehydration. T neonate with Hirschsprung's disease may have a worried frowning appearance, which, combined with thin featur makes the baby look like a little old man. Often the baby irritable and the head may be rolled from side to si Abdominal distension may hinder the normal respirat excursion, and breathing may be rapid and grunting character.

Vomiting was recorded in 53 cases (98%). Persist vomiting, especially when the vomitus was bile-stain usually led to prompt referral to hospital, but this did affect the mortality rate, because 7 died of the 23 patient whom vomiting began on the first day, and 11 died of the who began to vomit later (Fig. 2).

---

* Formerly Resident Assistant Surgeon, the Hospital for Sick Children, Great Ormond Street, London W.C.1. Present address: Department of Surgery, Health Centre for Children, Vancouver General Hospital, Vancouver, B.C., Canada.

† Nuffield Professor of Paediatric Surgery, the Institute of Child Health (University of London); Surgeon, the Hospital for Sick Children, Great Ormond Street, London W.C.1.

Abnormality of bowel habit was noted in 49 patients and was an even more common disturbance on the first day of life (28 cases) than was vomiting (Fig. 2). It was usually first manifest by the failure to pass normal meconium. Subsequently stools might be infrequent, abnormal in colour, loose, or offensive.

Abdominal distension was recorded in 51 patients (94%) and appeared in the first three days in 31 (60%) out of 51, most commonly on the second day of life (Fig. 2). The mortality was not closely related to the time of onset of distension.

Failure to progress is difficult to define, and its recognition may depend a good deal on the vigilance and experience of the nursing staff and the clinician. The main features are reluctance to feed or a poor performance during feeding, listlessness, irritability, and a failure to gain weight satisfactorily. This type of disturbance was found in 40 patients (74%) (Fig. 2), and the observation was often first made by the nursing staff, nearly always during the first week of life.

It is usually said that on rectal examination the anal canal and rectum feel narow and grip the finger. As the finger is withdrawn it may be followed by a forcible gush of flatus and liquid offensive pale faeces. These features are not always present, especially when the rectum has already been examined in this way on several occasions, and their absence does not exclude the diagnosis.

Confirmation of Diagnosis

So far the clinical features of the disease have been emphasized because the early diagnosis of Hirschsprung's disease in the neonatal period mainly depends on awareness of them and their recognition. Some support for this provisional diagnosis may come from a radiograph of the abdomen with the baby in the erect position, and in sufficiently fit babies it can be confirmed by *x*-ray examination after a barium enema. A radiograph taken with the baby erect will usually show the degree and distribution of gaseous distension of the intestine; further useful information may be obtained from a lateral erect exposure, since this often shows more clearly how far down into the colon and rectum the gaseous distension extends. In a neonate with a distended abdomen absence of gas from the pelvis, especially on an erect lateral radiograph, is suggestive of Hirschsprung's disease.

In the present series 27 patients were *x*-rayed after a barium enema, some in the first two or three days of life. The diagnosis of Hirschsprung's disease was correctly made in 24 instances, in one the appearances were equivocal, and in the remaining two patients the diagnosis was incorrect, but in both of them the rectum had been washed out before the barium examination. No complications were associated with the radiological examination in these 27 patients. The diagnosis may also be confirmed by histological examination of a biopsy specimen taken from the aganglionic bowel. Biopsy specimens were taken from the rectum in 21 patients in this series, of whom two died of peritonitis due to perforation during or soon after the biopsy was done.

Cause of Death

The causes of death of the 18 babies are shown in the Table. One (Case 5) was dead on arrival at the hospital and three (Cases 6, 7, and 11) were very ill when admitted. Some kind of severe infection occurred in all but one (Case 16), but in eight of these it was a direct consequence of the surgical treatment. In two patients (Cases 1 and 2) peritonitis was due to the bowel being perforated while the rectum and colon were being washed out, and in two others (Cases 3 and 4) peritonitis was secondary to perforation during or soon after diagnostic rectal biopsy. Five patients (Cases 5, 6, 7, 8, and 9) died of enterocolitis. One of these was dead on arrival at hospital with peritonitis due to perforation of the ascending colon secondary to enterocolitis. Two others (Cases 6 and 7) arrived already very ill with enterocolitis and survived colostomy for only a few hours. In two others (Cases 8 and 9) enterocolitis developed after the institution of a colostomy for the relief of low obstruction. Another child (Case 10) died of gangrene of the jejunum and ileum of uncertain cause 30 hours after an ileostomy had been made for relief of a long-segment obstruction.

A long segment of the bowel (more than the rectum and pelvic colon) was involved in 12 of the 54 patients of this series, of whom 8 died (67%), whereas for babies in whom only a short segment was involved the mortality was 24%. In five patients (Cases 11–15) a long segment of bowel was involved, the full extent of which was not recognized at the first operation. Repeated operations were needed for the relief of intestinal obstruction and were associated with infective complications; in four of these there were also obstructions due to adhesions. It may be very difficult to recognize exactly, by eye alone, the extent of the aganglionic segment at a primary laparotomy for relief of a neonatal intestinal obstruction. Whenever possible the diagnosis and the extent of the aganglionosis should be confirmed by the immediate

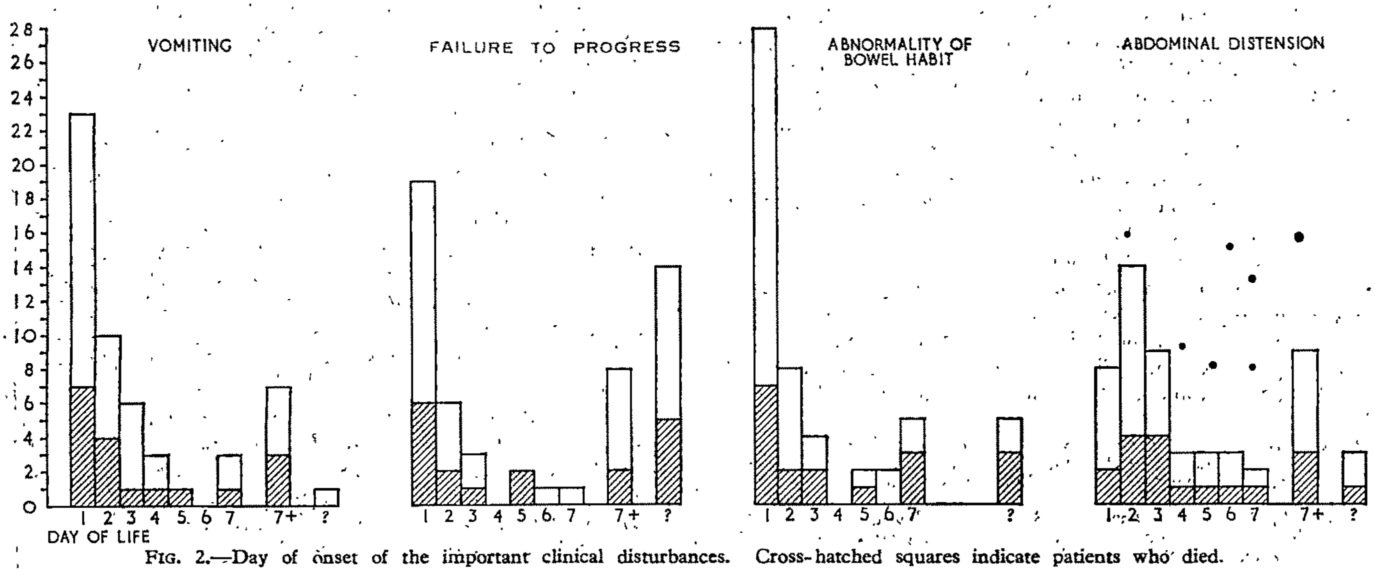


FIG. 2.—Day of onset of the important clinical disturbances. Cross-hatched squares indicate patients who died.

histological examination of a frozen section of a specimen from the bowel wall.

There were three mongols, of whom two died without any surgical treatment—one of bronchopneumonia due to aspiration of vomitus, and the other of cardiac failure. The third patient was treated conservatively for 30 days and then was subjected to a primary pull-through operation of the Soave type; after operation abdominal distension persisted except when relieved by bowel washouts per anum. This child died of cardiac failure at the age of 10 weeks, and necropsy showed a pelvic abscess and congenital defects.

Discussion

It is of the nature of Hirschsprung's disease that there is a high degree of intestinal obstruction from the time the bowel first develops in utero long before the baby is born. This is because the obstruction is due to the defective development of the nerve supply to the muscle coats of a varying length of the rectum and colon and very rarely of the small intestine (Swenson and Bill, 1948). Though in a few patients only a centimetre or two of the lowest part of the rectum may be aganglionic, and in such patients a satisfactory response may sometimes follow conservative treatment by repeated digital dilatation, the passage of rectal tubes, and rectal washouts, this response may be transient and the risks of perforation and water intoxication are well known. In those babies in whom the aganglionic segment extends above the lower two-thirds of the rectum it is unlikely that dilatation of the upper anal canal and lower rectum will be effective in relieving the obstruction. When the pelvic or more proximal parts of the colon are involved the narrow segment cannot be completely dilated, and bowel washouts are clearly useless and dangerous. A colostomy or ileostomy is essential for complete relief of the obstruction.

Details of Fatal Cases

Case No.	Sex	Age on Admission (Days)	Age at Death (Days)	Length of Segment	Cause of Death at Necropsy	Comments
1	M	3	15	Short	Peritonitis	Perforation during washout. Laparotomy; died 3 hours later
2	F	2	4	,,	,,	Perforation during washout. Colostomy; died 10 hours later
3	M	23	62	Long	Obliterative peritonitis	Perforation after rectal biopsy. Laparotomy, colostomy, ileostomy. 1 week later, small intestinal fistulae
4	M	8	21	,,	Peritonitis, bronchopneumonia	Ileostomy, perforation of rectal biopsy, peritonitis, laparotomy
5	M	5	5	Short	Enterocolitis, perforation of ascending colon, peritonitis	Dead on arrival
6	M	19	19	,,	Enterocolitis	Very ill on admission. Colostomy; died 5½ hours later
7	M	25	26	,,	Enterocolitis, necrosis of ileum	Very ill on admission. Peritonitis. Laparotomy, colostomy; died 8 hours later
8	M	8	17	,,	Peritonitis, enterocolitis	Gangrene of left iliac and transverse colostomies and colon
9	M	10	17	,,	Purulent colitis beyond colostomy, ? early enterocolitis above colostomy	Ill on admission. Colostomy sclerema 3rd to 5th postoperative days—subsided; sudden death on 7th day
10	M	2	4	Long	Gangrene of jejunum and ileum. ? Cause	Malrotation of midgut and Hirschsprung's disease to distal ileum; died 30 hours after ileostomy
11	M	14	20	,,	Septicaemia, multiple abscesses in lungs and heart	Admitted very ill after several operations elsewhere for "meconium obstruction." Ileostomy; died 8 hours later
12	M	1	50	,,	Multiple infections and abscesses	Colostomy on 12th day. Laparotomy 44th day for intestinal obstruction due to adhesions at biopsy site
13	M	27	76	,,	Multiple infections, dehydration	Ileostomy, rectal biopsy, laparotomy for obstruction due to adhesions. Repeated bouts of diarrhoea with parenteral therapy
14	M	3	67	,,	Septicaemia, lung abscesses, subacute intestinal obstruction	Original colostomy wrongly sited because of erroneous report on frozen section; repeated operations to resite colostomy and relieve adhesion obstructions
15	M	28	38	,,	Chronic peritonitis, perforated anterior duodenal ulcer	Colostomy 24 hours after admission, adhesion obstruction 4 days later. Laparotomy
16	M	12	37	Short	Cardiac failure, multiple anomalies	No surgical treatment. Mongol
17	M	24	48	,,	Bronchopneumonia, cardiac failure	No surgical treatment. Mongol
18	M	3	70	,,	Cardiac failure, pelvic abscess	Primary Soave rectosigmoidectomy; needed postoperative washouts. Mongol

In general the babies in this series were of normal size at birth. This is in contrast with the situation in atresia of the oesophagus or duodenum, in which about a quarter of the babies weigh less than 2.5 kg. (5½ lb.) (Waterston *et al.*, 1963; Young and Wilkinson, 1966), compared with only 3 (5.5%) in this series. It is of interest that only 10 out of 106 patients with meconium obstruction treated in this and another hospital weighed less than 2.5 kg. (5½ lb.) (Holsclaw *et al.*, 1965), a proportion not much different from that in the normal population. However, in meconium obstruction the mortality was higher (46%) in babies weighing 6 to 8 lb. (2.7 to 3.6 kg.). In this series of babies with Hirschsprung's disease there was not much variation in mortality rate with different birth weights. In an earlier report from this hospital Wyllie (1957) found the preoperative weights were below average for age, but this was because his patients were older and had failed to thrive. Only 33 of Wyllie's 157 patients were operated on in the first year of life.

Like Forshall (1964), we found few other congenital anomalies associated with Hirschsprung's disease, which in this way resembled meconium obstruction and was unlike oesophageal and duodenal atresia. Hofmann and Rehbein (1966), however, found other serious malformations in 17 (32%) of the 53 neonates in their series.

When persistent and detailed inquiry had been made clinical evidence of the disease during the first week of life was established in almost every child in this series. Vomiting (98%), abdominal distension (94%), and abnormal stools, constipation, or diarrhoea or both (98%) were the most important features and were usually present together. Though such disturbances might appear within a day or two of birth they were not invariable or progressive. Especially when only a very short segment of the rectum was involved, remission of the obstruction might follow digital rectal examination and the subsequent expulsion of gas and liquid faeces. In a few cases such a remission lasted several weeks or even months, but more often recurrent disturbances led to relief by operation. Hofmann and Rehbein (1966) found abdominal distension in all 53 of their neonates with Hirschsprung's disease and bilious vomiting in all but one, and that in 70% meconium had not been passed or had appeared in only small quantities. In the neonate episodes of vomiting of bile-stained fluid, especially if accompanied by abdominal distension, always justify the taking of a radiograph of the abdomen in the upright position to see if there is evidence of intestinal obstruction.

The best and safest way of confirming the clinical diagnosis is by radiological examination after a barium enema, provided that the bowel has not been washed out. Only in those babies whose general condition is too poor for radiological examination and who urgently require the decompression of their obstructed bowel should a colostomy be made without establishing the diagnosis; in these the barium-enema examination can be done a few days later. Rectal biopsy is difficult and dangerous in the neonate and may provide too little tissue for a sat-factory histological examination; it should be done only when the result of radiological examination is equivocal.

A third of the patients in this series died, a clear indication of the serious potentialities of Hirschsprung's disease. That such a high mortality should be found in a series of patients in whom the disease had been recognized within the first month of life adds weight to the former estimates (Bodian *et al.*, 1949; Eek and Knutrud, 1962) that 50% died in the first year of life.

The higher mortality in neonates has also been emphasized by Hofmann and Rehbein (1966): 15 of their 53 neonates died. They prefer to treat the condition by washouts and hot packs rather than by colostomy, to which they resorted only when conservative treatment failed. Only two of their patients died during conservative treatment and the remaining 22 survived subsequent resection of the aganglionic bowel. However, of the 31 in whom a colostomy had to be made, 8 died and 19 had a complicated course, and five more died subsequently after resection of the affected bowel.

It seems to us that when Hirschsprung's disease is diagnosed soon after birth the safest form of treatment is decompression of the obstructed bowel by a colostomy or ileostomy with as little delay as possible. Resection of the abnormally innervated segment of bowel should be delayed until the child is 1 year old or weighs 20 lb. (9.1 kg.).

It is not surprising that the mortality rate should be higher in the babies with the "long segment" type of disease, especially when the full extent of the lesion is not recognized at the first or subsequent operations to relieve the obstruction, and the colostomy or ileostomy is first made in aganglionic bowel.

In Hirschsprung's disease the term "abnormality of bowel habit" may imply either constipation or bouts of diarrhoea owing to the passage of faecal stained mucus round an impacted mass of faeces. In its most extreme form diarrhoea may be due to a sort of enterocolitis with mucosal ulceration and toxaemia that is often fatal. In another series of 47 patients with Hirschsprung's disease (Bill and Chapman, 1962) there were 24 with enterocolitis, of whom 21 were neonates and 8 died; though in this series enterocolitis did not occur after colostomy, it did in two of our patients (Cases 8 and 9). Bill and Chapman also found that patients who had once had enterocolitis were liable to its recurrence, especially after rectosigmoidectomy. Swenson and Davidson (1960) have reported a mortality rate of 33% in patients who were treated medically, but in those for whom a colostomy was made as soon as the disease was diagnosed the mortality rate was only 4%. It seems that the best way to prevent enterocolitis may be to make a colostomy as soon as the diagnosis of Hirschsprung's disease is made, but it must be recognized that this does not always provide complete protection from enterocolitis or prevent death from it.

Summary

Of 54 babies suffering from Hirschsprung's disease who were admitted within a month of birth, 18 (33%) died—5 of enterocolitis and 11 of other complications of the treatment; 2 mongols were not treated surgically.

The clinical disturbance associated with this form of congenital intestinal obstruction usually begins within the first two or three days after birth and is characterized by vomiting, abdominal distension, and abnormality of the bowel action. The clinical diagnosis was confirmed by *x*-ray examination after a barium enema in 24 out of 27 patients in this series; in one patient the appearances were equivocal and in two others the bowel had been washed out before the examination.

Neonatal intestinal obstruction due to Hirschsprung's disease should be relieved by a colostomy or ileostomy as soon as the diagnosis is established.

We are indebted to the late Mr. G. H. Macnab, Mr. D. J. Waterston, and Mr. H. H. Nixon for allowing us to include patients under their care in this survey.

REFERENCES

Bill, A. H., jun., and Chapman, N. D. (1962). *Amer. J. Surg.*, **103**, 70.
Bodian, M., and Carter, C. O. (1963). *Ann. hum. Genet.*, **26**, 261.
—— Stephens, F. D., and Ward, B. C. H. (1949). *Lancet*, **1**, 6.
Eek, S., and Knutrud, O. (1962). *J. Oslo Cy Hosp.*, **12**, 245.
Forshall, I. (1964). *J. roy. Coll. Surg. Edinb.*, **10**, 31.
Hofmann, S., and Rehbein, F. (1966). *Zbl. Kinderchir.*, **3**, 182.
Holsclaw, D. S., Eckstein, H. B., and Nixon, H. H. (1965). *Amer. J. Dis. Child.*, **109**, 101.
Swenson, O., and Bill, A. H., jun. (1948). *Surgery*, **24**, 212.
—— and Davidson, F. Z. (1960). *New Engl. J. Med.*, **262**, 64.
Waterston, D. J., Bonham-Carter, R. E., and Aberdeen, E. (1963). *Lancet*, **2**, 55.
Wyllie, G. G. (1957). Ibid., **1**, 850.
Young, D. G., and Wilkinson, A. W. (1966). Ibid., **2**, 18.

Overinflation of the Lungs in Coal Miners

COLIN OGILVIE,* M.D., M.R.C.P.; KEITH BROWN,† M.D., M.R.C.P.; W. E. KEARNS,‡ M.B., CH.B.

Brit. med. J., 1967, 3, 10–14

Coal miners whose chest radiographs are normal tend to be more breathless than non-miners of the same age-group, but a pattern of dysfunction distinct from chronic non-industrial lung disease has not been observed.

The purpose of this report is to compare the results of lung-function tests in coal miners referred to a physiological laboratory because of unexplained dyspnoea with those obtained in a group of men suffering from chronic non-specific lung disease.

Patients

The first group consists of 17 miners (two from Yorkshire and 15 from West Lancashire coal fields) who were referred during 1963–6 to a lung-function laboratory providing a routine service for the region. In each case the miner had been referred by a consultant physician because physical and radiological examination had failed to reveal an adequate cause for his disability. These 17 cases represent the total number of miners referred to the laboratory in this way. Apart from clinical or radiological signs compatible with either chronic non-specific lung disease or pneumoconiosis, no cardiac or pulmonary cause for dyspnoea could be found in any of these patients. The only miners attending the laboratory during 1963–6 and excluded from this report were those referred for routine preoperative assessment or for the investigation of a disease not directly related to their occupation (mitral stenosis, bronchiectasis, bronchial carcinoma, or tuberculosis).

---

* Consultant Physician.
† Senior Medical Registrar.
‡ Medical Registrar.
Regional Cardiothoracic Centre, Broadgreen Hospital, Liverpool 14.

The occupational history and the clinical and radiological findings for the 17 miners are recorded in Table I. The average age was 57 years at the time of the investigation. Only five of the miners were still working underground, the remainder having left the mines an average of five years previously. The average duration of underground work was 32 years, 12 of the 17 miners having worked underground for 30 or more years. Of the five with less than 30 years underground, two had worked in other dusty occupations (26 years in a lead mine and seven years in a granite quarry respectively). The 17 miners all complained of either moderate (grade 2) or severe (grade 3) dyspnoea on effort (see Methods). The average duration of effort dyspnoea was six years. Five miners denied having any cough, while 12 complained of cough with a variable amount of sputum. Most of them stated that cough and dyspnoea started together, but none was sure about the total duration of cough.

TABLE I.—*Occupational and Clinical History and Radiographic Findings in Group 1 (Coal Miners)*

Case No.	Years Underground	Years Since Leaving Mines	Symptoms	Grade of Dyspnoea	Signs of Bronchitis	*X*-ray Evidence of Pneumoconiosis
1	38	4	Cough and effort dyspnoea 5 years	3	Wheeze on forced expiration	None
2	38	7	Effort dyspnoea 6 years. No cough	2	None	Category 3
3	6*	8	Effort dyspnoea 10 years. No cough	2	"	" 1
4	45	2	Cough and effort dyspnoea 5 years	2	"	" 2
5	33	4	Cough and effort dyspnoea 4 years	2	Coarse basal crepitations	" 3
6	35	9	Cough and effort dyspnoea 9 years	3	Wheeze on forced expiration	None
7	30	10	Cough and effort dyspnoea 12 years	3	Generalized expiratory wheezing	"
8	6†	25	Effort dyspnoea 2 years. No cough	2	None	"
9	51	0	Effort dyspnoea 8 years. No cough	3	"	"
10	50	0	Cough and effort dyspnoea 1 year	2	"	"
11	17	8	Effort dyspnoea ? duration. No cough	3	Coarse basal crepitations	"
12	24	11	Cough and effort dyspnoea 15 years	3	Wheeze on forced expiration	"
13	31	0	Cough 5 years. Effort dyspnoea 1 year	2	None	Category 1
14	27	0	Cough and effort dyspnoea 6 months	2		" 1
15	35	2	Effort dyspnoea 19 years. Cough 1 year	3		None
16	42	1	Cough 2 years. Effort dyspnoea 1 year	2		Category 1
17	30	0	Cough 1 year. Effort dyspnoea 6 months	2	Wheeze on forced expiration	" 3
Mean	32	5				

* Plus 26 years in lead mines.
† Plus 7 years in granite quarry.

Physical signs of bronchitis were present in seven: expiratory wheeze was evident in five and coarse basal crepitations without wheeze in two others. The chest radiographs showed evidence of simple pneumoconiosis (categories 1–3) in eight cases and were clear in the remaining nine.

The second group consists of 15 male non-miners aged 50 and over referred to the laboratory as cases of chronic bronchitis and/or emphysema. These patients fulfilled the criteria required for a diagnosis of chronic non-specific lung disease: they were all suffering from chronic cough with sputum and/or persistent breathlessness *not* associated with localized lung disease of any kind, generalized specific infective diseases of the lungs, pneumoconiosis, generalized pulmonary fibrosis or granulomata, primary cardiovascular or renal disease, diseases of the chest wall, anaemia, or psychoneurosis (Ciba Guest Symposium, 1959). The 15 patients represent the total number of males aged 50 and over with chronic non-specific lung disease for whom adequate physiological data were available in the laboratory records.

Methods

The physiological techniques used are those described in previous publications (Ogilvie *et al.*, 1963), and include: (1) the subdivisions of the lung volume, including vital capacity (V.C.), functional residual capacity (F.R.C.), and residual volume (R.V.). F.R.C. and R.V. were measured by means of a closed-circuit helium method; (2) maximum voluntary ventilation at 80 respirations per minute (M.V.V.80); (3) maximum inspiratory and expiratory flow rates derived from the forced spirogram (M.I.F.R. and M.E.F.R.); (4) the forced expiratory volume in 1 second (F.E.V.$_1$); (5) arterial CO_2 tension by the rebreathing method (Pco_2); and (6) transfer factor for carbon monoxide (diffusing capacity, DL) by the single-breath technique.

The degree of dyspnoea was recorded for each miner before the physiological tests were carried out, according to the following grading:

Grade 1 (mild). Dyspnoea only on severe exertion such as running on the level or hurrying upstairs.

Grade 2 (moderate). Dyspnoea on one flight of stairs or walking up inclines. No dyspnoea when walking at a normal pace on level ground.

Grade 3 (severe). Dyspnoea when walking at a normal pace on level ground.

The normal values for lung volumes were predicted from the formula of Baldwin *et al.* (1948). The normal values for transfer factor were predicted from the formula of Ogilvie *et al.* (1957). The results in the two groups were also compared with those obtained in five normal men aged 50 and over studied in the same laboratory. These five men had been referred to general surgical clinics of the hospital from the same area as the

TABLE II.—*Physiological Findings in Group 1 (Coal Miners)*

Case No.	Age	Height		Weight		V.C. (l.)	F.R.C. (l.)	R.V. (l.)	T.L.C. (l.)	$\frac{R.V.}{T.L.C.}$ %	M.V.V. (l./min.)	$\frac{F.E.V._1}{V.C.}$ %	M.I.F.R. (l./min.)	M.E.F.R. (l./min.)	$\frac{M.I.F.R.}{M.E.F.R.}$	Transfer Factor (% Normal)	Pco (mm Hg)
		in.	cm.	lb.	kg.												
1	59	70	178	173	78·4	3·2	5·0	4·6	7·8	60	50	41	150	100	1·5	108	33
2	55	70	178	145	65·7	3·1	3·8	3·1	6·2	50	72	68	—	—	—	82	40
3	58	68	172	168	76·2	3·7	4·7	3·4	7·2	49	80	56	120	240	0·5	105	29
4	61	66	168	178	80·7	2·1	4·5	3·4	5·5	62	72	71	150	120	1·2	85	—
5	52	72	183	165	74·8	3·7	5·1	3·9	7·5	52	99	53	172	172	1·0	93	28
6	63	67	170	171	77·5	1·7	4·0	3·8	5·5	70	44	67	50	46	1·1	120	4
7	54	69	175	182	82·5	1·5	6·1	5·7	7·2	79	24	51	120	32	3·7	82	3
8	66	69	175	140	63·5	4·3	6·7	5·2	9·5	55	80	68	200	300	0·7	112	—
9	65	65	165	135	61·2	2·2	6·4	5·9	8·1	74	30	52	171	50	3·4	113	—
10	64	70	178	143	64·8	3·7	5·2	3·8	7·4	51	98	60	150	300	0·5	93	—
11	65	64	163	106	48·0	1·6	6·3	5·3	6·9	77	34	40	—	—	—	67	3
12	55	69	175	136	61·6	2·9	6·3	5·0	7·9	63	44	36	150	55	2·7	62	—
13	45	69	175	154	69·8	3·5	4·0	3·3	6·8	48	84	55	120	200	0·6	102	—
14	41	68	172	143	64·8	3·4	3·1	2·8	6·2	45	82	60	200	400	0·5	120	
15	61	63	160	113	51·2	2·4	4·0	3·5	5·9	60	50	52	86	120	0·7	103	
16	60	64	163	148	67·1	1·7	3·3	3·1	4·8	65	60	70	67	100	0·7	—	
17	52	66	168	165	74·8	3·5	4·2	3·1	6·6	46	86	70	120	120	1·0	130	
Mean	57	67	170	151	68·4	2·8	5·0	4·1	6·9	60	65	57	142	164	1·3	99	

TABLE III.—*Physiological Findings in Group 2 (Chronic Non-specific Lung Disease)*

Case No.	Age	Height		Weight		V.C. (l.)	F.R.C. (l.)	R.V. (l.)	T.L.C. (l.)	R.V./T.L.C. %	M.V.V. (l./min.)	F.E.V.$_1$/V.C. %	M.I.F.R. (l./min.)	M.E.F.R. (l./min.)	M.I.F.R./M.E.F.R.	Transfer Factor (% Normal)	Pco$_2$ (mm. Hg)
		in.	cm.	lb.	kg.												
1	50	68	172	187	84·8	1·8	3·9	3·5	5·3	66	21	30	150	12	12·5	86	64
2	59	63	160	128	58·0	1·8	3·0	2·7	4·5	60	36	52	150	80	1·9	90	50
3	56	65	165	145	65·7	2·2	6·1	5·4	7·6	71	30	36	194	30	6·5	78	—
4	53	68	172	154	69·8	1·9	3·9	3·2	5·1	63	26	37	97	21	4·6	38	—
5	56	65	165	157	71·2	1·7	5·9	5·6	7·3	76	24	38	154	26	5·9	74	—
6	55	68	172	122	55·3	2·4	6·3	5·4	7·8	70	26	28	167	17	9·8	55	—
7	57	68	172	143	64·8	3·0	4·9	4·3	7·3	59	52	40	150	75	2·0	29	41
8	61	68	172	147	66·6	1·9	2·9	2·6	4·5	58	45	48	150	35	4·3	65	37
9	67	67	170	125	56·6	1·8	4·8	4·5	6·3	72	26	37	100	10	10·0	10	43
10	62	67	170	115	52·1	2·2	5·0	4·4	6·6	67	38	46	187	33	5·7	7	—
11	62	67	170	135	61·2	2·6	5·1	4·1	6·7	61	40	42	162	58	2·9	29	32
12	70	69	175	126	57·1	2·8	4·6	3·8	6·6	57	38	36	193	40	4·8	9	—
13	51	69	175	143	64·8	2·6	6·8	6·2	8·8	70	40	41	143	30	4·7	17	—
14	59	65	165	109	49·4	2·6	4·4	3·0	5·6	54	38	39	92	36	2·6	33	—
15	56	69	175	175	79·3	2·8	3·5	2·7	5·5	49	24	20	130	27	4·8	13	31
Mean	58	67	170	141	63·9	2·3	5·4	4·1	6·4	63	34	39	148	35	5·5	42	43

TABLE IV.—*Physiological Findings in Five Normal Men*

Case No.	Age	Height		Weight		V.C. (l.)	F.R.C. (l.)	R.V. (l.)	T.L.C. (l.)	R.V./T.L.C. %	M.V.V. (l./min.)	F.E.V.$_1$/V.C. %	M.I.F.R.	M.E.F.R.	M.I.F.R./M.E.F.R.	Transfer Factor (% Normal)
		in.	cm.	lb.	kg.											
1	55	68	172	168	76·2	3·3	2·5	2·2	5·5	42	95	76	240	400	0·6	107
2	58	69	175	162	73·4	3·9	2·3	1·0	4·9	21	60	62	200	240	0·8	73
3	69	67	170	168	76·2	3·7	2·3	1·8	5·5	33	90	66	170	300	0·6	94
4	50	65	165	135	61·2	3·7	3·3	2·1	5·8	36	108	74	200	300	0·7	95
5	50	69	175	123	55·7	3·4	2·8	1·6	5·0	32	77	65	200	300	0·7	76
Mean	57	68	172	151	68·4	3·6	2·6	1·7	5·3	33	86	69	202	308	0·7	90

FIG. 1

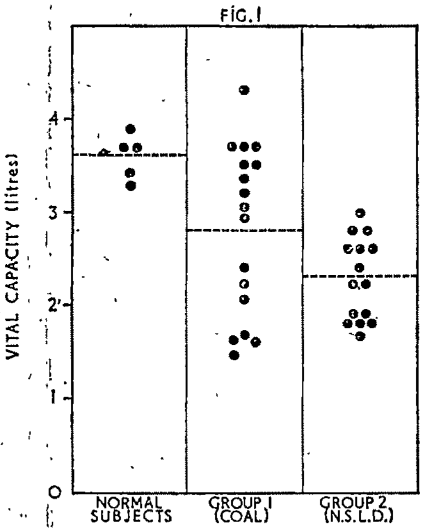


FIG. 2

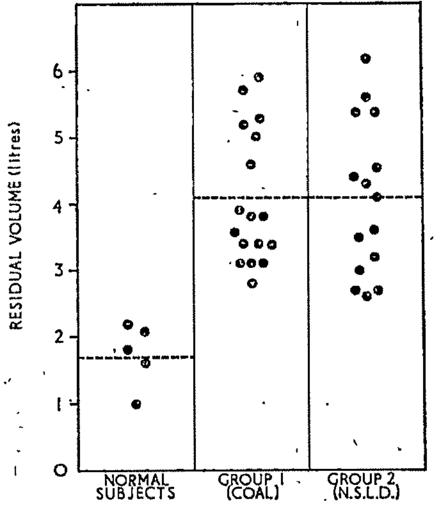


FIG. 3

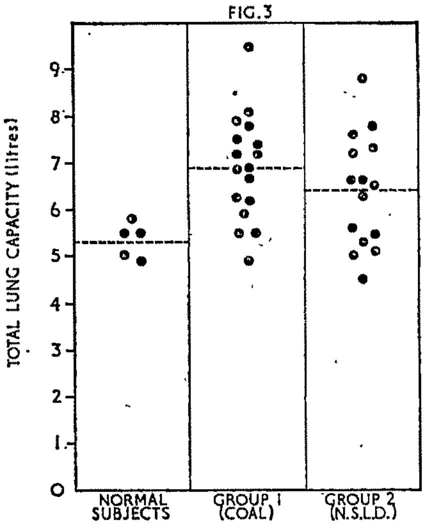


FIG. 4

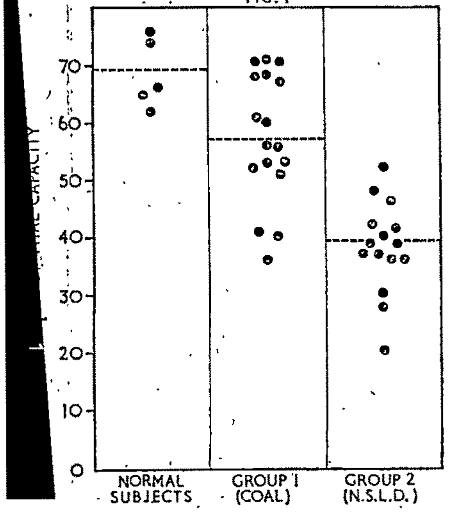


FIG. 5

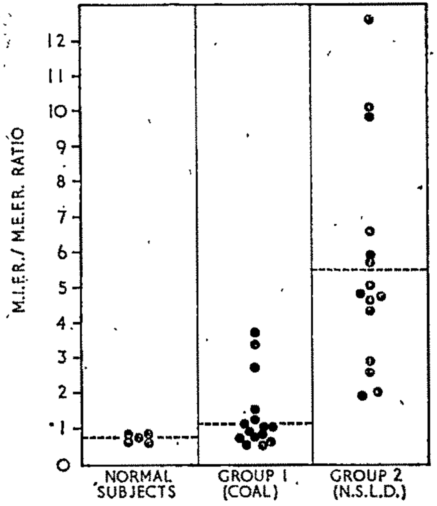
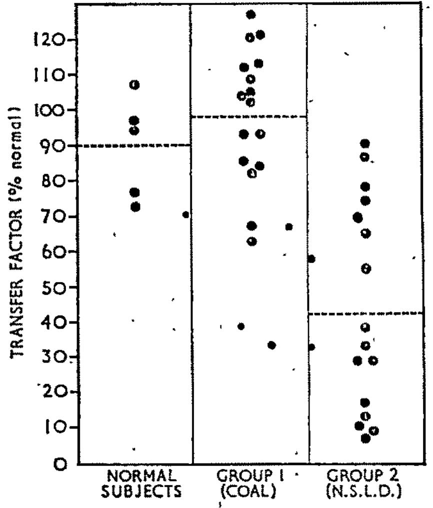


FIG. 6



G. 1.—Vital capacity. FIG. 2.—Residual volume. FIG. 3.—Total lung capacity. FIG. 4—F.E.V.$_1$ as percentage of vital capacity. FIG. 5.—M.I.F.R./M.E.F.R. ratio. FIG. 6.—Transfer factor.

miners and were all free of symptoms, signs, and radiological evidence of respiratory disease.

Results

The vital statistics and physiological findings in the two groups are shown in Table II (miners) and Table III (non-specific lung disease) and the results of the physiological tests are compared in Figs. 1 to 6. The results obtained in the five normal subjects are recorded in Table IV and are also shown in Figs. 1 to 6.

Vital Statistics.—The mean age was 57 years (range 41–66) in the miners (group 1) and 58 years (range 50–70) in patients with chronic non-specific lung disease (group 2). The mean height was 67 in. (170 cm.) (range 63–72 in.; 160–183 cm.) and mean weight 151 lb. (68.4 kg.) (range 106–182 lb.; 48–82.5 kg.) in group 1, and 67 in. (170 cm.) (range 63–69 in.; 160–175 cm.) and 141 lb. (63.9 kg.) (range 109–187 lb.; 49.4–84.8 kg.) respectively in group 2.

Lung Volumes.—In Table V the mean values for V.C., R.V., and T.L.C. are expressed as the percentage of predicted normal according to the formula of Baldwin *et al.* (1948). Results are shown for the two groups in the present study and for the five normal subjects. According to the formula of Baldwin *et al.* and the findings in our own normal subjects, the residual volume is increased to about two and a half times the predicted normal in both groups, while the total lung capacity is increased by nearly one-third in the miners and by nearly one-quarter in the patients with non-specific lung disease (see also Figs. 2 and 3).

TABLE V.—*Means of Lung Volume Fractions and M.V.V. Expressed as Percentage of Predicted Normal (By the Formulae of Baldwin et al., 1948)*

	Normal Subjects	Group 1 (Coal)	Group 2 (N.S.L.D.)
Vital capacity	100%	78%	64%
Residual volume	106%	255%	256%
Total lung capacity	102%	132%	123%
Maximum voluntary ventilation ..	106%	80%	41%

Ventilatory Capacity.—The impairment of ventilatory capacity was considerably greater in group 2 than in group 1, the mean M.V.V. having nearly twice the value in the latter group (see Table V). This difference was due to the greater degree of expiratory airways obstruction in group 2: the mean M.I.F.R. was approximately the same in the two groups, but the mean M.E.F.R. in group 2 was less than one-quarter of the value obtained in group 1. The values for the M.I.F.R./M.E.F.R. ratio and for the F.E.V.$_1$ as percentage of vital capacity are compared for the two groups in Figs. 4 and 5. It will be noted that in 12 of the miners but in none of the other group, the M.I.F.R./M.E.F.R. ratio was within the normal range (0.5–1.5). Eight miners, but none in the other group, showed a normal F.E.V.$_1$ as percentage of V.C. (over 60%).

Transfer Factor (Diffusing Capacity).—The mean transfer factor as percentage of predicted normal was 99% in group 1 and 42% in group 2. Fourteen of the 16 miners had a normal transfer factor (over 75%) as compared with 3 of the 15 patients in group 2 (see Fig. 6).

P_{CO_2}.—This was measured by the rebreathing method in seven patients from each group. The mean value for P_{CO_2} in these patients was 36 mm. Hg in group 1 and 43 mm. Hg in group 2. The P_{CO_2} was elevated in one patient from group 1 and in two patients from group 2.

Discussion

In any study of disability in coal miners the mode of selection is clearly important. In the present investigation the miners had all been referred by a general practitioner to a consultant physician and thence to a regional pulmonary function laboratory because physical and radiological examination had not revealed an adequate cause for their disability. Inevitably the question of eligibility for pension arose in a number of these patients, and in several the possibility of a "compensation neurosis" had been raised by the referring physician. It is not surprising, therefore, that more than half of these miners had no physical signs of bronchitis nor any radiological evidence of dust in the lungs and that only two (Cases 4 and 5) were in receipt of a pension for pneumoconiosis.

This group of miners had certain other features in common, less obviously related to the method of selection. Fifteen of the 17 were over the age of 50 and 12 had left the mines several years previous to the investigation. Twelve of the 17 had spent 30 years or more underground and, of the remaining five, two had been engaged in other forms of dusty work. Finally, they all showed an increase in residual volume, total lung capacity, and R.V./T.L.C.% comparable to that observed in patients with chronic non-specific lung disease but without a commensurate degree of expiratory airways obstruction or impairment of the transfer factor.

Several authors (Gilson and Hugh-Jones, 1955; Carpenter *et al.*, 1956; Higgins *et al.*, 1956; Leathart, 1959) have found that miners with normal chest radiographs have a poorer M.V.V. than those whose films show simple pneumoconiosis. Furthermore, Gilson and Hugh-Jones (1955) reported a close correlation between M.V.V. and dyspnoea in coal miners, but when a group in hospital was studied the correlation between R.V./T.L.C.% and dyspnoea was almost as good. In Fig. 7 M.V.V. has been plotted against R.V. for the miners in the present study and the grade of dyspnoea is indicated for each case. The eight miners with simple pneumoconiosis tend to have a higher M.V.V. and smaller residual volume (mean M.V.V. 80 l./min.; mean R.V. 3.3 l.) than the miners with clear films (mean M.V.V. 50 l./min.; mean R.V. 4.8 l.). Moreover, the grade of dyspnoea in these eight miners (grade 2) was less than in seven of the nine with clear films (grade 3). There appears, therefore, to be some relation between dyspnoea on the one hand and a low M.V.V. with increased residual volume on the other, but this relation is not necessarily a causal one, for there are many other variables of lung function which have not been measured in the present study. For example, uneven distribution of inspired gas (Gilson and Hugh-Jones, 1955), disturbances of the mechanical properties of the lungs (Leathart, 1959), and an increased alveolar-arterial Po$_2$ difference (Brasseur, 1963) have all been reported in coal miners.

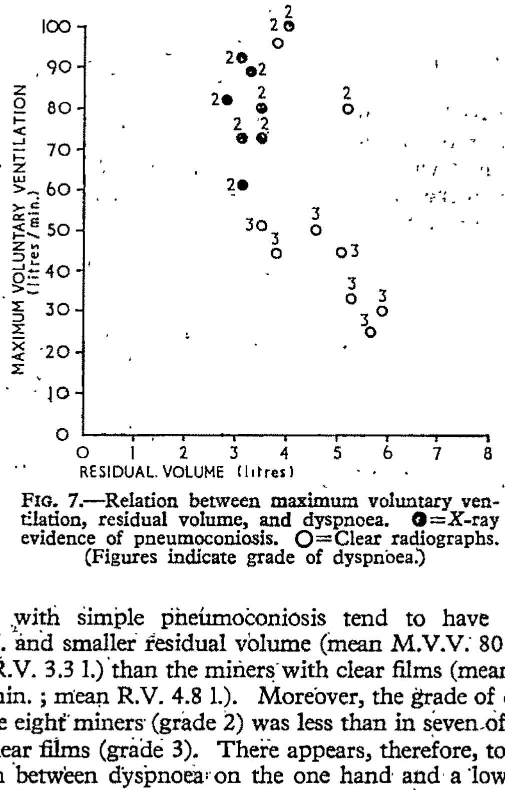


FIG. 7.—Relation between maximum voluntary ventilation, residual volume, and dyspnoea. ● = X-ray evidence of pneumoconiosis. ○ = Clear radiographs. (Figures indicate grade of dyspnoea.)

Carpenter *et al.* (1956) have suggested that the lower values for M.V.V. found in miners with clear films than in those with simple pneumoconiosis might be due to generalized emphysema in the former group, and Leathart (1959) supported this view. The finding of an increased residual volume among such miners in the present study is also in keeping with this suggestion. A possible explanation for this paradox has been offered by Rappaport (1966), who suggested that emphysema could mask the shadows cast by dust in the lungs. If emphysema is the cause of the increased residual volume found among the miners in the present study, then its physiological manifestations differ from those reported by Fletcher *et al.* (1963) for patients with primary emphysema. Fletcher's patients showed an increase in residual volume and R.V./T.L.C.% comparable to that found among the miners in the present series, but in addition there was severe airways obstruction and impairment of the transfer factor.

In their account of the pathogenesis of focal emphysema due to coal dust, Heppelston and Leopold (1961) pointed out that, initially, disruption of the alveoli is not a feature of this condition. Moreover, the bronchial smooth muscle is atrophic or absent and expiratory contraction of the bronchioles is diminished or abolished. Heppleston and Leopold attribute the alveolar dilatation to inspiratory traction upon the alveoli surrounding the deposits of dust rather than to expiratory airway obstruction. In the present investigation the finding among the coal miners of an increased residual volume with relatively less evidence of expiratory airway obstruction or impairment of gas transfer is compatible with Heppleston and Leopold's observations in focal emphysema. However, a normal transfer factor does not necessarily exclude alveolar destruction, and no conclusions can be drawn regarding the anatomical significance of our physiological findings. It is clear that a careful necropsy examination of the lungs of miners in whom physiological tests have been done during life is needed.

Summary

The physiological findings in 17 coal miners referred to a pulmonary function laboratory because of unexplained dyspnoea are compared with the findings in 15 patients referred with chronic non-specific lung disease and five normal subjects of the same age group.

The two groups of patients showed a comparable increase in residual volume, total lung capacity, and R.V./T.L.C.%, but expiratory airways obstruction and impairment of gas transfer were considerably less in the group of miners than in the patients with chronic non-specific lung disease.

The increase in residual volume was greater in the miners with clear radiographs than in those with simple pneumoconiosis. The increase in residual volume was also greater in those with a reduced M.V.V. and a high grade of dyspnoea, but it could still be detected in breathless miners with a normal M.V.V. and no evidence of expiratory airways obstruction.

It is suggested that the physiological findings in this group of miners are compatible with some of the reported pathological features of focal emphysema due to coal dust, but no conclusions can be drawn until necropsy studies are available for miners investigated during life.

We are indebted to the technical staff of the regional pulmonary function laboratory, Broadgreen Hospital, for their assistance in carrying out the tests reported in this paper; to Dr. James Carmichael, who read the chest radiographs; and to the consultant physicians who referred the patients for investigation. We are especially grateful to Dr. James MacArthur for his help and encouragement.

References

Baldwin, E. de F., Cournand, A., and Richards, D. W., jun. (1948). *Medicine (Baltimore)*, **27**, 243.
Brasseur, L. (1963). *L'exploration fonctionnelle pulmonaire dans la pneumoconiose des houilleurs.* Brussels.
Burrows, B., Niden, A. H., Fletcher, C. M., and Jones, N. L. (1964). *Amer. Rev. resp. Dis.*, **90**, 14.
Carpenter, R. G., Cochrane, A. L., Gilson, J. C., and Higgins, I. T. T. (1956). *Brit. J. industr. Med.*, **13**, 166.
Ciba Guest Symposium (1959). *Thorax*, **14**, 286.
Fletcher, C. M., Hugh-Jones, P., McNicol, M. W., and Pride, N. B. (1963). *Quart. J. Med.*, **32**, 33.
Gilson, J. C., and Hugh-Jones, P. (1955). *Spec. Rep. Ser. med. Res. Coun. (Lond.)*, No. 290.
Heppleston, A. G., and Leopold, J. G. (1961). *Amer. J. Med.*, **31**, 279.
Higgins, I. T. T., Oldham, P. D., Cochrane, A. L., and Gilson, J. C. (1956). *Brit. med. J.*, **2**, 904.
Leathart, G. L. (1959). *Brit. J. industr. Med.*, **16**, 153.
Ogilvie, C. M., Forster, R. E., Blakemore, W. S., and Morton, J. W. (1957) *J. clin. Invest.*, **36**, 1.
—— Harris, L. H., Meecham, J., and Ryder, G. (1963). *Brit. med. J.*, **1**, 1111.
Rappaport, I. (1966). Ibid., **1**, 1356.

Psychiatric Study of a Consecutive Series of 34 Patients with Ulcerative Colitis*

FRED FELDMAN, M.D.; DAVID CANTOR, M.D.; SIDNEY SOLL, M.D.; WILLIAM BACHRACH, M.D.

Brit. med. J., 1967, **3**, 14–17

The purpose of this study is to evaluate the role of psychiatric factors in the causation of ulcerative colitis by survey of a fairly long unselected series. Ulcerative colitis is still one of the most enigmatic of diseases, despite its position, paradoxically, as the "classic" psychosomatic illness. Its cause is believed by most gastroenterologists to be unknown, yet a large number of reports by psychiatrists discuss it as an unquestionably psychosomatic illness. The studies by physicians and surgeons of such medical factors as cause, course, complications, and drug treatment have been for the most part cautious, uncertain, and qualified (Crohn and Yarnis, 1951; Michener *et al.*, 1961; Hijmans and Enzer, 1962; Korelitz *et al.*, 1962; Edwards and Truelove, 1963, 1964; Rhodes and Kirsner, 1965). On the other hand, reports by psychiatrists of much smaller series (Engel, 1961; Finch and Hess, 1962; Fullerton *et al.*, 1962; Powles, 1964), sometimes random and unselected, have used such terms as "constantly show severe psychopathology," "uniformly show pathology," "in every case," and "the evidence is overwhelming, incontrovertible."

We are aware that psychiatrists recognize that the disease is one which may be multifactorial in origin, and that some of them regard the psychogenic component as only one factor out of many. Nevertheless, the presence of severe psychopathic disease is so consistently described that the impression is gained from leading psychiatric papers that an emotional component is necessary for the condition to exist. Both sophisticated psychiatric readers and general physicians seem to derive this notion from the psychiatric literature. One of the papers cited above (Fullerton *et al.*, 1962), for example, stated specifically that ulcerative colitis "represented a morbid grief reaction," and other papers circuitously or directly imply that emotional conflicts are a requisite though perhaps only partial cause.

---

* From the Department of Medicine and Department of Psychiatry, Cedars-Sinai Medical Center, Mount Sinai Division, Los Angeles, California.

The concept of "psychosomatic disease" has become a blurred one, and the term is used in three different ways:

(1) The "true" or "strict" psychosomatic diseases are those which *must* have a psychogenic component as part of the cause, or they cannot exist. The usual lists of "true psychosomatic illness" include duodenal ulcer, ulcerative colitis, hypertension, asthma, and neurodermatitis.

(2) Illnesses which appear physical in origin but may be exacerbated, triggered, or hastened by psychogenic factors (one might postulate heart disease in this category) would be regarded as not "truly psychogenic" illnesses but ones influenced by psychophysiological factors. Some physicians feel that the diseases listed under paragraph (1) above may often belong only to this second level, and that no true psychosomatic disease has as yet been verified.

(3) Illnesses whose cause and physical pathology are at present unknown—for example, most headaches, other pains—may be designated as "possibly psychosomatic." No proof exists.

The psychosomatic literature is often vague and confusing in its criteria for validating the psychogenic component, and thus proving it an indispensable element.

We are suggesting seven criteria in an attempt to summarize all indices used by psychiatrists to prove that a psychosomatic disease may exist. The seven criteria are: (1) a characteristic personality disorder of moderately severe to severe degree, or other definite psychiatric diagnosis; (2) a clearly emotional precipitating factor, chronologically related to the illness; (3) general stress, not necessarily symbolically related to the illness but perhaps cumulative; (4) basic emotional problems of long or short duration, with significant background features symbolically related to the illness; (5) alternation of symptoms, or syndrome shift; (6) characteristic patterns of illness in the life history; and (7) efficacy of psychotherapy.

Material

Thirty-four patients with ulcerative colitis were studied. Every known patient with ulcerative colitis admitted to the gastroenterology service between August 1964 and June 1966 was included.

Tables I and II list age group, sex, severity of disease, number of crises, and patients who have been treated psychiatrically.

TABLE I.—*Age Groups and Sex Distributions of 34 Ulcerative Colitis Patients*

Age Group	No. of Patients	Males	Females
10–20	9	2	7
21–30	10	4	6
31–40	8	5	3
41–50	5	5	—
51–60	1	—	1
61–70	1	1	—
Total	34	17	17

TABLE II.—*Other Clinical Data on 34 Ulcerative Colitis Patients*

Severity of disease	Mild	8
	Moderate	12
	Severe	14
No. of crises	1	15
	2	6
	More than 2	13
Response to medical treatment	Able to function normally	19
	Function normally but frequent visits to doctors	6
	Not satisfactory functioning	5
	Not known	4
No of patients with ileostomy		5
No. of patients who received psychiatric treatment		7

Two types of "control" groups were used. The first can be regarded as a control group only in the loosest sense, since it consisted of the general population, divided into normal and abnormal according to arbitrary criteria. The second control group comprised 74 patients. These were the first 74 consecutive patients admitted to the gastroenterology service while the study on ulcerative colitis was in process. No patients with large-intestine disease or regional enteritis were included.

Method

The team members consisted of a psychiatrist, a physician, and two gastroenterologists, one of whom was a Fellow in Psychosomatic Medicine. All four have had a long-standing interest in psychosomatic disease. (The psychiatrist is also a psychoanalyst, and a member of the American Psychoanalytic Association.)

Each patient first had two standard psychiatric interviews, of the free-association type, but eventually including a discussion of sufficient current and past material to yield data for scoring about 65 variables considered salient for personality evaluation. The first interview usually lasted two to three hours, and was conducted by the Fellow. He then reported his findings to the team in detail. The team, including the psychiatrist plus the Fellow and one of the other physicians, then conducted the second interview, which lasted about an hour. Subsequently, the team, including the psychiatrist, almost always saw the patient a second time, and then as often as possible during the stay in hospital. The Fellow continued to see each patient every day, and reported to the team twice a week. The minimum amount of psychiatric time spent with and discussing each patient was five to six hours, and the average 10 to 12 hours. In some cases the time spent was longer, since, for example, three patients remained in the hospital several months.

The psychiatric evaluation took into consideration all the descriptive and dynamic variables which a complete evaluation requires. Among them were symptoms, cognition, ego strengths, defensiveness, acting out, dependence, external problems, attitude toward illness, past history, anxiety, depression, personality type, background, parents, role reversal, siblings, psychosomatic relationships, and many others. All 65 variables were scored in every case, on a 1 to 5 basis, as explained below. As noted above, the scoring for the seven criteria was undertaken cautiously. Broad limits for "normality" were used. The criteria for placing a patient in the "predominantly normal," "normal aggressive," or "normal passive" groups were: (1) no moderately severe or severe personality disorders; (2) average or better ego strengths in the great majority of the 14 categories of ego strengths in the inventory; (3) no severe emotional problems or conflicts which would have required psychotherapy were it not for the physical illness; (4) no diagnosis of psychosis, impulse disorder, or moderate to severe psychoneurosis or depression; (5) evidence of constructive handling of life's anxieties and problems; and (6) no significant patterns of hypochondriasis or incapacity due to unexplained illness of any sort.

The entire process by which the decision about normality was made is too compendious to describe. However, it was thought to be so important that a 200-page handbook has been written, and used, to evaluate all of the 65 variables in the inventory. Criteria for scoring each variable as 1, 2, 3, 4, or 5 were given.

Each patient was diagnosed as "normal" or "abnormal" in each category of the protocol. "Normal" was scored as 3, 4, or 5, "abnormal" as 1 or 2. A normal distribution curve was used (Fig. 1). This curve refers to the general population—that is, an arbitrary assumption has been made that approximately 70% of the general population are "normal" and 30%

definitely "abnormal." We recognize the danger that such a decision may appear uncompromising and high-handed. We tried to take into consideration, for each patient, a comparison not only with the general population but also with the patient's cultural group.

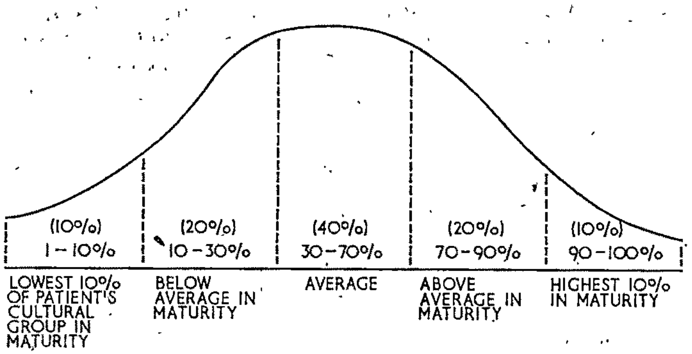


FIG. 1.—Normal distribution curve.

The final designation of normality or abnormality was made by discussion among all four investigators. No patient was placed in the normal group unless all four agreed.

Results in Ulcerative Colitis Patients

Personality Types and Psychiatric Illness.—Twenty-nine of the patients were regarded as essentially "normal" and five as "abnormal." The five abnormal personality types included one or more of the following character disorders to a significant degree: inadequate, infantile, passive, schizoid, depressive, or dependent. There were among the "normal" personalities mild to moderate personality characteristics in this incidence: passive-dependent, 8; passive-aggressive, 5; anxious, 1. Fifteen were classed as predominantly normal—that is, to have no or very mild character disorders. There was one psychopathic personality who was also diagnosed as "schizoid." There were no psychoses, severe psychoneuroses, or severe depressions.

Fig. 2 shows the data given above, and also the following precipitating factors and stresses.

Precipitating Factors and Chronological Relations.—In only 4 out of the 34 cases was a significant precipitating factor thought to have occurred close in time to the first attack of ulcerative colitis. In three cases there was a possible substantial emotional conflict. In 15 cases a moderately eventful emotional factor was present within six months of a *relapse* of the disease but not before its first occurrence. It must be noted that by this time almost every patient had been alerted to the "probable" emotional origin of ulcerative colitis, and was therefore often impressionable to what might otherwise be considered to be normal events. (*a*) No instances of extreme *separation anxiety* were found. No specific symbolic *separation factors* were regarded as pivotal. (*b*) There were no instances where fear of taking *forward steps* in career or marriage seemed crucial. In general, all 29 classed as "normal" were thought to have handled adolescent or adult responsibilities fairly well. There appeared to be no excessive fear that outgoing or aggressive behaviour was dangerous or destructive, and many of them had played football and other sports, had "hit back" when hurt, and had shown an ability to reach out to forward their ambitions when necessary. In general, then, our cases did not show the consistent presence of important precipitating factors.

General Conscious Stress, Not Necessarily Symbolically Related to the Illness, but Perhaps Cumulative.—This factor is difficult to evaluate, since every sensitive human being is aware of stress. We tried to be realistic in evaluating the degree of stress in a patient's life, and regarded as significant any degree of conflict beyond the average. In only five instances was a moderate to severe degree of stress present before the onset of the first attack. There were no other instances of "extreme stress" in the other 33 patients in the approximately five years preceding onset of the illness. In nine cases a moderate to moderately severe degree of stress was present before a *relapse.* There were no cases of *extreme* stress before relapses.

Basic or Nuclear Emotional Problems, of Long or Short Duration, with Significant Background Features, Symbolically or Unconsciously Related to the Illness.—There were 14 cases in which the total background, or dynamic, factors were such as to suggest the "possibility" of nuclear conflicts which might express themselves in somatic illness, if such conversion is thought possible. In no case was it felt that any of the possible nuclear conflicts showed a demonstrable symbolic relation to the ulcerative colitis. There were no instances of severe *role reversal* in childhood, for example. The extent of unusual aggressiveness in mothers and passivity in fathers was about average for the population. The type of "helplessness" described by Engel (1954, 1955, 1958) was considered to be present only as secondary to the illness itself. There was often no helplessness even in seriously ill patients. We found no notable prevalence of problems of bowel training or bowel preoccupation in the family.

Alternation of Symptoms, or Syndrome Shift.—No alternation of either psychiatric or physical symptoms with the ulcerative colitis was encountered in the patients' history or in their hospital course. *Headaches* were a complaint in six cases, but without significant reference to the severity of the ulcerative colitis symptoms. Mild to moderate *depression* was present in four cases; there was no alternation with the symptoms of colitis; if anything, the depression was severe only when the colitis symptoms were most severe.

Characteristic Patterns of Illness in the Life History.—There were a number of cases of mild hypochondriasis, but none was outstanding. Most of the patients had had relative freedom from physical and psychiatric illness.

Efficacy of Psychotherapy.—Of the 34 patients seven had undergone fairly extensive psychiatric treatment lasting from several months to eight years. In three cases it had aided the patients' adjustment to the disease, but in none did it have an appreciable effect on the course of the illness.

Results in Control Group

The patients in this group were as carefully examined and followed as were the patients with ulcerative colitis. The results are not described in detail here, but are compared with those of the ulcerative colitis patients in Fig. 2. In general, the control patients showed as much psychopathology as, or more than, the ulcerative colitis cases.

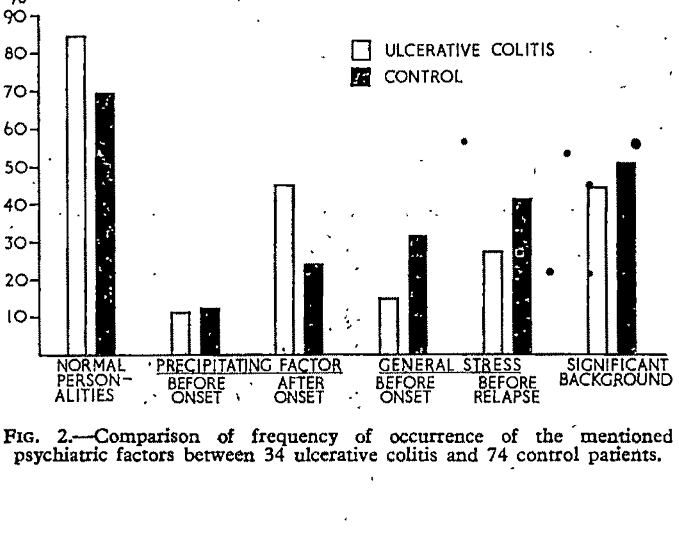


FIG. 2.—Comparison of frequency of occurrence of the mentioned psychiatric factors between 34 ulcerative colitis and 74 control patients.

Discussion

Essentially the 34 ulcerative colitis patients fall within the distribution of "normality" in our society as we have defined it. The question of whether or not an accurate psychiatric appraisal can be made in one or two interviews, plus observation of the patient for a brief period in the hospital, is a valid one. It may be answered in part by the experience of the psychiatrist in another situation where a similar type of evaluation proved successful. This involved eight years of experience in a low-cost psychoanalytic clinic, where patients were screened in one or two interviews by a team of two to four psychiatrists.

Our review of the literature became so lengthy that we have included it in a companion paper. In general, we found that our results were different from those of most psychiatrists but similar to those of the gastroenterologists.

Of approximately 300 reports a year in the world literature we estimate that about 10% are devoted primarily to the psychogenic aspects, another 20 to 30% mention psychiatric factors with uncertainty or partial acceptance, and the remaining 60 to 70% omit psychiatric aspects almost completely. Most of the psychiatric reports are subject to several criticisms. Many of them deal with only one or two patients analysed at great length, little attention being paid to the medical irregularities of the illness. Many of the studies are retrospective (Daniels *et al.*, 1962 ; Fullerton *et al.*, 1962 ; Langford, 1964), or deal with relatively large groups gathered from questionaries and not evaluated personally by the team (Weinstock, 1962). Many studies are of cases selected by other physicians and then referred to psychiatrists (Mohr, 1960 ; Sperling, 1960). In other instances no controls were used, or the criteria for emotional evaluation were not given, or cases were reported only if they had been in treatment (O'Connor *et al.*, 1964).

So far as we can tell, our series of 34 is the first in which a relatively large, consecutive, and unselected group of cases has been studied by the same team, using the same methods, planned in advance. There are two other studies in the literature, of about the same length, which may be comparable (Wittkower, 1938 ; Langford, 1964). Their cases were investigated less intensively than ours.

In our review we encountered the phenomenon of what might be called the innocent acceptance of previous reports (McDermott, 1966). Another observation is that in some of the papers written by teams of gastroenterologists and psychiatrists (or psychologists) there appears to be a split in the reactions of the two groups about the patients (Ehrenpreis *et al.*, 1960).

Summary and Conclusions

Thirty-four consecutive unselected cases of ulcerative colitis have been studied psychiatrically. They appeared to present essentially the usual distribution of emotional problems to be expected in a group of that size. This statement must be modified by several qualifications, particularly the difficulty in assessing deeper problems with our type of interviews. As many as possible of the emotional factors relating to psychosomatic illness mentioned in the psychiatric literature were found not to apply in any significant degree. Our series is small and no definitive conclusions are drawn. We do, however, raise the question whether the disease should be regarded as "psychosomatic."

Our results are presented with concern and caution, since large philosophical questions are raised. These questions concern: (1) the concept of "normality" and our recognition that the assumption of 70% "normality" is open to criticism ; (2) the reliability of diagnostic criteria in psychiatry as compared with other fields of medicine ; (3) the symbolic significance of diarrhoea in ulcerative colitis, taking into consideration the fact that the motility of the bowel in ulcerative colitis patients is different from that found in "functional" colonic disorders (Almy *et al.*, 1949 ; Chaudhary and Truelove, 1961) ; and (4) the central problem of whether primary psychosomatic disease exists, and, if so, how it can be explained.

REFERENCES

Almy, T. P., Kern, F., jun., and Tulin, M. (1949). *Gastroenterology*, **12**, 425.
Chaudhary, N. A., and Truelove, S. C. (1961). Ibid., **40**, 1, 18.
Crohn, B. B., and Yarnis, H. (1951). *N.Y. St. J. Med.*, **51**, 2129.
Daniels, G. E., O'Connor, J. F., Karush, A., Moses, L., Flood, C. A., and Lepore, M. (1962). *Psychosom. Med.*, **24**, 85.
Edwards, F. C., and Truelove, S. C. (1963). *Gut*, **4**, 299.
—— —— (1964). Ibid., **5**, 1.
Ehrenpreis, T., Ericsson, N. O., Billing, L., Lagercrantz, R., and Rudhe, U. (1960). *Acta paediat. (Uppsala)*, **49**, 810.
Engel, G. L. (1954). *Amer. J. Med.*, **16**, 416.
—— (1955). Ibid., **19**, 231.
—— (1958). *Amer. J. dig. Dis.*, **3**, 315.
—— (1961). *Gastroenterology*, **40**, 313.
Finch, S. M., and Hess, J. H. (1962). *Amer. J. Psychiat.*, **118**, 819.
Fullerton, D. T., Kollar, E. J., and Caldwell, A. B. (1962). *J. Amer. med. Ass.*, **181**, 463.
Hijmans, J. C., and Enzer, N. B. (1962). *Pediatrics*, **29**, 389.
Korelitz, B. I., Gribetz, D., and Danziger, I. (1962). *Ann. intern. Med.*, **57**, 582.
Langford, W. S. (1964). *Clin. Proc. Child. Hosp. (Wash.)*, **20**, 89.
McDermott, J. F. (1966). *Psychosomatics*, **7**, 163.
Michener, W. M., Gage, R. P., Sauer, W. G., and Stickler, G. B. (1961). *New Engl. J. Med.*, **265**, 1075.
Mohr, G. J. (1960). *Amer. J. Gastroent.*, **34**, 42.
O'Connor, J. F., Daniels, G., Karush, A., Moses, L., Flood, C., and Stern, L. O. (1964). *Amer. J. Psychiat.*, **120**, 738.
Powles, W. E. (1964). *Canad. Psychiat. Ass. J.*, **9**, 51.
Rhodes, J. B., and Kirsner, J. B. (1965). *Surg. Gynec. Obstet.*, **121**, 1303.
Sperling, M. (1960). *Int. J. Psycho-Anal.*, **41**, 450.
Weinstock, H. I. (1962). *J. psychosom. Res.*, **6**, 243.
Wittkower, E. (1938). *Brit. med. J.*, **2**, 1356.

Pernicious Anaemia among Asians in Singapore

F. J. JAYARATNAM,* M.B., B.S., M.R.A.C.P. ; CHENG SIANG, SEAH,† M.D., M.R.C.P.ED.
J. L. DA COSTA,‡ M.B., B.S., M.R.C.P.ED., M.R.C.P.GLASG.
KHENG-KHOO, TAN,§ M.B., B.S., D.C.P., DIP.PATH., M.C.PATH. ; W. O'BRIEN,|| O.B.E., M.D., F.R.C.P.

Brit. med. J., 1967, 3, 18–20

In an investigation of 40 consecutive cases of megaloblastic anaemia admitted to the Medical Unit, Thomson Road General Hospital, Singapore, from mid-1962 until the end of 1965, six patients (four Chinese and two Indians) were found to fulfil all the criteria for a diagnosis of pernicious anaemia. All six had megaloblastic marrows, histamine-fast (maximal stimulation) achlorhydria, very low serum vitamin-B$_{12}$ levels, and an inability to absorb this vitamin orally, this inability being corrected by the addition of intrinsic factor. These cases are worth reporting, because pernicious anaemia has not hitherto been reported in Singapore and Malaysia, and also because of the paucity of reports of pernicious anaemia in Chinese and Indians.

Methods

The following investigations were carried out:

Haematological investigations included an estimation of the haemoglobin, total red and white cell, platelet, and reticulocyte counts, packed cell volume, mean corpuscular volume, mean corpuscular haemoglobin concentration, and examination of smears of the peripheral blood film and bone marrow. Serum vitamin B$_{12}$ and folic acid assays were carried out in the Hammersmith Postgraduate Medical School, London, through the courtesy of Professor D. L. Mollin. The method of vitamin-B$_{12}$ assay was that of Mollin and Ross (1957), using *Euglena gracilis*, while folic acid assays were carried out by employing *Lactobacillus casei* as a test organism (Waters and Mollin, 1961). An augmented histamine test meal examination was carried out as described by Kay (1953), and the Crosby capsule (Crosby and Kugler, 1957) was used for gastric biopsies.

In order not to miss other causes of vitamin-B$_{12}$ deficiency, the following investigations were also made: a careful dietary survey by a qualified dietitian, examination of stools for ova, cultures of stools, a barium-meal examination with follow-through, a xylose-tolerance test, and an estimation of the total fat content of stools for five consecutive days while on a diet containing 75 g. of fat a day.

When all preliminary investigations were completed, a therapeutic trial with vitamin B$_{12}$ was carried out in each case ; 10 μg. of vitamin B$_{12}$ was administered intramuscularly once weekly, the haematological response being charted by means of daily reticulocyte counts and weekly haemoglobin estimations, total red cell counts, and packed cell volumes.

Finally, the absorption of vitamin B$_{12}$ with and without the simultaneous administration of hog intrinsic factor was estimated by Schilling's (1953) method, using ^{58}Co-labelled vitamin B$_{12}$. In four patients vitamin-B$_{12}$ absorption with and without the simultaneous administration of intrinsic factor was also determined by the modified faecal excretion technique of Mollin *et al.* (1957) and by a scintillation count over the liver one week after the administration of the test dose of vitamin B$_{12}$ (Glass *et al.*, 1954).

Clinical Findings

Of the six patients four were Chinese and two were Tamils, immigrants from the South of India. Four were males and two were females, their ages varying from 50 to 68 years (Table I). Their modes of presentation varied: three complained of pallor and two of progressive breathlessness on exertion ; one complained of fever and diarrhoea for a few days and had not noticed his pallor ; and two complained of paraesthesiae, weakness of both legs, and unsteadiness of gait. Though three patients had excessive melanotic pigmentation over the face, hands, and soles, only one had noticed this pigmentation.

TABLE I.—*History and Clinical Findings*

Case No.	Race	Age	Sex	Complaints	Physical Findings
1	Indian (Tamil)	62	M	Melanotic pigmentation. Paraesthesiae in lower limbs. Sore tongue	Pallor. Glossitis. Melanotic pigmentation. Subacute combined degeneration of cord
2	Chinese	68	F	Pallor. Exertional dyspnoea	Pallor. Loss of vibration sense in lower limbs
3	Indian (Tamil)	54	M	Fever. Diarrhoea	Pallor. Melanotic pigmentation
4	Chinese	68	M	Anorexia. Pallor	Pallor. Melanotic pigmentation
5	,,	64	F	Exertional dyspnoea	Pallor
6	,,	50	M	General weakness. Pallor. Paraesthesiae in lower limbs	Pallor. Glossitis. Subacute combined degeneration of cord

Physical examination revealed the presence of moderately severe pallor of the conjunctivae and mucous membranes in all the patients. Three had an even melanotic pigmentation involving the face, particularly the circumoral area, the dorsum and palms of the hands, and the dorsum and soles of the feet. Glossitis was present in only two patients. Abnormal neurological signs were confined to three: an Indian (Case 1) and a Chinese (Case 6) had the classical signs of subacute combined degeneration of the cord in the lower limbs, and a Chinese (Case 2) had loss of vibration sense in the lower limbs.

Results of Investigations

These results are summarized in Table II. All the patients were anaemic (haemoglobin varied from 4.3 to 6.2 g./100 ml.) with macrocytic well-haemoglobinized red cells, megaloblastic bone marrows, and histamine-fast achlorhydria (Kay, 1953). Serum vitamin-B$_{12}$ levels before treatment were very low, varying from 10 to 40 μμg./ml. The serum folic acid levels, which were estimated simultaneously, were normal, and varied from 4.5 to 25.1 mμg./ml.

Gastric biopsies in five patients revealed severe atrophic gastritis ; the sixth patient refused consent for a biopsy. The results of the Schilling tests confirmed the diagnosis of pernicious anaemia in these patients. Absorption of vitamin B$_{12}$

---

* Senior Registrar, Medical Unit, Thomson Road General Hospital, Singapore.

† Consultant Physician and Head, Medical Unit, Thomson Road General Hospital, Singapore.

‡ Late Senior Registrar, Medical Unit, Thomson Road General Hospital, Singapore. Present address: Department of Medicine, General Hospital, Singapore.

§ Senior Pathologist, General Hospital, Singapore.

|| Colonel, R.A.M.C. Late Consultant Physician, British Military Hospital, Singapore. Present address: The Queen Alexandra Military Hospital, Millbank, London S.W.1.

was negligible in the absence of intrinsic factor, but was enhanced to a normal range by the simultaneous administration of intrinsic factor. None of the patients had any renal dysfunction which would have rendered the Schilling test unreliable. However, in four patients the absorption of ^{58}Co-labelled vitamin B_{12} was also determined by the faecal excretion technique of Mollin *et al.* (1957) and the hepatic uptake method of Glass *et al.* (1954), and the results obtained confirmed those obtained by Schilling's method. Finally no evidence of malabsorption was found in any of the patients. Microscopical examinations and cultures of the stools, fat content of the stools, xylose-absorption tests, and barium studies were all normal.

Response to Vitamin-B_{12} Therapy

After completing investigations, 10 µg. of vitamin B_{12} was administered intramuscularly weekly. All six patients responded with a reticulocytosis, the peak reticulocyte count varying from 14 to 23% and occurring on the fifth to the sixth day after the first dose of vitamin B_{12}. Two patients (Cases 1 and 6) who presented with subacute combined degeneration of the cord improved rapidly with specific therapy. The other four remained well on maintenance vitamin B_{12} therapy.

TABLE II.—*Results of Investigations*

Case No.	Peripheral Blood		Megaloblastic Marrow	Serum Iron (µg./100 ml.)	Serum Folic Acid (mµg./ml.)	Serum B_{12} (µµg./ml.)	Urinary Excretion of Oral ^{58}Co B_{12} without Intrinsic Factor (Schilling's Test)	Urinary Excretion of Oral ^{58}Co B_{12} with Intrinsic Factor (Schilling's Test)	Oral ^{58}Co B_{12} Absorption without Intrinsic Factor (Faecal Excretion Method and Hepatic Uptake)	Oral ^{58}Co B_{12} Absorption with Intrinsic Factor (Faecal Excretion Method and Hepatic Uptake)	Histamine-fast Achlorhydria	Gastric Biopsy	Reticulocyte Peak after Intramuscular Vitamin B_{12}
	Hb (g./100 ml.)	Macrocytosis											
1	4·7	+	+	123	8·7	40	1%	22%	Not done	Not done	+	Not done	16%
2	4·9	+	+	130	10	20	1%	20%	Not done	Not done	+	Severe atrophic gastritis	14%
3	4·7	+	+	143	4·5	15	1·5%	18%	3·5%	64·2%	+	,,	23%
4	4·3	+	+	220	5·1	30	0·25%	21%	4%	53%	+	,,	14%
5	6·2	+	+	150	14·8	40	3%	30%	15%	72%	+	,,	14%
6	6·	+	+	230	25·1	10	1·8%	11%	3%	49%	+	,,	20%

Discussion

Pernicious anaemia of the Addisonian type is probably rare among Asians, though reports of its occurrence can be found in the literature. Friedlander (1934) discussed the racial incidence of the disorder and noted its rarity in Negroes and even in the dark-skinned white races—for example, Italians and Greeks. Das Gupta and Chatterjea (1951) reviewed Indian publications and found a few reports (Taylor and Chitkara, 1940; Chhuttani, 1948); in the same article they described three well-documented cases of megaloblastic erythropoiesis, achlorhydria, and subacute combined degeneration of the cord improving after treatment with crude liver extract. These three patients, they stated, were found "after a careful examination of a very large number of Indian patients with macrocytic anaemia during a period of 15 years." Since then a few more instances have been added in publications from India; Konar (1951) and Misra and Singh (1961) each described one case.

The paucity of reports (in English) of pernicious anaemia in Chinese patients is even more pronounced. Morris (1929) found six cases in the hospital records of Central and North China, but these were not documented, and in his own experience there were no proved cases. Yang and Keefer (1931) reported on two cases of pernicious anaemia in Chinese living in the U.S.A. Both were cases of Minot's and apparently were typical. Schwartz and Rappolt (1945) described three Chinese who suffered from this condition in Chicago; the diagnosis was made on clinical grounds and a satisfactory response to administration of liver extract.

The evidence thus far does indicate that pernicious anaemia of the Addisonian type is uncommon among Asians. This, however, may not be a true evaluation for the future. It remains to be seen whether an increasing awareness of its occurrence and the availability of the more recent tools of investigation—for example, radioactive vitamin B_{12} and its absorption tests—will alter the present concept of its rarity among Asians.

The six cases described in this paper formed part of the group of 40 consecutive cases of megaloblastic anaemia mentioned above. Of the remaining 34 patients, 30 were found to have nutritional folic-acid deficiency, two were vegans suffering from nutritional vitamin-B_{12} deficiency, and two had a haemolytic anaemia complicated by secondary folic-acid deficiency. On the basis of our experience with this group of patients we can conclude that though the majority of Asians with megaloblastic anaemia in Singapore suffer from nutritional folic-acid deficiency, there is yet a distinct minority who suffer from pernicious anaemia and who need specific vitamin-B_{12} therapy. Four of our six pernicious anaemia patients were Chinese, and belonged to a racial group which forms 70% of the total population of the State of Singapore. The remaining two patients were South Indian Tamils belonging to a racial group which forms 6% of the total population of the State. Another noteworthy feature was that three of the six patients—two Indians and one Chinese—had marked melanotic pigmentation of the face, particularly the circumoral area, the palms and dorsum of the hands, and the dorsum and soles of the feet. The pigmentation gradually disappeared approximately four to six weeks after the administration of vitamin B_{12}. Cases of pernicious anaemia are commonly described as presenting with pallor and a lemon-yellow tint of the skin. However, a minority may have excessive melanotic pigmentation. Sir William Osler (1916) mentions that there might be "a brownish tinge of the skin (sometimes associated with leucoderma) deep enough to suggest Addison's disease." Though Baker *et al.* (1963) described similar pigmentation in patients with nutritional vitamin-B_{12} deficiency, it is worth reiterating its occasional presence in patients suffering from pernicious anaemia also.

Summary

During a period of three and a half years six cases of pernicious anaemia in Asians were detected among routine admissions to a local medical unit in Singapore. Four were Chinese and two were Indians, and in all six the criteria for a diagnosis of pernicious anaemia were fulfilled. All made an excellent response to vitamin-B_{12} therapy.

We are grateful to Professor D. L. Mollin for carrying out the vitamin-B_{12} and folic-acid assays. We wish to thank Major G. Vasey, R.A.M.C., and Mr. John Baxter, of the Radioisotope Diagnostic Laboratory, British Military Hospital, Singapore, for carrying out the vitamin-B_{12} absorption tests. We are indebted to

Mr. V. Jayasekeran, of the Haematology Laboratory, Thomson Road General Hospital, Singapore, for carrying out most of the routine haematological investigations on our patients.

REFERENCES

Baker, S. J., Ignatius, M., Johnson, S., and Vaish, S. K. (1963). *Brit. med. J.*, **1**, 1713.
Chhuttani, P. N. (1948). *Indian med. Gaz.*, **83**, 508.
Crosby, W. H., and Kugler, H. W. (1957). *Amer. J. dig. Dis.*, **2**, 236.
Das Gupta, C. R., and Chatterjea, J. B. (1951). *Blood*, **6**, 631.
Friedlander, R. D. (1934). *Amer. J. med. Sci.*, **187**, 634.
Glass, G. B. J., Boyd, L. J., Gellin, G. A., and Stephanson, L. (1954). *Arch. Biochem.*, **51**, 251.
Kay, A. W. (1953). *Brit. med. J.*, **2**, 77.
Konar, N. R. (1951). *Indian med. Gaz.*, **86**, 237.
Misra, S. S., and Singh, B. N. (1961). *J. Indian med. Ass.*, **36**, 105.
Mollin, D. L., Booth, C. C., and Baker, S. J. (1957). *Brit. J. Haemat.*, **3**, 412.
—— and Ross, G. I. M. (1957). *Vitamin B_{12} and Intrinsic Factor*, edited by H. C. Heinrich, p. 413. Stuttgart.
Morris, H. H. (1929). *China med. J.*, **43**, 768.
Osler, William (1916). *The Principles and Practice of Medicine*, 8th ed., p. 736. London.
Schilling, R. F. (1953). *J. Lab. clin. Med.*, **42**, 860.
Schwartz, S. O., and Rappolt, L. A. (1945). *Arch. intern. Med.*, **75**, 404.
Taylor, G. F., and Chitkara, N. L. (1940). *Indian med. Gaz.*, **75**, 16.
Waters, A. H., and Mollin, D. L. (1961). *J. clin. Path.*, **14**, 335.
Yang, C. S., and Keefer, C. S. (1931). *Nat. med. J. China*, **17**, 218.

Effects of Rabies Vaccine in Man

J. C. M. SHARP,* M.B., CH.B., D.P.H.; SHEILA McDONALD,† M.D.

Brit. med. J., 1967, 3, 20–21

Few opportunities are available in the United Kingdom to study the effects of rabies vaccine in man. Immunization is restricted to those exposed to a definite risk of infection as the course is prolonged, is painful, and may be associated with complications such as peripheral neuritis, dorsolumbar myelitis, and acute ascending Landry type myelitis; major paralytic incidents develop in about 1 in 6,000 persons given treatment (Parish and Cannon, 1962).

In 1965 an opportunity arose in Edinburgh to study the effects of the Semple vaccine, a killed virus suspension of rabbit origin, which was used to immunize 20 persons who had been exposed to infection from a rabid leopard cub.

Epidemiological History

On 30 October 1965 a 3-month-old leopard arrived at Edinburgh Zoo by air from Nepal. On arrival the animal was emaciated and attempts to force-feed it failed. The animal's condition deteriorated and four days later it was transferred to the Royal (Dick) Veterinary College in Edinburgh, where it died the next day. Encephalitis was found at post-mortem examination and inclusion bodies in the brain tissue suggested the diagnosis of rabies. The animal's head was sent to the Central Veterinary Laboratory, Weybridge, Surrey, for further examination.

At the zoo it was found that four adults (A, B, C, and D) and three children (E, F, and G) had received bites, scratches, and licks from the leopard (Table I). Three adults (A, B, and C) and one child (E) who had been bitten on their hands were given a single dose of antiserum and with the others were started on a 14-day course of Semple vaccine before rabies was confirmed. One week later a further five persons (H, I, J, K, and L) admitted contact with the leopard and were also given vaccine. Four were employees of British European Airways at Edinburgh Airport, who had allowed the animal to lick their abraded hands. The fifth (L) had fed the animal at the zoo but had later left for other employment.

On 2 December the laboratory at Weybridge confirmed the diagnosis of rabies after mice inoculation tests. It was then decided to vaccinate eight other persons who had been at some risk. Four (M, N, O, and P) were zoo employees who had not previously admitted their contact with the animal. The others were a kennel maid (Q) and three veterinary surgeons (R, S, and T) at the Royal (Dick) Veterinary College, who had had their scratched hands in the animal's mouth. The four contacts (A, B, C, and E) most seriously at risk and one other (D) were given further treatment. Four (A, B, D, and E) were given six additional doses of vaccine, but C, who became unwell, received only four doses. The first four doses were given daily, beginning one week after completion of the original 14-day course; the remaining two booster doses were given to A, B, D, and E at 10-day intervals.

Three other persons had been in contact with the animal, but as they had not been bitten, scratched, or licked, no vaccine was given. In all, 20 persons were vaccinated (12 males and 8 females). Their ages ranged from 8 to 59.

The Vaccine and its Administration

The vaccine, obtained from the Lister Institute of Preventive Medicine, Elstree, Herts, was a sterile preparation of killed rabies virus in 0.5% phenolized saline containing a 4% suspension of the brains of rabbits that had died after inoculation with "fixed" rabies virus. Graded doses were given, varying from 2 to 4 ml. for the adults and from 1.5 to 2.5 ml. for the children. The daily injections were made subcutaneously into alternate sides of the anterior or lateral abdominal wall. All

---

* Senior Medical Officer, Health and Social Services Department, Edinburgh.
† Lecturer in Bacteriology, University of Edinburgh.

TABLE I.—*Prophylactic Treatment Given to Persons At Risk in Relation to the Extent of their Exposure to Infection*

	Group at Greater Risk							Group at Lesser Risk												
Contact:	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T
Degree of exposure to infection	BL	BL	B	S	B	SL	SL	L	L	L	L	S	S	L	L	L	H	H	H	H
Antiserum given ..	+	+	+	–	+	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Volume of vaccine given (ml.) ..	66	66	58	66	42	29	29	All received 41												

B = Bite. L = Lick. S = Scratch. H = Handled mouth.

vaccinated were encouraged to lead a normal life but warned to avoid excessive fatigue and alcohol during vaccination (Parish and Cannon, 1962) and for 10 days after the course.

Reactions

Six persons had their vaccine course interrupted because they felt unwell. Thirteen reported symptoms by the fourth day. A further three complained by the end of the first week and the remaining four reported symptoms by the 13th day (Table II). The earliest symptoms were increasing physical lethargy (17 cases), sleepiness during the day (16), and difficulty in wakening in the morning (10). Only L and T had no such complaints.

TABLE II.—*Day of Onset and Severity of Reactions in Relation to Age of Contacts*

	Group at Greater Risk							Group at Lesser Risk													
Contact:	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T
Age in years ..	41	25	59	22	8	11	11	40	34	32	25	35	15	27	27	22	35	23	44	42
Day of onset of reaction after start of vaccine course ..	2nd	2nd	8th	6th	4th	4th	4th	4th	3rd	3rd	3rd	10th	7th	3rd	2nd	7th	3rd	3rd	10th	13th
Severity of reactions	+ +	+ +	+ + +	+ +	+ +	+	+	+ + +	+ +	+	+	+	+ +	+ +	+ +	+	+	+ +	+ +	+

+ + + = Severe. + + = Moderate. + = Minimal.

Nineteen persons complained of erythema, induration, and tenderness around the injection sites. Pruritus was reported by 15 persons, including J, who had no other local symptoms. Axillary lymphadenopathy was observed in seven persons, two of whom (R and H) also developed inguinal adenitis.

Mental symptoms such as impaired concentration (14 cases) and forgetfulness (11) also occurred during the first week. Six persons reported episodes of confusion of thought, three of whom also experienced amnesia. Difficulty in getting off to sleep or nightmares were reported by six persons, one of whom had frequent nocturnal emissions.

Headaches of varying severity and frequency were experienced by 13 persons. Three persons, including two of the children, had difficulty with visual focusing. Single fainting attacks were reported by two persons during the first week. Episodes of acute nervous tension and frontal headache were experienced by C after the 18th injection. These symptoms, which recurred with diminishing frequency for six weeks, resulted in his being confined to bed at home.

Neurological symptoms developed in six persons. The most seriously affected was H, who developed acute left-sided motor and sensory disturbances, including paresis of the deltoid, triceps, and hemidiaphragm on the seventh day. This resulted in his admission to hospital, where his vaccine course was completed under corticosteroid cover. Temporary paraesthesia of the extremities was reported by I and T. H and I also complained of intention tremor when writing. Intermittent weakness of the quadriceps was reported by N, while R experienced frequent twitching in unrelated muscle groups.

Less common experiences were dryness of the mouth with marked thirst (A, B, and D), anorexia (B), frequency of micturition (A), difficulty in maintaining urinary flow (H), diarrhoea (D and O), low backache (D and N), and alopecia (C).

Discussion

Though many of the reactions experienced by the 20 vaccinated persons were minimal, some of which were reported in retrospect only, two persons (C and H) were seriously ill and absent from work for two and three months respectively. Others suffered severe discomfort.

Several persons aggravated their symptoms by failing to restrict physical exertion. However, the three children and M (aged 15) were not seriously affected despite continuing normal physical activities. It may be that susceptibility to vaccine reactions increases with age. The two persons most seriously affected were aged 59 (C) and 40 (H).

Some of the symptoms described above may have been psychological in origin, but this report does show that a high incidence of reactions can follow immunization with the Semple vaccine. Passive immunization with rabies antiserum may give better protection than active immunization, but to be of value it must be administered within 72 hours of exposure. Until more conclusive evidence is available, active immunization will continue to be part of post-exposure treatment (Hildreth, 1963). Attempts to develop vaccines less hazardous than the Semple preparation have not been entirely successful. The duck embryo vaccine was thought to be devoid of the tissue component responsible for neurological complications, but this has not been substantiated. The high-egg-passage Flury vaccine which is used for pre-exposure immunization is not recommended for post-exposure treatment (Horsfall and Tamm, 1965). Post-infection treatment of guinea-pigs has also shown that the protection given by the duck embryo or the high-egg-passage Flury vaccine is less than that given by the Semple vaccine (Veeraraghavan and Subrahmanyan, 1963).

Though quarantine arrangements are approved by the Department of Agriculture and Fisheries in Scotland, only verbal instructions are given to zoos regarding precautions to be taken with imported animals. Written instructions, however, are issued to all other registered quarantine stations. In view of the incident reported here, it is strongly recommended that similar written instructions be given to and be implemented at zoos. This report emphasizes the importance of restricting human access to animals in quarantine, thus minimizing the number of persons exposed to possible infection and subsequently to the hazards of immunization.

Summary

An outline is given of the reactions experienced by 20 persons who were immunized with Semple rabbit-brain vaccine after exposure to infection from a rabid leopard cub. Two persons were seriously ill and others suffered severe discomfort. The importance of restricting human access to animals in quarantine in order to reduce the number of persons requiring vaccination is emphasized.

We wish to thank Dr. J. L. Gilloran, Medical Officer of Health, City of Edinburgh, for permission to publish this paper; also Dr. A. Jamieson, Mr. J. Norval, veterinary inspector, and the Tropical Diseases and Infectious Diseases Unit of the Edinburgh City Hospital for their valuable assistance.

REFERENCES

Hildreth, E. H. (1963). *Ann. intern. Med.*, 58, 883.
Horsfall, F. L., and Tamm, I. (1965). *Viral and Rickettsial Infections of Man*, 4th ed., p. 828. London.
Parish, H. J., and Cannon, D. A. (1962). *Antisera, Toxoids, Vaccines and Tuberculins in Prophylaxis and Treatment*, 6th ed., p. 221. Edinburgh.
Veeraraghavan, N., and Subrahmanyan, T. P. (1963). *Bull. Wld Hlth Org.*, 29, 323.

P25569

Thymectomy in Subacute Sclerosing Leucoencephalitis

O. KOLÁŘ,* M.D., C.SC.; M. OBRUČNÍK,† M.D., DR.SC.; L. BĚHOUNKOVÁ,‡ M.D., C.SC.
J. MUSIL,§ M.D.; V. PĚNIČKOVÁ,|| M.D.

Brit. med. J., 1967, **3**, 22–24

Subacute sclerosing leucoencephalitis is a well-known inflammatory affection of the central nervous system occurring predominantly during childhood and adolescence. Clinically, the initial phase of mental disturbances is followed by extrapyramidal signs associated with hyperkinesis. The E.E.G. is typical. In the cerebrospinal fluid gamma-G-globulins are raised and qualitatively altered. Subacute sclerosing leucoencephalitis is nearly always fatal, death occurring within a few months or some years after onset of the initial signs.

Sixty-nine patients with subacute sclerosing leucoencephalitis have been observed by us, six of whom are still alive. We think its incidence has increased in Czechoslovakia during the past 20 years, and we have therefore tried to find new methods of treatment. The present report deals with one patient with subacute sclerosing leucoencephalitis who was treated by thymectomy.

Case Report

Towards the end of his 13th year the patient showed a deterioration in his intellectual capacity, and his school results became unsatisfactory. There was a slow development of periodic choreiform hyperkineses of the muscles of the face and hands, particularly of the right one, together with a slight flexion of the trunk. In May 1965 he began to complain of deteriorating vision. He was no longer able to dress himself nor could he use common objects, such as a knife and fork. In September he had his first generalized epileptic fit.

On examination he could control his movements only with difficulty; he was negativistic and repeated sentences and words in a stereotyped way, and joked inappropriately. Hypertonia of the muscles and higher postural reflexes appeared, which were more marked in the right hand and foot, while there was also choreoathetosis, repeated at intervals of four to nine seconds. There was an inconstant Chaddock sign and fanning of the toes, more consistently on the right, but no patellar or ankle clonus was ever elicited. No sensory loss was found. Psychiatric findings suggested a hebephrenic syndrome arising out of leucoencephalitis. The E.E.G. picture showed periodic, high, diffuse delta waves typical of subacute sclerosing leucoencephalitis. In the cerebrospinal fluid there were 3 cells/cu. mm., predominantly lymphocytoid with reticulomonocytic elements; the total proteins were 45 mg./100 ml., the colloidal gold curve was 666543110; immunoelectrophoresis revealed a gamma-C-fraction and an increase in the anodic part of gamma-G-globulins. In the ventricular fluid 58 mg. of total protein per 100 ml. was found and the gold curve was 455543210.

The complement-fixation reaction (Běhounková, Kadlec, and Kolář, 1966), with 0.3 ml. of the patient's C.S.F. and a standardized antigen prepared from the brain of a patient with subacute sclerosing leucoencephalitis, was strongly positive (+ + +). The antigen used in the complement-fixation test was tested on 26 patients with subacute sclerosing leucoencephalitis, from 0.1 to 0.5 ml. of spinal fluid being used. With one exception the complement-fixation reaction in cerebrospinal fluid was positive at various degrees (+ to + + +) in these patients. The antigen as described here is not absolutely specific for subacute sclerosing leucoencephalitis, as it reacted to the spinal fluid of five patients out of a total of 288. These five all had inflammatory diseases of the brain.

The complement-fixation reaction is graded according to the amount of complement used in comparison with a control; + indicates use of 1 to 2 units, + + corresponds to 2 to 3 units, and if more than 3 units of complement are used the reaction is graded + + +. The antigen did not react with the serum of the control subjects, but with the sera of two out of 26 patients with subacute sclerosing leucoencephalitis, and then only with an intensity of +.

Radiological investigation showed enlargement of the spleen, liver, and thymus (Fig. 1). In the serum the acid-phosphatase concentration was 7.7 units/100 ml., and the alkaline-phosphatase concentration 20.0 units/100 ml. The levels of fibrinogen, plasmin, plasmogen, and antiplasmin were within physiological limits. Brain biopsy showed a perivascular mononuclear infiltration, particularly around the veins, and a pericapillar increase in acid mucopolysaccharides (stained with alcian blue). Inclusion bodies were not found. Immunoelectrophoresis of brain tissue extract demonstrated as increase in gamma-G-globulins. By means of the transbronchial diagnostic pneumomediastinum with oxygen (Pěgřim, Ríha, and Simeček, 1957), hyperplasia of the thymus was shown. Attempts

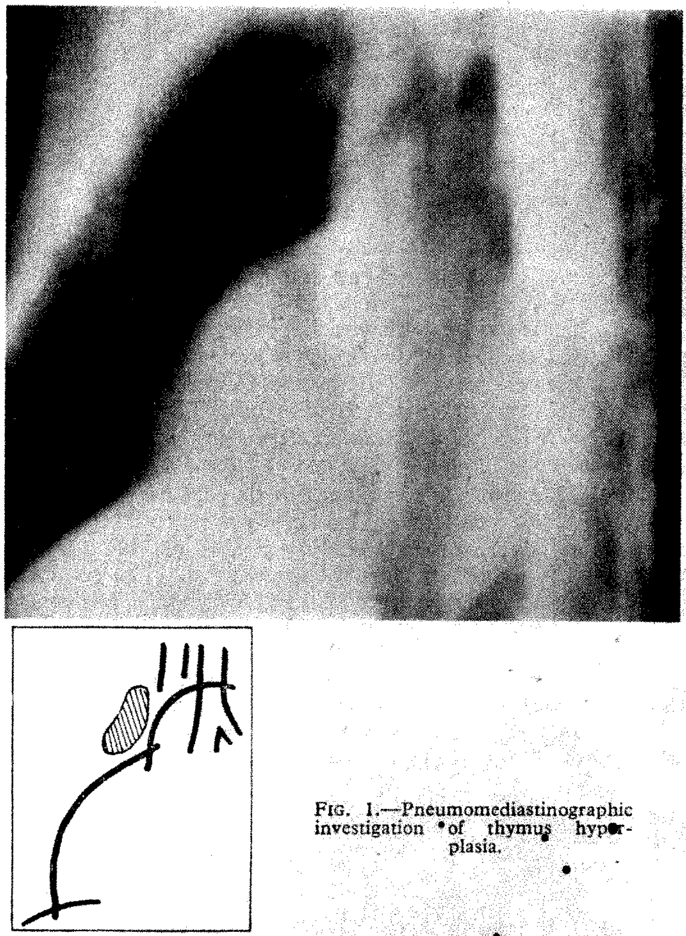


FIG. 1.—Pneumomediastinographic investigation of thymus hyperplasia.

---

* Assistant Professor, Department of Neurology. Present address: Section of Neuropathology, Department of Pathology and Neurology, Indiana University School of Medicine.

† Professor, Director, Department of Histology and Embryology.

‡ Lecturer, Department of Microbiology.

§ Senior Consultant in Chest Diseases.

|| Senior Consultant in Neurology.

From the Clinic of Neurology, Department of Histology and Embryology, Department of Microbiology, and Clinic of Lung Diseases, Palacký University, Olomouc, Czechoslovakia.

at virological isolation from the biopsied brain material and from the C.S.F. were persistently negative.

Despite corticosteroid treatment the symptoms steadily got worse. Because enlargement of the thymus had been found thymectomy was performed in November 1965; the thymus weighed 19.8 g. Histologically the thymus showed disappearance of the border between the cortex and the medulla of the thymus, hyperplasia of the reticular cells (Fig. 2), and numerous enlarged cystically altered Hassall's corpuscles (Fig. 3). Histochemically the substance in Hassall's corpuscles showed a positive reaction after staining by periodic-acid–Schiff. Alcian blue staining reaction was also positive.

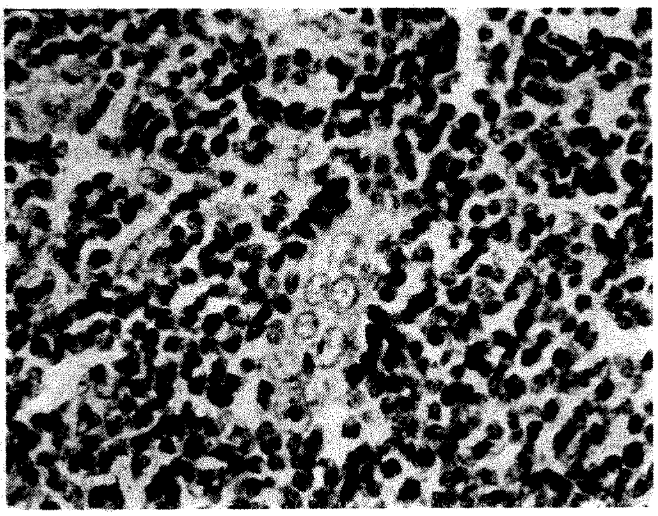


FIG. 2.—Collection of hyperplastic reticular cells. (H. and E. ×126.)

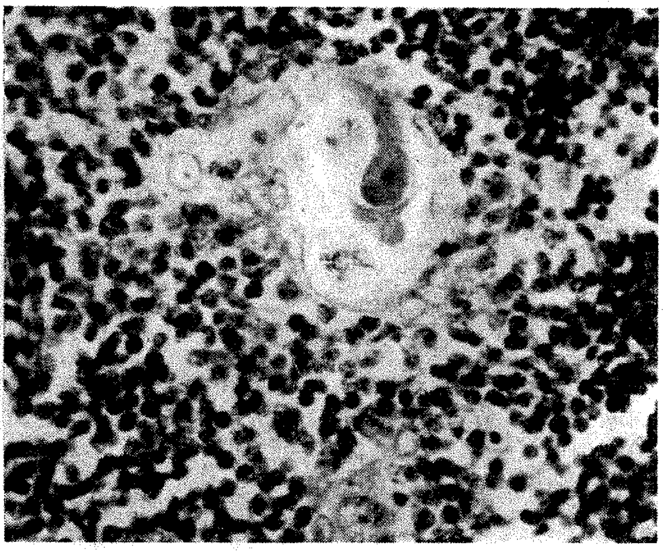
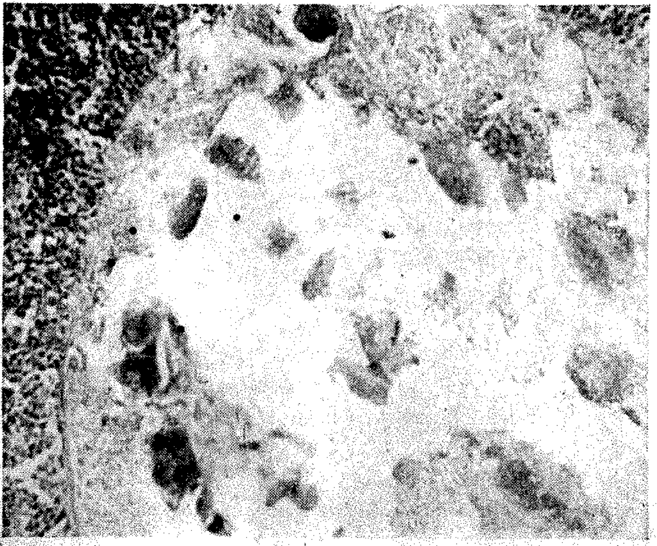


FIG. 3.—Above, Hassall's corpuscle with atypical arrangement of reticular cells. (H. and E. ×106.) Below, Cystically changed Hassall's corpuscle. (H. and E. ×63.)



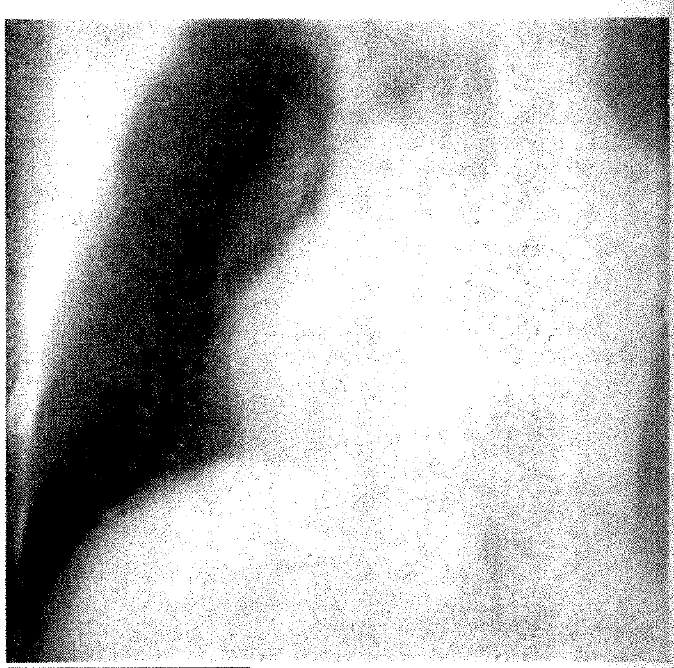
Within two weeks of thymectomy the patient's hebephrenic syndrome had improved, and this improvement has been maintained, together with a diminution in the extrapyramidal signs. After four months a repeat examination of the C.S.F. was carried out. This showed a concentration of 40 mg./100 ml. (with 22% of gamma-globulin) and a gold curve of 223321000. Autoantibodies were still present in the C.S.F. The E.E.G. picture still showed typical pseudorhythmic R-complexes. Agar-gel electrophoresis of the serum showed two abnormal fractions of gamma-G-globulins of slow electrophoretic mobility. The acid-phosphatase concentration fell to 5.9 units/100 ml.

The duration of subacute sclerosing leucoencephalitis from the onset of the first clinical signs of the disease has so far been more than two and a half years.

Control Examination.—Seventeen months after thymectomy the patient is free of seizures and hyperkinesias. Pyramidal signs are lacking. This improvement of the neurologic syndrome is unfortunately not matched by a similar alleviation of the psychologic impairment. The patient is imbecile, though he can take care of his needs, and recognizes relatives and physicians. He is still on prednisone and antiepileptics.

Discussion

Enlargement of the thymus was also seen in three other patients out of nine with subacute sclerosing leucoencephalitis examined by pneumomediastinum produced by the transbronchial route with oxygen. Fig. 4 shows thymic hyperplasia in a 15-year-old boy with subacute sclerosing leucoencephalitis. In the course of prolonged treatment with corticosteroids,



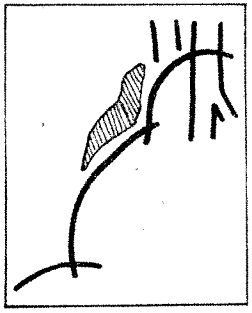


FIG. 4.—Thymus hyperplasia in a 15-year-old boy with subacute sclerosing leucoencephalitis

the clinical picture showed apparent stabilization of the abnormal neurological signs in these patients, and the 15-year-old boy has so far lived for more than four years since the onset of the illness.

Subacute sclerosing leucoencephalitis is accompanied by an increase and a qualitative change in the cerebrospinal fluid gamma-G-globulins (Kolář, 1966a) and by appearance of autoantibodies against the brain-tissue antigen in the C.S.F. of subacute sclerosing leucoencephalitis patients (Běhounková *et al.*, 1966). The symptoms and laboratory manifestations of subacute sclerosing leucoencephalitis may have a remittent course. Other manifestations of the disease include splenomegaly, hepatomegaly, and pathological changes, mainly in the cathodic part of the serum gamma-G-globulins (Kolář, 1966c ; Kolář, Obručník, Fárková, Dvořák, and Musil, 1967).

Examination of biopsy or necropsy brain tissue from patients with subacute sclerosing leucoencephalitis has shown mainly perivenous collection of mononuclear cells which probably contain glycolipoprotein complexes, since these fluoresce when examined by ultraviolet light. Moreover, the presence of abnormal gamma-G-globulins in these specimens from patients with subacute sclerosing leucoencephalitis has also been shown (Kolář, Dencker, Obručník, Černá, and Skatula, 1966).

The perivascular mononuclear infiltrates in the brain, persisting for months to years, the increase and the qualitative changes of gamma-G-globulins in brain tissue, the participation of the extraneural reticuloendothelial system in the development of subacute sclerosing leucoencephalitis, together with the presence of antibodies against a brain-tissue extract used as antigen in the cerebrospinal fluid, all suggest a neuroimmunopathological basis for this disease. This process seems to be not completely analogous with the immunological events leading to experimental allergic encephalomyelitis.

Involvement of the thymus in the development of autoimmune processes, particularly those in which delayed hypersensitivity is concerned, is now generally accepted (Good, Finstad, Peterson, Kellum, and Surtherland, 1965 ; Loghem, 1965). Nevertheless, thymectomy, especially in older subjects, does not prevent the appearance of autoantibodies (Kerr, Duran, Thomas, and Wright, 1965). So far the therapeutic effects of thymectomy in myasthenia gravis have not necessarily been found to be beneficial. Some improvement after thymectomy was described in a patient with systemic lupus erythematosus (Mackay, Goldstein, and McConchie, 1963), but this could be attributed to prednisolone therapy.

The improvement in the neuropsychiatric symptoms in our patient with subacute sclerosing leucoencephalitis is noteworthy, though it can hardly be ascribed to the corticosteroid therapy, which was given in small doses. Nevertheless, a spontaneous remission of the subacute sclerosing leucoencephalitis, which was accompanied also by a fall in the cerebrospinal fluid gamma-G-globulins, cannot be excluded in this case.

Thymic hyperplasia in patients with subacute sclerosing leucoencephalitis suggests that the "central" lymphoid tissue may play a part in the development of the disease. Possibly the thymus influences the development of subacute sclerosing leucoencephalitis unfavourably by supporting the autoimmune histotoxic process, but the right moment to recommend thymectomy in patients with subacute sclerosing leucoencephalitis will be determined only by careful study of further cases of the disease.

Summary

Enlargement of the thymus may be found in some patients in the course of subacute sclerosing leucoencephalitis. We describe a case of subacute sclerosing leucoencephalitis treated by thymectomy in which considerable improvement resulted.

We thank Professor V. Rapant, M.D., Dr.Sc., head of I Clinic of Surgery, Palacký University, Olomouc, for his co-operation.

REFERENCES

Běhounková, L., Kadlec, A., and Kolář, O. (1966). *Acta Univ. Olomuc.*, **40**, 333.

Good, R. A., Finstad, J., Peterson, R. D. A., Kellum, M., and Surtherland, D. E. R. (1965). *Molecular and Cellular Basis of Antibody Formation.* Prague.

Kerr, J. H., Duran, C. G., Thomas, H., and Wright, R. (1965). *J. Neurol. Neurosurg. Psychiat.*, **28**, 429.

Kolář, O. (1966a). *Klin. Wschr.*, **44**, 279.

—— (1966b). *Wien. Z. Nervenheilk.*, Suppl. No. 1, p. 208.

—— (1966c). *Z. Immun. Allergieforsch.*, **131**, 236.

—— Dencker, S. J., Obručník, M., Černá, I., and Skatula, Z. (1966). *Dtsch. Z. Nervenheilk.*, **188**, 222.

—— Obručník, M., Fárková, H., Dvořák, V., and Musil, J. (1967). *J. neurol. Sci.* In press.

Loghem, J. J. van (1965). *Ser. Haematol.*, **9**, 1.

Mackay, I. R., Goldstein, G., and McConchie, I. H. (1963). *Brit. med. J.*, **2**, 792.

Pěgřim, R., Ríha, V., and Simeček, C. (1957). *Rozhl. Tuberk.*, **17**, 100.

Renal Colic

JAMES A. RHIND,* F.R.C.S.

Brit. med. J., 1967, **3**, 24–25

Since 1958 an "immediate" intravenous pyelogram (I.V.P.), taken while the pain is actually present, has been used in the routine investigation of cases of suspected renal colic admitted to the Pontefract General Infirmary. This is a busy hospital, and it has often been necessary for the consultants to delegate to junior staff the responsibility for the initial diagnosis and supervision of the *x*-ray films, which were often taken by junior radiographers during the evening and the night. The details of the *x*-ray examination have varied, but in general we have taken a control film, and films 10 and 30 minutes after the injection of the intravenous medium. Further films were taken until the ureter was outlined ; this may not happen until as long as 24 hours, but the rate of appearance of the nephrogram can be a guide to the timing of the later films.

While a typical attack of renal colic can be recognized confidently, in the atypical attack an immediate intravenous pyelogram showing delayed excretion, a nephrogram, and slow filling of the kidney drainage system compared with the normal side provides impressive confirmation of the obstruction to the kidney and permits the use of strong analgesics. The further management of the case depends on the demonstration of the cause of the obstruction.

Results

The results in the 146 cases in which immediate I.V.P. was carried out were: stones in 84 cases, abnormal *x*-ray films in 27, normal *x*-ray films in 31, and other diseases in 4.

---

* Consultant Surgeon, Pontefract and Castleford Hospital Group, Pontefract, Yorkshire.

Stones

We were impressed by the number of stones revealed by this routine. In some cases several films were required before an apparent phlebolith in the pelvis was indicated as a calculus by coincidence with the termination of a dilated ureter, the diagnosis being confirmed by the disappearance of the shadow after passage of a stone. In other cases a large shadow was quickly proved to be a ureteric calculus. During the same period ureteric calculi were discovered in outpatients referred after an attack of renal colic or with other urinary symptoms, and the management of these cases (called "late I.V.P.") is compared with the cases of immediate I.V.P. in the accompanying Table. A further group of cases we have called "delayed I.V.P." These patients were admitted to hospital with renal colic, but an immediate I.V.P. was not taken because either the pain had ceased or pressure of work in the *x*-ray department prohibited the examination. In these cases the I.V.P. was usually taken about four to seven days after admission.

Fate of Calculi in the Ureter

	Size of *X*-ray Shadow of Stone	I.V.P.					
		Immediate		Delayed		Late	
		Passed	Op.	Passed	Op.	Passed	Op.
Abdominal ureter	3 mm. or less	6	1				1
	4 ,, ,, more	2	6		1		5
	Not known	3	2		1		2
	Total ..	11	9	0	2	0	8
Pelvic ureter	2 mm. ..	32		2		3	
	3–5 mm.	21		4		8	1
	6 mm. or more	2	3	1	1		3
	Not known	6		4		7	3
	Total ..	61	3	11	1	18	7

It is apparent that most of the stones revealed by the immediate I.V.P. are small, are at the lower end of the ureter, and pass spontaneously. Operative intervention was more common when the immediate I.V.P. showed a stone in the abdominal ureter; ureterolithotomy in this area is easy and safe, and failure of the stone to move for a few days was usually taken as an indication for operation. How many of these stones would have passed is uncertain, but the occasional stone which moved slowly was a source of anxiety for weeks. The late I.V.P. series showed a much smaller proportion of small stones and more of these cases were treated by operation; in four cases the kidney was so damaged that nephrectomy was performed. It would seem that the agonizing pain of renal colic requiring admission to hospital implies a healthy kidney and the recent movement of a small stone to the ureter, from which it will probably soon pass. The kidney that has been damaged by the growth of a larger calculus in the ureter can manage only a feeble protest which brings the patient to the outpatient clinic.

Abnormal X-ray Films

In 27 cases the immediate I.V.P. showed some or all of the signs of obstruction—namely, delayed excretion, nephrogram, hydronephrosis, and delayed emptying of the ureter—but without the shadow of a stone being visible. In five of these cases the examination was not continued long enough to demonstrate the whole ureter. In two the patient failed to empty the bladder, and the lower end of the ureter was obscured. In only one case did we find that faecal and gas shadows prevented adequate examination of the ureter. Thus in 19 there was evidence of obstruction without stones. Two of these patients subsequently passed stones. In the stone series occasionally a ureteric shadow disappeared during the course of the examination, with passage of a calculus, but the signs of obstruction persisted for a little time. We are prepared to accept the thesis that in the absence of other disease renal colic is always due to the presence of a stone.

Normal X-ray Films

If the pain of renal colic is due to a rise in pressure in the ureter and kidney pelvis, it is difficult to see how this can occur without radiological abnormality. In 31 cases the immediate I.V.P. was normal though the diagnosis of renal colic seemed well established by a typical history, the presence of red cells on microscopy of the urine, redness and swelling of the ureteric orifice on cystoscopy, or the passage of a calculus. In some cases an overzealous junior resident carried out an immediate I.V.P. even though the patient's pain had disappeared on admission to hospital. In other cases the *x*-ray department could not arrange an I.V.P. for some hours and the pain disappeared during the period of waiting. Strong analgesics are required for the relief of the pain of renal colic and it may be impossible to say whether the disappearance of the pain is due to the analgesic or the actual relief of the obstruction. Each of these explanations probably applied in some cases, but unfortunately our records are not detailed enough to be sure that they explain all the normal I.V.P.s. Nevertheless, we are left with a strong feeling that a normal I.V.P. taken while the patient has continuing pain makes the diagnosis of renal colic unlikely.

Other Diseases

This series included one case of renal tumour with haematuria, pyelonephritis, massive hydronephrosis, and renal arterial embolism.

Discussion

An immediate I.V.P. for all cases of renal colic imposes a heavy strain on an *x*-ray department, but the value of the examination justifies the procedure. A normal I.V.P. requires serious reconsideration of the diagnosis, while the proof of renal obstruction reassures the doctor in continuing analgesia. The demonstration of a small stone (4 mm. or less) at the lower end of the ureter—and this will be the case in a great number—allows the patient to be sent home if the general practitioner will provide suitable analgesia. It is important that these patients are seen in the outpatient clinic until the stone has been passed. A larger stone (4 mm. in the upper ureter or 6 mm. in the pelvic ureter) may need early operation unless it is moving quickly. Perhaps the general adoption of this policy might prevent the tragedy of the late case which requires removal of a destroyed kidney rather than ureterolithotomy.

Summary

Investigation of 146 cases of renal colic by immediate intravenous pyelography showed that most cases are due to calculi, and that the few that need operation can be selected at an early stage.

Asymmetrical Rheumatoid Arthritis after Poliomyelitis[*]

E. N. GLICK,[†] M.B., M.R.C.P., D.PHYS.MED.

Brit. med. J., 1967, 3, 26–29

An outstanding feature of rheumatoid arthritis is its tendency to be bilateral and symmetrical. This is one of the generally accepted diagnostic criteria, as suggested by the American Rheumatism Association (Ropes *et al.*, 1958). Jacqueline (1953) and Thompson and Bywaters (1962) have described unilateral rheumatoid arthritis, sparing the paralysed side, after hemiplegia. The only report of similar sparing of a paralysed limb after lower motor neurone paralysis is that by Kamermann (1966), though Heberden's nodes formation limited to the non-paralysed hand has been described after lower motor neurone paralysis by McEwen (1940), Hench (1940), and Stecher and Karnosh (1947) and after hemiplegia by Coste and Forestier (1935), Forestier (1935), and Winter (1952).

This paper records 12 cases of rheumatoid arthritis developing in patients previously paralysed by poliomyelitis, in whom the paralysed limbs have been spared totally or partially by the arthritic process.

In addition, a woman of 84 was seen who started with low-grade rheumatoid arthritis at the age of 57. She had had a virtually complete right hemiplegia since encephalitis at the age of 2, and the arthritis was almost entirely confined to the normal left arm and leg.

During the course of this investigation several patients with osteoarthritis after poliomyelitis were also seen. On superficial analysis they would appear to fit in with the findings of Glyn *et al.* (1966) that osteoarthritis predominantly affects the non-paralysed limbs.

Case Material

Cases 1 and 2 were seen in clinics at the London Hospital. A search through the hospital records brought to light Cases 3 and 4; the former patient had died and the latter had removed and could not be found. Cases 5 and 6 were contacted through the co-operation of the British Polio Fellowship, who published a notice in their *Bulletin* asking for anyone with arthritis and polio who was willing to volunteer details. These were the only two with rheumatoid arthritis of those who replied, and they were seen by me.

These six cases formed the material for a communication to the Heberden Society in May 1966. Subsequently, several physicians offered details of similar cases known to them; these are Cases 7–12. I did not examine these patients but have seen the *x*-ray pictures. I know of no other cases of rheumatoid arthritis occurring after poliomyelitis. All but one patient (Case 10) were women.

Dr. A. J. Popert (Droitwich) sent details of a patient with atypical polyarthritis who had polio at the age of 5, resulting in a weak left leg and flail left foot. At the age of 24, arthritis began in the left knee, spread rapidly to the right knee, and then became generalized. She is anodular and seronegative. There are marked sacroiliac changes. Now, at the age of 32,

Summary of Salient Features of 12 Cases

Case No.	Age	Extent of Paralysis and Degree (0 – + + +)	Arthritis		Serology	Subcutaneous Nodules	*X*-ray Findings
			Duration (Years)	Distribution			
1	67	Left leg + + +	5	Right hip and knee. Both hands and elbows	–	0	Symmetrical erosions in hands. Gross changes in right hip and knee, but none in left hip and knee
2	46	Right leg + +	12	Generalized but mild. Symmetrical in upper limbs. Left knee definitely the most affected joint with recurrent effusions	+ +	0	Erosions of hands and wrists, worse on right. No gross changes in lower limbs
3	61	Left leg +	22	Generalized and mainly symmetrical, but right knee seems to have been much more troublesome than the left	+	Both elbows	Not available
4	25	Right leg + +	2	Left knee only. (Synovial biopsy typical of R.A.)	–	0	Osteoporosis of left knee
5	38	Trunk +. Left leg + + +. Right hip +	2	Symmetrical involvement of elbows, wrists, and hands. Gross changes in right knee and minor involvement of right ankle	–	0	Erosions of both carpi. Gross destruction of right knee
6	45	Right leg + +. Left leg +	11	Fairly symmetrical bilateral involvement of upper limbs. Both knees troublesome. Left ankle and foot worse than right	–	0	Erosive changes in hands. (No recent bilateral films of lower limbs)
7	76	Right arm + +. Right leg +	20	Virtually unilateral, involving only the unparalysed left arm and leg	+	Left elbow	Erosive changes in left hand and foot
8	53	Left leg + + +	14	Generalized. Symmetrical in upper limbs. Unilateral in lower limbs—right knee and ankle only	–	0	Joint space narrow in both knees, but very much more so on right
9	57	Left arm + + +. Right leg + +	31	Generalized. Changes in right hand and wrist more marked than in left. Left knee and foot more severely affected than on right	+ +	Right elbow and left leg	Erosive changes more marked in right arm and fingers. Gross cartilage loss in left knee but not in right. Subluxation of metatarsophalangeal joints of feet, more marked on left
10	45	Right arm + +	7	Bilateral involvement but less marked in right elbow, wrist, and hand. (Psoriasis of skin but no features typical of psoriatic arthropathy)	Not done	0	Slight erosive changes in right wrist but not in fingers. Marked erosions of left hand and wrist. Erosive changes in feet, more marked on right
11	62	Right arm + + +. Right leg + +	4	Pains in left shoulder, hand, ankle, and foot. Left index metacarpophalangeal joint swollen (i.e., not definite R.A.)	–	0	Joint narrowing limited to metacarpophalangeal joint of left index
12	73	Left shoulder + + +	2	Both hands, wrists, and ankles. Right shoulder	+ +	0	Destructive changes in both wrists and several finger joints

---

[*] I gratefully acknowledge the co-operation of the following physicians: Dr. W. S. Tegner (London), Dr. R. M. Mason (London), and Dr. N. Bennett-Jones (Whiston), who allowed me to examine and report on patients under their care; Dr. Charlotte Feldman (London), Dr. D. N. Golding (Harlow), Dr. H. Jacobs (London), Dr. M. R. Jeffrey (Harrogate), and Dr. M. Wilkinson (Bridge of Earn), who sent details of their patients. I wish to thank the British Polio Fellowship for their co-operation.

[†] Consultant in Physical Medicine, Metropolitan Hospital, London E.8.

there are few changes in the upper limbs or left leg, but the disease is still active in her neck, right knee, and right ankle.

Findings

The Table summarizes the salient features of each case. It can be seen that the greater the severity of the paralysis the more pronounced the sparing of the joints of that limb. Thus very little arthritis was discovered in flail limbs. In fact, it seemed that it was the joints normally controlled by the paralysed muscles that escaped the arthritis (Figs. 1–4). There was good correlation between the clinical and radiological findings.

Subcutaneous nodules were present in three cases (Nos. 3, 7, and 9). In Cases 7 and 9 the nodules occurred on the non-paralysed limbs but not on the opposite, paralysed, side. This was particularly striking in Case 9.

Discussion

These findings illustrate that joints controlled by paralysed muscles show less involvement and destruction when rheumatoid arthritis develops. This is in marked contrast to the denervated neuropathic joint in which hypertrophic and destructive changes are very severe.

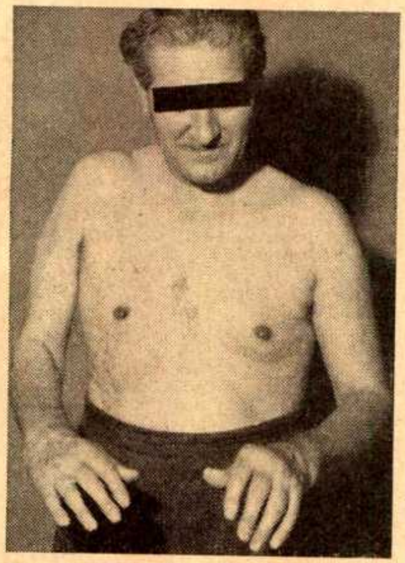


FIG. 1.—Case 10. Wasting of right shoulder muscles. More severe changes in left metacarpophalangeal and proximal interphalangeal joints with ulnar deviation.

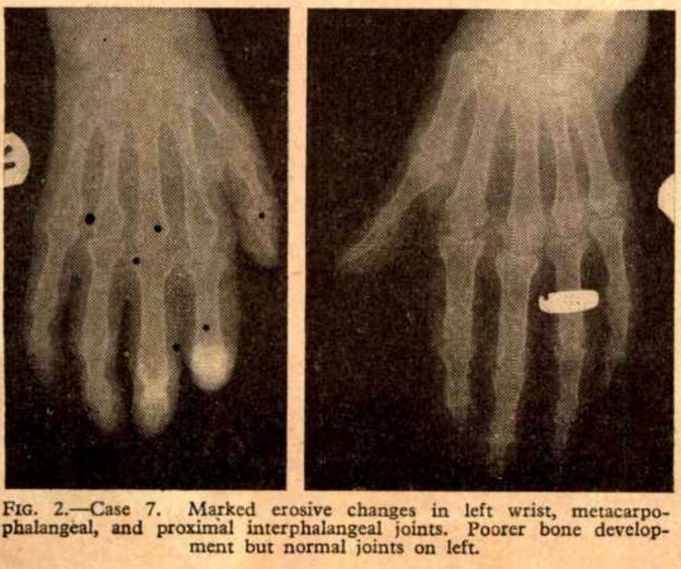


FIG. 2.—Case 7. Marked erosive changes in left wrist, metacarpophalangeal, and proximal interphalangeal joints. Poorer bone development but normal joints on left.

Of particular interest was the observation that subcutaneous nodules did not appear on the paralysed limbs. In their case in which an arteriogram was taken, Thompson and Bywaters (1962) found abnormalities on both sides, but these were more intense on the non-paralysed side. It would be of interest to have had similar investigations in this series, but in those patients under my clinical supervision this procedure did not seem worth while.

In their consideration of the protective effect of the hemiplegia Thompson and Bywaters (1962) came to the conclusion that the most reasonable explanation for the immunity of the paralysed side to the development of rheumatoid arthritis was the relative lack of use and function. They quoted some studies of vascular responses which were the same in the hemiplegic and non-hemiplegic limbs. Kamermann (1966) also regarded the protective effect as being due to comparative disuse rather than to the neurological lesion.

Castillo *et al.* (1965) have shown that the development of cystic erosions in rheumatoid arthritis is related to the degree of physical activity. Van Dam (1964) found no significant difference between the right and left hands in rheumatoid arthritis with regard to cartilage thinning, but erosions and cysts were more frequent on the right. In a review of 300 consecutive rheumatoid patients Glick (1966) attempted a correlation between right- or left-handedness and the severity of the disease in the two wrist joints and found just significantly more severe arthritis in the wrist of the dominant limb. In patients whose work was classified as heavy, and where marked asymmetry might have been expected if

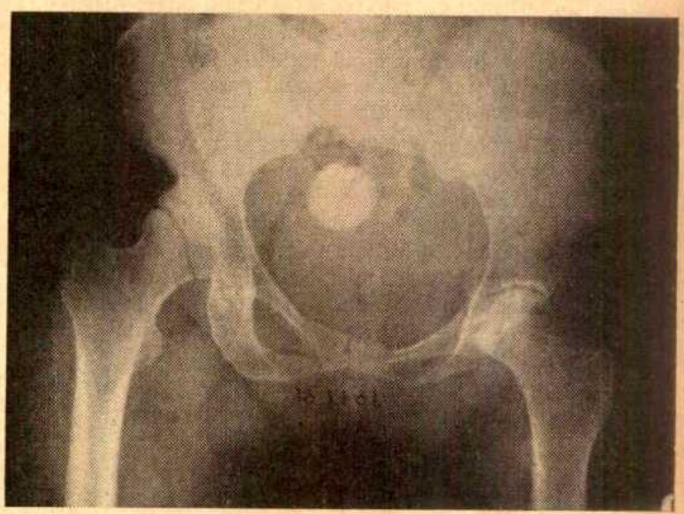


FIG. 3.—Case 1. Gross destruction of right hip joint. Decreased bone development on left, but normal joint.

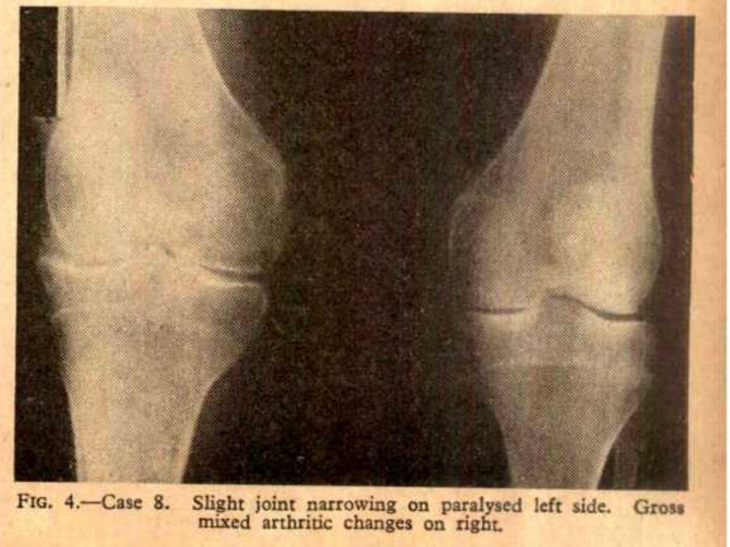


FIG. 4.—Case 8. Slight joint narrowing on paralysed left side. Gross mixed arthritic changes on right.

mechanical factors were dominant, the symmetry of the disease in many of the patients was perhaps more striking than the difference between right and left. Nevertheless, the more active limbs did seem to develop the more severe arthritic changes, and the wrist involvement did appear to begin at an earlier stage. Asymmetry was noted to be more common in seronegative cases. In the present series both seronegative and seropositive cases showed asymmetry.

The experiments of Courtwright and Kuzell (1965) are very pertinent. In 20 out of 31 rats with adjuvant polyarthritis, prior section of one sciatic nerve appeared to delay the onset and diminish the severity of the arthritis in the operated limb. Similar but less marked sparing of joints resulted from prior fracturing of the femur. These two workers attributed their results to an interruption of the normal neurological control of the limb concerned rather than to mechanical factors, but the findings of this series, and their results, also correlate with different experimental work.

Dumonde and Glynn (1962), after rendering rabbits hypersensitive to their own fibrin, were able to produce an arthritis with histology similar to rheumatoid arthritis by intra-articular injection of fibrin.

Norton and Ziff (1966) injected colloidal gold particles into a joint. At synovectomy, about an hour later, these were found deep in the synovial membrane. They consider that the joint space is in continuity with the synovial extracellular space and regard the gold particles as having been mechanically propelled into their deep situation.

If, therefore, fibrin or some other immunizing agent—perhaps a globulin complex present in the joint space—is forced into the synovium by exercise or joint movements, it might be expected that in rheumatoid arthritis joint usage would increase the severity of the disease and paralysis would minimize the inflammatory process.

The actual mechanical factor involved may be the intra-articular pressure. Dixon and Grant (1964) have shown the high pressure reached when a joint is used actively, and though this work has not been repeated on joints of paralysed limbs it is reasonable to assume that, whatever stresses occur in such joints, the intra-articular pressure does not reach the levels produced in normal limbs. It is conceivable that capsular and ligamentous stresses might even be higher in a paralysed weight-bearing limb.

Glyn *et al.* (1966) have studied the incidence of osteoarthritis in people with limb paralysis occurring after poliomyelitis. They found a positive correlation between the severity of degenerative joint changes and the power of the muscles controlling the joint. The flail limbs were relatively free from arthritis. However, it is not clear how much can be inferred between the two different types of arthritis.

What does seem clear is that after muscle paralysis the associated joints show less destructive changes of both degenerative and inflammatory arthritis than joints in the non-paralysed limbs.

The problem arises of how far these findings should influence decisions regarding rest and exercise in the management of arthritis.

Summary

Details are given of 12 cases of rheumatoid arthritis occurring in people previously paralysed by poliomyelitis. Joints controlled by the paralysed muscles were less affected than those in the contralateral non-paralysed limb. This sparing effect was most marked in completely flail limbs.

Subcutaneous nodules showed similar asymmetrical distribution in two patients.

It is suggested that decreased intra-articular pressure might be an important factor in this apparently mechanical effect.

References

Castillo, B. A., El Sallab, R. A., and Scott, J. T. (1965). *Ann. rheum. Dis.*, **24**, 522.
Coste, F., and Forestier, J. (1935). *Bull. Soc. méd. Hôp. Paris*, **51**, 772.
Courtwright, L. J., and Kuzell, W. C. (1965). *Ann. rheum. Dis.*, **24**, 360.
Dam, G. van (1964). In "Radiological Aspects of Rheumatoid Arthritis," *Excerpta med. Fdn. int. Congr. Ser.*, No. 61, p. 63. Amsterdam.
Dixon, A. St. J., and Grant, C. (1964). *Lancet*, **1**, 742.
Dumonde, D. C., and Glynn, L. E. (1962). *Brit. J. exp. Path.*, **43**, 373.
Forestier, J. (1935). *Rev. neurol.*, **63**, 442.
Glick, E. N. (1966). *Proc. roy. Soc. Med.*, **59**, 555.
Glyn, J. H., Sutherland, I., Walker, G. F., and Young, A. C. (1966). *Brit. med. J.*, **2**, 739.
Hench, P. S. (1940). *J. Amer. med. Ass.*, **115**, 2025.
Jacqueline, F. (1953). *Rev. Rhum.*, **20**, 323.
Kamermann, J. S. (1966). *Ann. rheum. Dis.*, **25**, 361.
McEwen, C. (1940). *J. Amer. med. Ass.*, **115**, 2024.
Norton, W. L., and Ziff, M. (1966). *Arthr. and Rheum.*, **9**, 589.
Ropes, M. W., Bennett, G. A., Cobb, S., Jacox, R., and Jessar, R. A. (1958). *Bull. rheum. Dis.*, **9**, 175.
Stecher, R. M., and Karnosh, L. J. (1947). *Amer. J. med. Sci.*, **213**, 181.
Thompson, M., and Bywaters, E. G. L. (1962). *Ann. rheum. Dis.*, **21**, 370.
Winter, S. (1952). *N.Y. St. J. Med.*, **52**, 349.

Adverse Reactions from the Illicit Use of Lysergide

THOMAS H. BEWLEY,* M.D., F.R.C.P.I., D.P.M.

Brit. med. J., 1967, 3, 28–30

Lysergide (lysergic acid diethylamide ; L.S.D.) is a drug with marked effects on the mind. Illegal use of the drug in the United States has led to reports of untoward and adverse reactions (Cohen and Ditman, 1962, 1963 ; Ludwig and Levine, 1965 ; Frosch *et al.*, 1965). Severe abnormal reactions have also occurred in the United Kingdom when the drug has been obtained illicitly and taken without medical supervision, and some are reported here.

Case 1

A youth aged 19 was educated at a grammar school but failed G.C.E., and after leaving school at the age of 16 never worked. He then lived a vagrant existence and at different times took marijuana, oral amphetamines, intravenous heroin and cocaine, and methylamphetamine hydrochloride (Methedrine) intramuscularly. He had always obtained drugs illegally. When he first took L.S.D. he had a short-lived paranoid psychotic reaction.

"I had a bad trip the first time I took it. I thought I was in a different place to where I was. I was very frightened ; I thought people were coming after me. All these red people were coming after me for some reason. I was very scared and ran out of the room. I thought they would get me. I did not know if they were the devil's people or something. I was running about the streets scared. I don't know what happened for about four hours ; I was very frightened and running about the streets."

---

* Consultant Psychiatrist, Tooting Bec Hospital, London S.W.17.

Despite the unpleasantness of this first experience he continued to experiment with L.S.D., but did not have a similar reaction on subsequent occasions. "I never had a bad trip since then. I use it to expand my mind. I'm not against it now. I get a really wonderful experience. I use it for relaxation with music. I underestimated it the first time I took it. It took me unawares."

His current problem is physical dependence on heroin.

Case 2

A man aged 24 had a normal upbringing and education at a secondary modern school until he was 15. Then he had periods in an approved school, Borstal, and two years' imprisonment for receiving. He had taken dexamphetamine since the age of 16 and also marijuana, heroin, and cocaine. He had a cocaine psychosis with hallucinations on one occasion. He took L.S.D. once and found that he became acutely depressed and suicidal. "I felt like jumping into a pond. I had a crazy urge to." He found the experience sufficiently frightening and unpleasant to have no desire to repeat it. He had a history of depressive reactions and he slashed his wrists on one occasion in hospital, after attending the funeral of his best friend, who had committed suicide.

Case 3

A man aged 21 had a normal childhood and had done well at grammar school until he was 17, when he left after taking O levels. He then did hotel and catering training for two years and obtained a job as assistant manager of an off-licence. He was described as quiet and studious up to the age of 19. He had his own car and saved money. He started taking amphetamines at 18, and this was succeeded by experimentation with all forms of drugs. He took heroin, cannabis, and "sleeping tablets" irregularly. He tried L.S.D. once and found the effects pleasant at the time. "At first it was a vague dream. I was semi-floating. There's nothing you can't do. You throw your problems aside, think you are God." However, he had severe panic attacks later. "The after-effects were too terrifying. I would not want to repeat it. I was violently sick for a few days, my head was spinning, and I could hardly stand. I was in a deep depression and thought someone was watching me all the time. I would wake in a cold sweat, find myself lying in bed paralysed. Once you move your arm you are all right, you sit up after 20 minutes. It's frightening, you wake up and don't know if you are awake or not." He had no desire to take L.S.D. again. He had become heavily dependent on alcohol and was drinking a bottle of brandy a day, mixing it with Pernod. He had been incapable of working for two months and had spent all his savings and sold his car.

Case 4

A man aged 21 had had a very disturbed childhood and upbringing. His parents were divorced and remarried, and he was brought up by various relatives and in foster-homes. He had nocturnal enuresis until the age of 15. He was in the Merchant Navy for three years (aged 16–19). After this he had not worked. He lived with a prostitute, sold hashish, and touted for blue films in the West End of London. He was currently on probation for living on immoral earnings. He attended a V.D. clinic regularly, having had gonorrhoea several times according to his own account. He had taken amphetamines and marijuana since the age of 18, and had once jumped in front of a taxi while under the influence of amphetamines. He started taking L.S.D. and took it three times in a week. He found it produced pleasant reactions at first but later unpleasant ones, and he stopped taking it.

"It was great when it first happened, but after a while I began to get the horrors. It frightened me and I started to fight under it. Once when on L.S.D. I used violence. Two of us had taken L.S.D., me and this girl. There were two other couples, one couple I knew well, the other I did not. I thought this bloke was trying to get off with this girl I was taking a trip with. We were talking, laughing, drinking. In the hall there were me and this girl and the other fellow. He said, 'Go away please.' I went mad and started to fight him, but I cooled down quickly. I said, 'Go away for a minute.' I was frightened of him, so afterwards I apologized. I did not know how to apologize enough."

After this he stopped taking L.S.D., but continued to smoke marijuana. He found that although he had never had any unpleasant effects from smoking cannabis before he used L.S.D., when he smoked it again, after his experimentation, he began to get recurrent short-lived psychoses. "I used to smoke hashish till I could not think. I'd smoke myself silly with some friends. If I smoked with them I'd smoke an awful lot. Now, more recently, I've realized it was since taking L.S.D. I was getting more horrors. I keep getting double meanings. I was really terrified the night before last, I was just smoking hash at the time, I could see the effects like L.S.D. I thought they were wanting to kill me. I was sitting looking at myself in a mirror. They were talking about vans. I thought it was all directed at me, it was driving me nuts. I thought people were going to kill me. It was worse than after I had the L.S.D."

He found these reactions sufficiently alarming to wish to try to give up all use of drugs.

Case 5

A man aged 20 died from severe laceration of the brain associated with a fracture of the left parietal region caused by falling from a fourth-storey window on to a brick wall. This appeared to have followed his first experimentation with L.S.D.

He was a musician living in furnished rooms and had no past history of mental illness or instability. He had previously smoked marijuana and belonged to a group of people who used drugs and were interested in them. He was anxious to try the effects of L.S.D., and arranged to do this with two friends, one of whom had taken the drug before and who possessed some. On the day that this was arranged both these friends apparently changed their minds and did not go round to his room. That evening he was seen to climb out of the window of his attic room, having first broken the glass; he stumbled, slid down the roof, and fell to his death. The door of his room was found to be locked and barricaded on the inside with a chair against the door. The room was in complete disorder, with clothing, bedding, and furniture strewn all over the room. No one else was present. The gas-stove and the electric-light fittings were broken. All the windows in the room were broken, including the one he had got out of.

At necropsy it was not possible to confirm the presence of L.S.D., though it appears likely that it had been taken. There was no evidence at necropsy that he had taken any other drugs, such as amphetamines.

Case 6

A man aged 20 died from multiple injuries (fractured skull, fractured pelvis, fractured right tibia and fibula) caused by jumping or falling 60–70 ft. (18–21 m.) from a church roof. He was a bricklayer's labourer and had no history of serious illness or accident, nor was there any history that he had previously taken L.S.D. On the Saturday night before his death he apparently went to a club in Soho with a girl, who could not subsequently be traced. On Sunday morning at 10 o'clock he was found lying naked in the forecourt of a church in Highgate. His clothes had been left in a neat pile on the roof. Necropsy showed that he had died from multiple severe injuries, and analysis of specimens of blood (peripheral), liver blood, heart blood, bile, and stomach contents gave the following results (Dr. Ann E. Robinson): "(1) Routine screening tests for alcohol and 5,5-disubstituted barbituric acid derivatives in the peripheral blood sample were negative. The stomach contents also gave negative results from these substances. (2) The specimens of bile (6 ml.) and the remaining peripheral blood (11 ml.) were examined for the presence of lysergic acid diethylamide (L.S.D. 25). A substance was detected in both of these samples which had properties consistent with those of L.S.D. 25, though unequivocal proof of identity of the recovered substance was lacking."

It seems likely that this man had taken L.S.D. at some stage after his visit to the club and had then climbed to the top of a church, taken all his clothes off, put them in a neat pile, and jumped or fell to his death. It is possible that he had a psychotic reaction or he may have had such changes in mood (euphoria or elation) that he believed he could float safely down.

Discussion

There has been an increase recently in the use of L.S.D. in this country on a casual basis and not under medical supervision. Use in this way as a "mind-expanding" drug has been extensively discussed in the press and on television, and has been advocated in non-medical journals. After a similar interest in the non-medical uses of the drug and extensive self-medication by fringe groups in New York there was a sudden upsurge of admissions to Bellevue Hospital with acute reactions from its use (Frosch *et al*., 1965). These fell into three groups: (1) acute panic reactions; (2) recurrence of symptoms while abstaining from the drug, which was more likely to occur after multiple ingestion; and (3) prolonged psychosis.

Cases 1, 2, and 5 reported here appeared to be acute panic reactions, and Cases 3 and 4 a recurrence of symptoms in a period of abstinence. Case 4 also showed signs of a prolonged psychosis. Case 6 may have been due to disordered judgement or a psychotic reaction. Prolonged adverse reactions, including chronic hallucinatory states, also occur (Rosenthal, 1964). Owing to the fashion of using sugar cubes as a vehicle for black market L.S.D. it can also be taken accidentally—for example, by children—and three such cases have been reported. One of these sustained a dissociative state, accompanied by anxiety and visual illusions, that lasted for several weeks (Cohen, 1966). Cases 5 and 6 show the need to look for L.S.D. and amphetamines at necropsy in deaths of this type, lest some be wrongly attributed to suicide.

Despite the statements of the protagonists of the use of this drug that it is safe, L.S.D. can be dangerous when taken casually—for example, when not taken by selected patients under strict medical supervision and with the use of proper safeguards. The incidence of adverse effects associated with controlled use of the drug by physicians suggested that in medical hands it was an exceptionally safe drug (Levine and Ludwig, 1964).

Summary

Recently there has been an increase in the use of lysergide (lysergic acid diethylamide; L.S.D.) obtained illicitly. Adverse reactions are not uncommon, and six (two fatal) cases are reported.

I am grateful to Professor F. E. Camps, Dr. A. Robinson, and Mr. F. F. Haddock for help with information about some of these cases.

REFERENCES

Cohen, S. (1966). *Psychosomatics*, **7**, 182.
—— and Ditman, K. S. (1962). *J. Amer. med. Ass.*, **181**, 161.
—— —— (1963). *Arch. gen. Psychiat.*, **8**, 475.
Frosch, W. A., Robbins, E. S., and Stern, M. (1965). *New Engl. J. Med.*, **273**, 1235.
Levine, J., and Ludwig, A. M. (1964). *Comprehens. Psychiat.*, **5**, 314.
Ludwig, A. M., and Levine, J. (1965). *J. Amer. med. Ass.*, **191**, 92.
Rosenthal, S. H. (1964). *Amer. J. Psychiat.*, **121**, 238.

Preliminary Communications

Trephine Biopsy for Diffuse Lung Lesions

Brit. med. J., 1967, **3**, 30–32

Drill biopsy of various tissues by means of a dental drill and cylindrical rotating cutting needle was described by Kirschner (1935). The technique was modified by Christiansen (1940) and further results with this method were reported by Ellis (1947). A high-speed pneumatic drill was used by Deeley (1960). Within the thorax, these authors confined themselves to the diagnosis of peripheral tumours adherent or adjacent to the chest wall, and, despite the theoretical advantages of the procedure over other methods of lung biopsy, interest in it has lapsed because of this limited application. It is our purpose to show how high-speed drill biopsy can be extended to the diagnosis of diffuse pulmonary conditions.

The extremely fast cutting edge provided by the air-drill was found to be effective in obtaining specimens from the lung at necropsy, but the small trephine described by Deeley failed to provide adequate specimens of diffuse lesions from inflated lung. To overcome this difficulty a large trephine with special features was designed by one of us (S. J. S.) and proved successful experimentally and in practice.

INDICATIONS

Indications include diffuse and localized lesions of the lung or pleura where a definitive diagnosis is required for the purpose of treatment, prognosis, or a claim for industrial compensation.

There are no specific contraindications other than bullae, cysts, or aneurysms, but it is wise to avoid patients with a bleeding diathesis or insufficient respiratory reserve to risk a pneumothorax. Some upper-lobe lesions may prove inaccessible and those adjacent to the mediastinum are best avoided.

METHOD

The apparatus consists of a small Desoutter pneumatic drill easily held in the hand and driven by compressed air from a cylinder fitted with a reducing valve. A speed of up to 15,000 revolutions per minute at a pressure of 100 lb./sq. in. (7 kg./sq. cm.) is controlled by a trigger. The spindle of the drill is connected by a Luer fitting to a hollow trephine 7.5 cm. long and 3 mm. in external and 2.1 mm. in internal diameter, with a right-angled smooth cutting edge. The trephine is rifled internally for 5 mm. behind the cutting edge to guide the specimen into its lumen, and fitted with a sharp-pointed keyed stylet projecting 2.5 mm. beyond the end (Fig. 1).

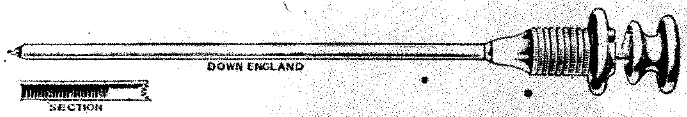


FIG. 1.—Lung biopsy trephine for use with high-speed air-drill. Length 7.5 cm., external diameter 3 mm., internal diameter 2.1 mm. Internal rifling for 5 mm. at end. Sharp-pointed keyed stylet fitted.

The first step is to choose a suitable site with chest radiographs and markers. If the lesion is diffuse and bilateral the most convenient position is usually the eighth right intercostal space posteriorly with the patient sitting across the bed and leaning forward, but an axillary or anterior approach may be used with the patient lying down. Premedication is not usually necessary, but it is essential to demonstrate the apparatus to familiarize the patient with the whistling noise produced by the air-drill. At the same time the patient should be instructed not to move, cough, or breathe deeply during the drilling process, but breath-holding is not necessary.

The trephine, previously sterilized, is flushed with 3.8% sodium citrate, and about 5 ml. of the citrate is left in a 20-ml. syringe. After infiltration with local anaesthetic a small skin incision is made with a scalpel. The trephine, with the pointed stylet in position, is introduced and, unless a specimen of pleura is required, the point is gently pushed through the parietal pleura. The stylet is then removed and the drill is attached to the trephine. The patient is told to keep still. The trigger is pressed and the trephine, revolving at maximum speed, is steadily pushed into the lung almost as far as the hub ; this should take about three seconds. The drill is then detached from the trephine and replaced by the 20-ml. syringe, which is used to provide suction to retain the specimen while the trephine is withdrawn. The specimen is ejected into filter paper in a funnel and the liquid allowed to run through. Finally it is transferred into fixative.

RESULTS

The results of the first 100 consecutive biopsies, performed from 1962 to 1966, are shown in Table I. A successful biopsy is defined as one where adequate material for histological examination was obtained. The first 21 biopsies, mostly of pleura, were performed with the small trephine, and though it proved successful for thickened pleura or solid lung lesions all the attempts to obtain specimens from lung with diffuse lesions failed.

TABLE I.—100 *Biopsies of the Lung and Pleura with a High-speed Air-drill*

	Total	Successful	Complications	
			Pneumothorax	Haemoptysis
		Small Trephine		
Lung	7	3	1	—
Pleura	14	12	—	—
		Large Trephine		
Transitional stage while undergoing development:				
Lung	17	9	6	1
Pleura	12	10	1	1
Final stage with rifling and pointed sytlet added:				
Lung	38	33 (87%)	7	6
Pleura	12	10	—	—
Totals	100	77	15	8

Subsequent biopsies were performed with the large trephine. There was a transitional stage during which modifications to the trephine were reflected in improving results in lung biopsy. Finally, when rifled and fitted with the pointed stylet, 33 out of 38 (87%) lung biopsies were successful at the first attempt, the majority being diffuse lung conditions (Table II).

TABLE II.—*Histological Findings in* 38 *Lung Biopsies With the Large Trephine*

Histological Diagnosis of Biopsy Specimen		
Number attempted		38
Number successful		33
Organizing pneumonia	3	
Lung abscess	1	
Tuberculosis	3	
Sarcoidosis	5	
Asbestosis	2	
Berylliosis	2	
Diffuse interstitial pulmonary fibrosis	2	
Non-specific pulmonary fibrosis	2	
Emphysema	1	
Alveolar proteinosis	1	
Eosinophilic vasculitis	1	
Adenocarcinoma	3	
Squamous carcinoma	1	
Undifferentiated carcinoma	3	
Normal lung	3	

Complications.—Complications were not serious. Routine post-biopsy radiographs showed that pneumothorax occurred in 15% of cases, but it was usually shallow and asymptomatic (Table I). In most instances the lung re-expanded uneventfully, but one patient required aspiration of air to relieve dyspnoea and another two with surgical emphysema needed an intercostal tube. Only one of the eight haemoptyses consisted of more than transient staining. It amounted to 50 ml. and ceased within half an hour. None of the patients complained of significant pain. There was no instance of air embolism or of invasion of the biopsy track by infection or neoplasm.

CASE REPORTS

Case 1.—A 59-year-old male electroplater complained of three months' increasing dyspnoea on exertion. He had a few crepitations at both bases. A chest radiograph (Fig. 2) showed bilateral diffuse nodular shadowing confluent in the hilar regions. Sputum examination for acid-fast bacilli and neoplastic cells was negative and bronchoscopy showed no abnormality. Drill biopsy of the right lower lobe showed distension of the alveolar spaces with granular periodic-acid/Schiff-positive material, the picture being that of alveolar proteinosis (Fig. 3). He improved clinically and radiologically without treatment.

Case 2.—A 45-year-old man who worked with beryllium-copper alloys complained of two years' increasing dyspnoea on exertion, with cough and scanty sputum. There were no abnormal physical

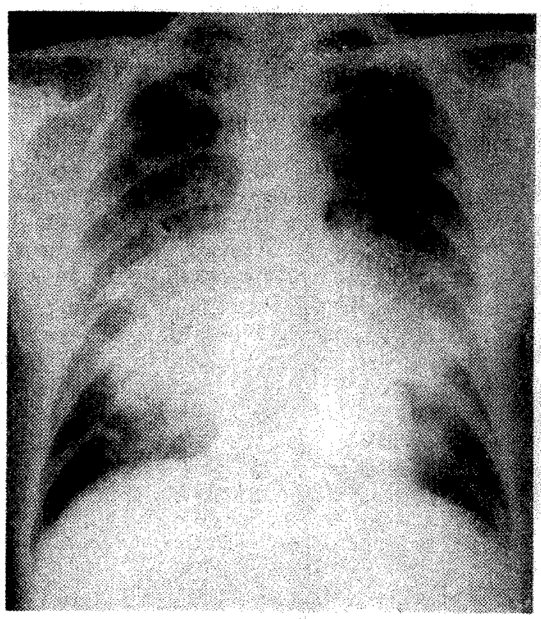


FIG. 2.—Case 1. Bilateral diffuse nodular shadowing confluent in the hilar regions.

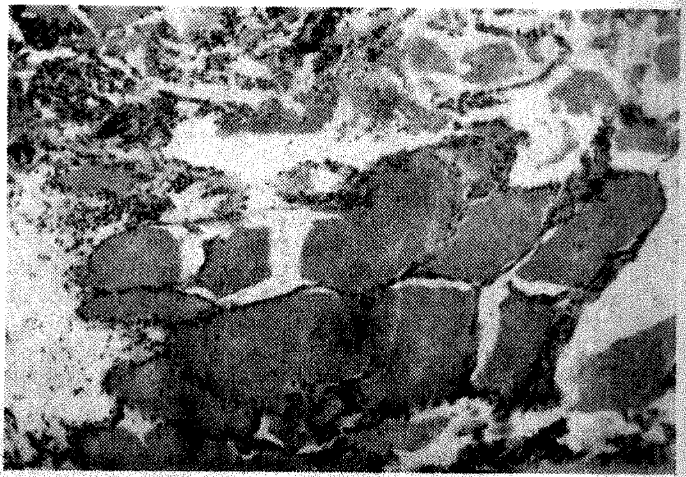


FIG. 3.—Case 1. Alveolar proteinosis. (H. and E. ×90.)

signs. Chest radiography showed bilateral granular and nodular shadowing. A patch test for berylliosis was negative. Drill biopsy of the right lower lobe showed miliary granulomata, the outstanding feature of which was the presence of numerous conchoid bodies. The appearances were those of chronic berylliosis. A shallow right pneumothorax resulted from the drill biopsy but absorbed uneventfully. Treatment was started with corticosteroids, but without appreciable clinical or radiological improvement. He was awarded 20% industrial compensation.

DISCUSSION

The first systematic approach to percutaneous lung biopsy was the needle aspiration method described by Martin and Ellis (1930). This technique produces a small specimen and has chiefly been used by investigators such as Lauby, Burnett, Rosemond, and Tyson (1965) for the differential diagnosis of pulmonary tumours.

In order to obtain a larger specimen for the study of diffuse lesions interest has recently centred on special needles incorporating a cutting mechanism. Manfredi, Rosenbaum, and Behnke (1963) published the results of 18 lung biopsies and advocated the use of a Franklin–Silverman needle. Smith (1964a) reviewed the literature and reported a series of 61 patients who had needle biopsy of the lung—39 with a Vim–Silverman and 22 with a Jack needle. In an addendum further experience with the Jack needle was mentioned, but he subsequently recorded one fatal pulmonary haemorrhage and recommended that the procedure should be performed in an operating theatre with a thoracic surgeon available (1964b). Krumholz and Weg (1966) obtained lung tissue in 56 out of 65 (86%) biopsies with a Franklin–Silverman needle on patients with diffuse lung lesions, chiefly sarcoidosis or interstitial fibrosis. Complications included 12 pneumothoraces, six of which required intubation, and two haemoptyses of 40–50 ml. Another patient with pulmonary hypertension, not included in the series, had a 750-ml. haemoptysis. A disadvantage of their method is that the patient has to hold his breath for 15–30 seconds.

Apart from the work of these authors, most of the reported techniques of needle biopsy have been directed towards a diagnosis of peripheral thoracic tumours, and biopsy of diffuse lung lesions has usually been performed by open thoracotomy according to the method described by Andrews and Klassen (1957). Although this ensures an adequate specimen of lung for histological examination, it entails a major surgical procedure and is subject to the usual complications of thoracotomy.

In our experience high-speed air-drill biopsy with the large trephine has proved successful in obtaining adequate specimens of diffuse lung lesions without the need for major surgery. It is performed at the bedside, thereby saving time in the operating theatre, although it is wise to arrange thoracic surgical cover. From the patient's point of view it is quick and painless, and breath-holding is not required. A further advantage is that the procedure can be repeated if an adequate specimen is not obtained or as a means of assessing the patient's progress.

SUMMARY

One hundred biopsies of the lung or pleura have been performed with a high-speed air-drill over the last four years. A specially designed trephine, 2.1 mm. in bore, proved successful in obtaining adequate specimens from patients with diffuse lung lesions. With this trephine in its final form 33 out of 38 (87%) lung biopsies were successful. Conditions such as sarcoidosis, berylliosis, alveolar proteinosis, and eosinophilic vasculitis were successfully diagnosed. Complications were not serious and pneumothorax, which occurred in 15% of cases, was usually asymptomatic.

We wish to thank the physicians and surgeons of the London Chest Hospital, in particular Dr. E. H. Hudson, for their support. We are indebted to Mr. K. G. Moreman for the photomicrograph and the Photographic Department of the Royal Marsden Hospital for the illustrations.

S. J. STEEL, M.D., M.R.C.P.,
Consultant Physician to the Romford Group of Hospitals and Clinical Assistant to the London Chest Hospital.
D. P. WINSTANLEY, M.R.C.P., M.C.PATH.,
Consultant Pathologist to the London Chest Hospital.

REFERENCES

Andrews, N. C., and Klassen, K. P. (1957). *J. Amer. med. Ass.*, **164**, 1061.
Christiansen, H. (1940). *Acta radiol. (Stockh)*, **21**, 349.
Deeley, T. J. (1960). *Acta Un. int. Cancr.*, **16**, 338.
Ellis, F. (1947). *Brit. J. Surg.*, **34**, 240.
Kirschner (1935). *Schweiz. med. Wschr.*, **65**, 28.
Krumholz, R. A., and Weg, J. G. (1966). *J. Amer. med. Ass.*, **195**, 38.
Lauby, V. W., Burnett, W. E., Rosemond, G. P., and Tyson, R. R. (1965). *J. thorac. cardiovasc. Surg.*, **49**, 159.
Manfredi, F., Rosenbaum, D., and Behnke, R. H. (1963). *Ann. intern. Med.*, **58**, 773.
Martin, H. E., and Ellis, E. B. (1930). *Ann. Surg.*, **92**, 169.
Smith, W. G. (1964a). *Thorax*, **19**, 68.
—— (1964b). *Lancet*, **2**, 318.

Medical Memoranda

Agranulocytosis Coincident with Amodiaquine Therapy

Brit. med. J., 1967, **3**, 32–33

Agranulocytosis is recognized as a rare complication of amodiaquine therapy. Love, Foulk, Williams, and Mitchell (1953) reported two cases of leucopenia ; Yates, Leeper, and Fishler (1955) reported a case of pancytopenia ; and Kennedy (1955) described a case of absolute neutrophil leucopenia. Glick (1957) described fatal agranulocytosis following 200 mg. of amodiaquine daily for eight weeks, and Perry, Bartholomew, and Hanlon (1962) an almost fatal reaction with hepatitis and agranulocytosis after 200 mg. daily for seven days.

This paper reports four cases (one fatal) in which agranulocytosis occurred coincident with taking amodiaquine as a malaria suppressive.

CASE 1

A previously healthy 20-year-old man, resident in Papua for only one week, was admitted to hospital with high fever, malaise, and a sore throat. He had taken 150 mg. of amodiaquine once or twice daily for three weeks, that dose having been prescribed in error as a malaria suppressive. He had never taken amodiaquine before, and was not taking any other drug. Haemoglobin was 14.1 g./100 ml., and the total leucocyte count 3,000/cu. mm., with no granulocytes. Bone-marrow aspiration showed an almost complete absence of developing granulocytes. Paul–Bunnell test was negative.

He was extremely ill from the onset, running a high fever and vomiting intermittently. A small blister on the knee developed into a spreading cellulitis from which *Pseudomonas pyocyanea* was isolated, the same organisms also being cultured from the blood stream. In spite of broad-spectrum antibiotics, digitalis, and corticosteroids he died on the fifth day in a state of " Gram-negative shock." Blood counts are shown in the Table.

CASE 2

A previously healthy man aged 30 was admitted to hospital with headache, fever, anorexia, joint pains, diarrhoea, and a sore throat. Haemoglobin was 14.4 g./100 ml., leucocyte count 2,000/cu. mm., with only 2% granulocytes. Thinking that he had malaria, the patient had taken 450 mg. of amodiaquine daily for five days. He had been in Papua for only four weeks, and had taken 300 mg. of amodiaquine twice weekly during this time. He was not taking other drugs, and had not had antimalarials before.

Being allergic to penicillin, he was treated with oxytetracycline, and later, when he developed a painful infected haemorrhoid, erythromycin and streptomycin were added. Fever persisted for 16 days and granulocytopenia for three weeks. He was discharged with a leucocyte count of 4,000/cu. mm., and 30% granulocytes (see Table).

CASE 3

A 57-year-old woman complained of pain in the back and epigastrium for one week and was thought to have cholecystitis. Haemoglobin was 11.7 g./100 ml., and there were 2,800 leucocytes/cu. mm., with 40% granulocytes. One week later, after a further attack of pain, the leucocyte count was 3,200/cu. mm., with an almost complete agranulocytosis. She had been in Papua for one month, and had taken 300 mg. of amodiaquine weekly. She had never taken this drug before, and was not having any other drugs.

She was admitted to hospital and treated with penicillin. On the third day her temperature was 103° F. (39.4° C.) and streptomycin was added. The agranulocytosis persisted, and on the fourth day prednisolone 15 mg. q.i.d. was begun. Two days later the percentage of granulocytes had increased, and by the third week the leucocytes showed a normal distribution (see Table). A Paul–Bunnell test performed in the third week was negative.

CASE 4

A 65-year-old man complained of severe sore throat, malaise, and earache. He was treated with penicillin, but three days later was unable to swallow because of pain. He was admitted to hospital, where haemoglobin was found to be 13.5 g./100 ml., leucocytes 1,100/cu. mm., with complete agranulocytosis. Pus from his inflamed ear gave a profuse growth of *Ps. pyocyanea.* He had been in Papua for 10 weeks, and had taken 300 mg. of amodiaquine weekly, but no other drugs.

He was treated with penicillin and oxytetracycline, but continued to run a fever of up to 104° F. (40° C.) for six days, after which his condition slowly improved. By the eleventh day his count had risen to 5,800/cu. mm., with 47% granulocytes (see Table), and he was then discharged.

Day of Illness	Case 1		Case 2		Case 3		Case 4	
	W.C.C.	G.	W.C.C.	G.	W.C.C.	G.	W.C.C.	G.
1	3,000	(0)	2,000	2%	2,800	40%	1,100	(0)
2	550	(1)	—	—			700	(0)
3	850	(0)	1,600	(2)				
4	600	(0)	—	—			800	(2)
5	650	(0)						
6			1,400	(2)			2,000	12%
8					3,200	(11)		
9								
10			1,300	(8)	3,500	(1)		
11					1,500	(10)	5,800	47%
12								
13			1,600	(2)				
14					1,000	15%		
15								
16			1,600	(5)	3,000	36%		
17								
18			1,600	(few)				
19					6,200	22%		
20			1,500	10%				
23					7,000	65%		
24			4,000	30%				

W.C.C. = Total leucocyte count. G. = Number of granulocytes either as a percentage of the total count or, where figure is in parentheses, total number found after a search for five minutes.

DISCUSSION

In all four cases amodiaquine was the only drug known to have been ingested in the month preceding the illness. In all four the granulocytes were the only elements of the blood to be affected, red cells, other leucocytes, and platelets remaining normal.

It has not been possible to prove that the agranulocytosis was caused directly by amodiaquine. In Cases 1 and 2 the possibility is strengthened by the fact that the drug was taken in excessive dosage (as in other fatal and near fatal cases reported). It is important for practitioners in temperate zones to familiarize themselves with correct dosage schedules for antimalarials.

The three non-fatal cases occurred in the same month, in European persons newly arrived in Papua. This suggests the possibility of an infectious disease or some other factor common to all three, either causing agranulocytosis or rendering them susceptible to the effect of amodiaquine. No such factor could be traced.

The amodiaquine taken by all four patients was Camoquin 150-mg. tablets. Tablets supplied in Cases 2 and 3 were referred to the manufacturer, and were reported to conform with official standards.

The cause of death in Case 1 appears to have been *Ps. pyocyanea* septicaemia, which was not recognized until the patient was in extremis. Corticosteroids did not seem to have a significant influence on the course of the illness, and were not given to two of the patients who recovered.

Thanks are due to Dr. R. F. R. Scragg, Director of Public Health, Territory of Papua and New Guinea, and to Dr. A. Tonakie and Dr. C. H. Campbell for permission to publish cases under their care.

ADDENDUM.—Since this report was written there has been a further fatal case of agranulocytosis in a 47-year-old Australian missionary at Wewak. He was admitted to hospital under the care of Dr. Vaughan with cellulitis of the foot, and had recently suffered from two boils and a paronychia. Bone-marrow and blood examination showed almost complete agranulocytosis, with thrombocytopenia. Despite intensive antibiotic treatment he developed acute gingivitis, pharyngitis, and otitis externa, and died after a few days. Cultures from blood, foot, throat, and ear all grew *Ps. pyocyanea.* He had taken 300 mg. of amodiaquine weekly since arrival in the Territory of Papua and New Guinea ten weeks previously, with an additional 2,100 mg. during the five days prior to admission. The only other drugs taken had been Aspro and tetracycline.

KATHLEEN BOOTH, M.D., M.C.PATH.,
Haematologist, Taurama Hospital, Port Moresby, Papua.
K. LARKIN, M.B., B.S.,
General Practitioner, Port Moresby, Papua.
I. MADDOCKS, M.D.,
Lecturer in Medicine, Papuan Medical College, Boroko, Papua.

REFERENCES

Glick, L. (1957). *Brit. med. J.*, 1, 932.
Kennedy, A. F. (1955). Ibid., 2, 475.
Love, J., Foulk, R., Williams, R. G. W., and Mitchell, R. B. (1953). *Amer. J. med. Sci.*, 225, 26.
Perry, H. O., Bartholomew, L. G., and Hanlon, D. G. (1962). *J. Amer. med. Ass.*, 179, 598.
Yates, J. E., Leeper, R. W., and Fishler, M. C. (1955). *Kaiser Fdn med. Bull.*, 3, 193.

Sudden Onset of Psychosis in Association with Vitamin-B_{12} Deficiency

Brit. med. J., 1967, 3, 34

Psychiatric disturbance due to avitaminosis B_{12} is well documented (Holmes, 1956 ; Wiener and Hope, 1959 ; Fraser, 1960 ; Smith, 1960), but the precipitation of such a situation by folic acid cannot fortunately be common, since the dangers of neurological damage by folic acid in the presence of vitamin-B_{12} deficiency are now well known (Spies and Stone, 1947 ; Israëls and Wilkinson, 1949 ; Conley and Krevans, 1955). The results were so dramatic in a case which recently came to our attention that we feel the details are deserving of record.

CASE HISTORY

A 53-year-old housewife presented in February 1966 with a four-year history of intermittent numbness and tinglings in the arms and legs which had been diagnosed elsewhere at the onset as being due to cervical spondylosis and treated by neck traction with partial relief. After a minor traumatic episode six months before presentation the symptoms had become more pronounced and unremitting and she had also developed weakness of fine movements of the hands. During the last six months she had felt depressed.

On inquiring into her past history it was found that she had been treated by "acid" for anaemia 15 years previously—this was probably hydrochloric acid—and that it had been discontinued after some 12 months. In March 1965 she was admitted to another hospital for hysterectomy for menorrhagia. At this time a blood count showed: Hb 50% (7.4 g./100 ml.) ; P.C.V. 25% ; M.C.H.C. 30% ; W.B.C. 4,000/cu. mm., normal differential ; reticulocytes 6% ; M.C.D. 7.8 μ by halometry ; appearances of film compatible with rapid red cell regeneration with some hypochromia, but macrocytosis not striking. A histidine loading test for formiminoglutamic acid was weakly positive. Blood transfusion, iron, and folic acid were given with good response, but tests to exclude vitamin-B_{12} deficiency were not carried out and she continued taking folic acid, 10 mg. t.d.s., until admission.

On examination she was a fit-looking, well-nourished woman who appeared depressed. There was no clinical anaemia, but glossitis was severe. In the central nervous system she was orientated in time and space. Cranial nerves were normal. Power was generally diminished in all four limbs, especially in the distal muscle groups. She had impaired sense to pinprick of the hands and feet and impaired proprioceptive and vibration senses of the feet and lower legs. Tendon reflexes were symmetrically depressed, the supinator and knee reflexes being absent. Gait and Romberg's tests were normal.

Investigations showed: Hb 12.4 g./100 ml., with normal indices and normal film ; W.B.C. 4,500/cu. mm., with normal differential ; E.S.R. 3 mm. in first hour ; total serum protein 5.7 g. (albumin 3.2 g.). Electrophoresis showed slight increase in β-globulin. Liver-function tests were normal. Pyruvate-tolerance test: fasting, 2.55 mg./100 ml. ; 30 minutes after 50 g. of glucose, 4.0 mg./100 ml. ; 60 minutes, 3.7 mg./100 ml. ; 120 minutes, 2.8 mg./100 ml. The normal blood pyruvate level is 0.5 to 1 mg./100 ml. and after glucose should not exceed 1.4 mg./100 ml.

Four days after admission she suddenly became frankly psychotic with delusions, requiring large doses of chlorpromazine. The mental picture was characterized by confusion with paranoid delusions and auditory hallucinations. She was convinced that others in the ward were saying horrible things regarding her and that she was about to undergo a serious brain operation.

Vitamin-B_{12} deficiency was suspected, and after the injection of cyanocobalamin 1,000 μg. for the Schilling test her mental aberration started to improve within 24 hours, and after 48 hours there was marked improvement. The Schilling test showed only 5.3% excretion of the oral dose in 24 hours, rising to 13.3% after 100 mg. of hog intrinsic factor.

Further investigation by Kay's augmented histamine test meal showed achlorhydria, and a barium meal with follow-through was normal apart from a bald gastric fundus. Bio-assay showed serum vitamin B_{12} 62 μμg./ml. and folate 100 mμg./ml. Xylose excretion was 2.1 g. after a 5-g. dose. Faecal fats were 12.8 g. in the first 24 hours, 7.8 g. in the second 24 hours, and 6.4 g. in the subsequent 24-hour periods.

Within a few days the mental symptoms had completely resolved, and over the ensuing weeks there was considerable symptomatic improvement in the peripheral neuropathy and she had only occasional mild paraesthesiae in the hands and feet. The power has improved, but at the time of writing impaired vibration sense and diminished tendon reflexes were still present.

COMMENT

The evidence of vitamin-B_{12} deficiency secondary to pernicious anaemia seems conclusive from the bio-assay and Schilling test results in this case, though there would also seem to be an element of malabsorption in the small intestine not involving vitamin B_{12}, as shown by the high faecal fat excretion values. The rapid improvement in the mental symptoms after parenteral vitamin B_{12} strongly favours deficiency of this vitamin as the cause of the psychosis, which began with dramatic suddenness at a time when the blood picture was normal and the clinical findings indicated peripheral neuropathy rather than the spinal involvement typical of subacute combined degeneration of the cord. A similar sequence of events was described in three cases by Strachan and Henderson (1965). It was fortunate that the psychosis developed while the patient was under observation in hospital so that treatment could be instituted promptly. We feel that this case illustrates once again the danger of prolonged folic acid therapy without prior exclusion of vitamin-B_{12} deficiency.

We wish to thank Dr. J. W. Aldren Turner for permission to publish details of this case.

ROSALINDE SMITH, M.B., B.S.,
Late Medical Registrar.
R. A. M. OLIVER, D.M.,
Consultant Haematologist.
Croydon General Hospital, Surrey.

REFERENCES

Conley, C. L., and Krevans, J. R. (1955). *Ann. intern. Med.*, 43, 758.
Fraser, T. N. (1960). *Lancet*, 2, 458.
Holmes, J. M. (1956). *Brit. med. J.*, 2, 1394.
Israëls, M. C. G., and Wilkinson, J. F. (1949). Ibid., 2, 1072.
Smith, A. D. M. (1960). Ibid., 2, 1840.
Spies, T. D., and Stone, R. E. (1947). *Lancet*, 1, 174.
Strachan, R. W., and Henderson, J. G. (1965). *Quart. J. Med.*, 34, 303.
Wiener, J. S., and Hope, J. M. (1959). *J. Amer. med. Ass.*, 170, 1038.

Current Practice

Clinician's Approach to Respiratory Viruses

NEVILLE C. OSWALD,* T.D., M.D., F.R.C.P.

Most clinicians dismiss the laboratory aspects of virology as being too difficult. They are aware that considerable advances have been and are being made and that some hundreds of viruses, many of which are pathogenic to man, can be positively identified by one means or another. Unhappily, these advances have been achieved by techniques which are not readily understood by clinicians, who are often at variance with virologists when it comes to the collection of specimens and the interpretation of results. Maybe they are at fault in failing to appreciate the difficulties of viral identification and in being intolerant of delays in the reporting of results which perforce are frequently negative. Whatever misunderstandings there may be, the fact remains that the science of virology is firmly in the grip of virologists and epidemiologists at the present time. Clinical virology as a subject is virtually non-existent, principally because of the lack of contact between clinicians and virologists and of course the lack of antiviral remedies. In practice this means that clinicians are useful chiefly for gathering material for field trials or for supplying random samples to be tested at leisure for the purpose of prevalence studies. Incidentally this situation is not peculiar to Britain.

None can deny the clinical importance of respiratory viruses, in that they contribute to the vast problem of acute respiratory disease which is responsible directly or indirectly for roughly one-quarter of all visits to general practitioners, one-quarter of all sickness absence in the working population, and one-tenth of deaths from all causes. Indeed, the sheer weight of clinical experience qualifies practising physicians who possess no more than a rudimentary knowledge of laboratory techniques at least to ponder on the problems confronting them. Their main concern is with the rapid identification of organisms when it may have some bearing on treatment. This is certainly not the case in the great majority of viral illnesses, which are comparatively trivial and of short duration. For example, Hope-Simpson (1966) estimates that only one patient in twenty with a cold in the head visits his doctor. Should pneumonia develop, the situation is quite different. Then any positive information is useful, provided that it is forthcoming while the disease is still active. Evidence of infection by influenza virus immediately raises the question of the extent to which the virus is responsible for the degree of illness and the extent of the consolidation, and of the possibility of staphylococcal superinfection. A patient with a positive test, for example, for adenovirus or respiratory syncytial (R.S.) virus may be saved from unnecessary antibiotic therapy when the pneumonia is slow to clear. Pneumonias caused by the mycoplasma, rickettsia, and psittacosis groups respond favourably to the tetracyclines; alas, they remain undiagnosed for the most part under existing conditions. This is particularly unfortunate in the case of mycoplasma infections, which probably account for about 10% of all primary pneumonias, with much higher figures having been recorded in children and young adults (Chanock *et al.*, 1963). High titres of serum antibody often develop early, and if facilities existed for the speedy testing of single specimens of blood, treatment with dimethylchlortetracycline could be started without undue delay, in anticipation of a fourfold rise in titre between the paired sera.

The Viruses

The term "respiratory viruses" is open to several interpretations. Some—for example, enteroviruses, chicken-pox, and measles—frequently propagate in the upper air passages and are disseminated from them without necessarily causing respiratory symptoms. Others are established agents of acute respiratory disease, of which the most important to be discovered so far are the influenza and parainfluenza viruses, adenoviruses, respiratory syncytial virus, rhinoviruses, and the Coe strain of Coxsackie virus. There are also the somewhat larger rickettsia, psittacosis, and mycoplasma groups, though of course they are no longer regarded as true viruses. The principal means of identification of these organisms are by cultural methods, electronmicroscopy, and immunological techniques.

The Table shows the current standard culture media and the times taken for isolation. Fairly rapid primary isolation can sometimes be achieved, with the exception of rhinoviruses and *Mycoplasma pneumoniae*, but further tests for typing are essential before a firm opinion can be given. While cultivation is fundamental to the study of viral illnesses, it has many disadvantages in clinical practice. Respiratory secretions need to be collected within four days of the onset of symptoms (Higgins *et al.*, 1964), and even then the number of positive results is unlikely to exceed 30% (M.R.C., 1965). A final report, including typing, is rarely available within a fortnight from the taking of the specimen. A formidable variety of tissue cultures needs to be maintained. For these reasons existing cultural methods have little to offer for the day-to-day management of patients in general hospitals with acute respiratory infections.

Time Taken for Isolation of Organisms and Media Used. Specimens Taken at 1–5 Days. Typing Time Additional

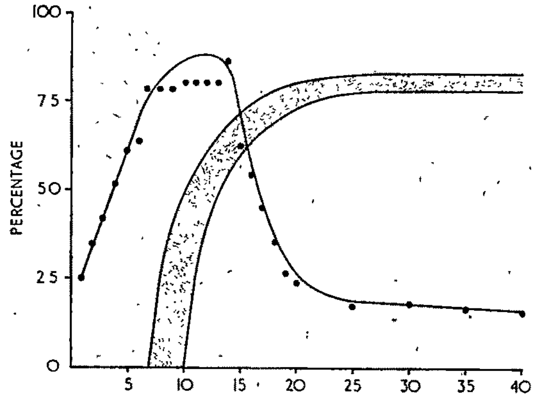
Organism	Isolation	Medium
Influenza	3–21 days	Eggs; monkey kidney
Parainfluenza	3–21 „	Monkey kidney
Adenovirus	3–30 „	HeLa cells
Rhinovirus	1–2 months	Embryo kidney WI.38
R.S. virus	5–21 days	HeLa cells
M. pneumoniae	1–3 months	Agar; broth
Q fever	4–14 days	Eggs
Psittacosis	5–30 „	Mice; eggs

Electronmicroscopy presents exciting possibilities for early diagnosis, particularly since the introduction of negative-staining techniques (Smith and Melnick, 1962; Williams *et al.*, 1962). It is useful in differentiating groups of viruses—for example, myxoviruses, adenoviruses, and rhinoviruses; it cannot be used to distinguish between members of groups. It has the great advantage that, should virus particles exist in sufficient numbers, group identification can be carried out quickly. The classical example, of course, is smallpox, which can be recognized within a quarter of an hour of the receipt of a specimen of secretion (Cruickshank *et al.*, 1966). Whether this method will ever be usefully applied to acute respiratory infections remains to be seen. Unfortunately, respiratory viruses tend to be comparatively sparse, making identification of extracellular forms in respiratory secretions very difficult. Examination of ultra-thin sections of secretions, with a view to seeing developing particles within the cut cells, may eventually be a fruitful if laborious technique. Positive results are clinically most desirable in pneumonia, so that specimens of sputum would seem to be the most appropriate, taken during the early stages when the infected cells are most likely to be shed.

---

* St. Bartholomew's Hospital, London E.C.1, and Brompton Hospital, London S.W.3.

Various immunological tests are currently available, of which the complement-fixation test, despite its disadvantages, remains a standard laboratory procedure. It can be applied to infections by all the organisms under discussion, with the exception of rhinoviruses, with a view to determining a rise in titre of antibodies which takes place usually between 7 and 21 days from the onset of symptoms. The shaded area in the Chart indicates the likelihood of finding a significant titre according to the day of illness. The area rises to a figure of 75–80%, which varies to some extent with the organism tested. The continuous line in the Chart shows the percentage of patients in hospital with pneumonia according to the day of illness, and demonstrates that the great majority of them are in hospital during the time that the titre would be expected to be raised.



Percentage of patients in hospital with pneumonia according to day of illness. Based on 350 consecutive patients admitted to St. Bartholomew's Hospital in 1963–5 with a diagnosis of primary pneumonia. Median hospital stay 14 days. Shaded area indicates possible percentage of positive complement-fixation tests by days of illness for the common respiratory viruses.

Other immunological tests exist which are not yet generally applicable to the range of respiratory viruses. Fluorescent antibody staining of secretions shows promise (Hers, 1963) and has been developed for influenza virus (Liu, 1956). Non-specific fluorescence causes difficulties, but the method has the great advantage that it is immunologically specific for the viruses tested. The possibility of haemabsorption of cells in sputum is being studied with a view to the early diagnosis of infection by myxoviruses. Gel diffusion has already been successfully used to identify smallpox antigens in secretions (Dumbell and Nizamuddin, 1959). It has also demonstrated antigens of laboratory-grown respiratory viruses when the viruses are available in concentrated form. The low concentration of virus in respiratory secretions has so far precluded its application to acute respiratory disease.

Clinician's Dilemma

Clinicians regard respiratory virology as something of an enigma at the present time. How far should they become involved in it? Should they become involved at all? If they should, how should they set about it? Few hospitals have their own virus laboratories, most of the work being done in the 60 regional and area laboratories of the Public Health Laboratory Service (P.H.L.S.). The P.H.L.S., a successor of the Emergency P.H.L.S. of the second world war, exists "to make a continuous study of how communicable microbial diseases are spread and what advice may be offered about how to control them," and "the duty of the service is to gather as good a sample of relevant information as can be secured and dealt with" (Howie, 1965). This has been the policy up to now—namely, that the virological resources of the country have been directed primarily to epidemiology, and nobody can blame the service, which is short of both virologists and technicians, for apparent delays in the reporting on specimens from individual patients. However, a sense of urgency is rapidly developing. More viruses are being discovered, more is being learnt of their behaviour, and rapid methods of identification are being devised. Overshadowing these considerations is the probable development of specific antiviral compounds in the very near future.

Already drug houses are pressing for clinical trials. The testing of compounds will raise considerable problems. Quite apart from their possible toxicity and range of potency, trials will have to be conducted in naturally occurring outbreaks with all the uncertainties of early diagnosis, and in voluntarily infected individuals, bearing in mind the difficulties in inducing infection and the risks involved. Clinical and statistical appraisal will be far from easy. These matters will need to be left in the hands of experts in the first instance. How hospital clinicians without immediately available virological facilities will become involved remains to be determined. The time is not yet ripe for the establishment of routine virus laboratories in general hospitals, nor does the staff exist to man them. However, some bridges must soon be erected between hospitals and the virologists' strongholds. These might take the form of laboratory technicians trained in the collection of specimens in the first instance. Beyond that lie token laboratories under the general supervision of virologists, the day-to-day work being carried out by senior technicians.

For more ambitious schemes, serious thought should be given to the extent to which Ph.D.s can be entrusted with routine laboratory work. Those clinicians who have been privileged to visit virus laboratories cannot fail to have been impressed by the continuous attention to detail which is necessary if disasters are to be avoided. A blown fuse to a refrigerator or the changing of a junior technician can wreck a month's work. There would seem to be much in favour of training more Ph.D.s for these responsibilities, thus leaving medically qualified virologists freer to concentrate on their special interests.

Conclusion

It seems that clinicians will become increasingly involved with respiratory virology. Already virus tests can assist materially in the management of individual patients. The hope is that when effective antiviral compounds become available clinicians will be afforded the opportunity to use them intelligently.

My thanks are due to Dr. R. B. Heath for his comments on this article.

References

Chanock, R. M., Mufson, M. A., Somerson, N. L., and Couch, R. B. (1963). *Amer. Rev. resp. Dis.*, **88**, Part 2, p. 218.
Cruickshank, J. G., Bedson, H. S., and Watson, D. H. (1966). *Lancet*, **2**, 527.
Dumbell, K. R., and Nizamuddin, M. (1959). Ibid., **1**, 916.
Hers, J. F. P. (1963). *Amer. Rev. resp. Dis.*, **88**, Part 2, p. 316.
Higgins, P. G., Boston, D. G., and Ellis, E. M. (1964). *Mth. Bull. Minist. Hlth Lab. Serv.*, **23**, 93.
Hope-Simpson, R. E. (1966). *Proc. roy. Soc. Med.*, **59**, 638.
Howie, J. W. (1965). *Lancet*, **1**, 501.
Liu, C. (1956). *Proc. Soc. exp. Biol. (N.Y.)*, **92**, 883.
Medical Research Council Working Party on Acute Respiratory Virus Infections (1965). *Brit. med. J.*, **2**, 319.
Smith, K. O., and Melnick, J. L. (1962). *Science*, **137**, 543.
Williams, M. G., Almeida, J. D., and Howatson, A. F. (1962). *Arch. Derm.*, **86**, 290.

TODAY'S DRUGS

Aerosols in Asthma and Vaccines

The Committee on Safety of Drugs publishes leaflets in its Adverse Reactions Series from time to time. Number five of this series has been published recently, on reactions to aerosols in asthma and to vaccines. The text is given below.

Aerosols in Asthma

A small number of reports of sudden and unexplained deaths of asthmatic patients has reached the Committee. In some instances the circumstances of the deaths were strongly suggestive of overdosage from aerosols containing bronchodilating drugs. Moreover, recent reports in the medical press suggest a possible link between the excessive use by patients of such aerosols and a recorded rise in the death rate from bronchial asthma. This possibility is still under investigation.

In proper dosage bronchodilating drugs given by inhalation are of great value to sufferers from asthma. However, excessive dosage does not increase the degree of relief obtained from these preparations and may be positively dangerous. Prescribers are advised to give patients careful instruction in the use of aerosols for the relief of asthma and to warn them of the dangers of excessive use.

The Committee on Safety of Drugs wish to remind prescribers of the possibility of overdosage with aerosols containing bronchodilating drugs for the relief of asthma. Overdosage is particularly likely to occur with *pressurized* aerosols.

Vaccines

The Committee on Safety of Drugs wish to draw the attention of doctors to the importance of reporting adverse reactions to vaccines and other immunological agents. Such products fall within the Committee's definition of drugs and suspected reactions to them should be reported on yellow cards.

Trivial reactions, such as slight pyrexia or local tenderness, need not be reported. Neither is it necessary to report morbilliform rashes after measles vaccine. Such events as hyperpyrexia, meningism, prolonged drowsiness, and convulsions should be reported on yellow cards.

In the report, the name of the manufacturer and the batch number of the vaccine should be given. It would also be helpful to record the time interval between inoculation and the occurrence of the reaction.

If there is any doubt whether a reaction is serious enough to warrant a report—*report it.*

ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Cardiac Catheterization after Myocardial Infarction

Q.—*Are there any indications for intracardiac catheterization immediately after a coronary thrombosis?*

A.—In the vast majority of patients there is no indication for intracardiac catheterization after a myocardial infarction. Very occasionally, however, the question of surgical treatment of a complication such as a ruptured interventricular septum or mitral incompetence (due to malfunction of the papillary muscles) may arise. Under these circumstances cardiac catheterization and angiocardiography might well have to be performed to confirm the nature of the complication and to determine its severity.

Slow-release Corticosteroids in Hay-fever

Q.—*Is there a place for injections of slow-release, long-acting corticosteroids in the treatment of hay-fever?*

A.—Hay-fever is as a rule an inconvenient disorder rather than a disabling one. Most patients can obtain adequate relief with antihistamine drugs or nasal inhalation of preparations containing a small quantity of corticosteroid derivatives. Others may be relieved by desensitization with pollen extract before or during the season.

Slow-release, long-acting corticosteroids have been reported to be an effective form of treatment.[1] No controlled trial, however, has been carried out to confirm this. Though a single injection of corticosteroid is unlikely to be harmful, it temporarily suppresses the adrenal glands and its therapeutic effect cannot be relied on. It might be justifiable to use this form of treatment in a patient who had bad hay-fever and who wished to be free from symptoms for some special purpose, such as taking an examination. But a short course of oral corticosteroids would be equally effective and the dose more easily controlled. In my opinion the use of systemic corticosteroids is rarely justified in uncomplicated hay-fever.

REFERENCE

[1] Marshall, B. Y., *Practitioner*, 1965, **194**, 676.

Treatment of Bell's Palsy

Q.—*What is the present-day treatment of Bell's palsy? Have corticosteroids any place?*

A.—Many patients with Bell's palsy in whom there is physiological block without denervation make a complete and fairly rapid recovery. Matthews[1] found that 65% of a series seen at hospital within six days of the onset fell within this group. In the group with denervation improvement may not start for three to four months, and in nearly all patients incomplete and associated movements are common. Tests for excitability in the facial nerve are claimed[2] to distinguish between physiological block and denervation as early as 72 hours after the onset of facial palsy, and galvanic stimulation of the tongue[3] is also used in early differentiation. Administration of cortisone,[4] galvanic stimulation of the facial muscles,[5] and repeated cervical sympathetic blockade[6] have all been used in controlled trials and are reported to have no beneficial effect. Recently Taverner and his colleagues[7] have used corticotrophin gel given by intramuscular injection for ten days. Of 77 patients treated 64 recovered completely and 13 developed denervation. From previous studies they report that the expected results in 77 successive patients with Bell's palsy would be 47 complete recoveries and 30 with denervation.

REFERENCES

[1] Matthews, W. B., *Brit. med. J.*, 1961, **2**, 215.
[2] Campbell, E. D. R., Hickey, R. P., Nixon, K. H., and Richardson, A. T., ibid., 1962, **2**, 7.
[3] Peiris, O. A., and Miles, D. W., ibid., 1965, **2**, 1162.
[4] Tavener, D., *Lancet*, 1954, **2**, 1052.
[5] Mosforth, J., and Taverner, D., *Brit. med. J.*, 1958, **2**, 675.
[6] Fearnley, M. E., Rainer, E. H., Taverner, D., Boyle, T. McM., and Miles, D. W., *Lancet*, 1964, **2**, 725.
[7] Taverner, D., Fearnley, M. E., Kemble, F., Miles, D. W., and Peiris, O. A., *Brit. med. J.*, 1966, **1**, 391.

Gammaglobulin in Early Pregnancy

Q.—*How often should gammaglobulin be administered in early pregnancy as a prophylactic against rubella?*

A.—Evidence suggests that one injection of gammaglobulin is a prophylactic against rubella. It may prolong the incubation period if the disease is to appear. It is not yet certain that it diminishes the number of foetal abnormalities, but it seems likely.[1]

REFERENCE

[1] *Amer. J. Dis. Child.*, 1965, **110**, 345.

NEW APPLIANCES

Inexpensive Heat-exchanger System for the Rygg Bag Oxygenator

Mr. **DONALD LONGMORE**, consultant physiologist, National Heart Hospital, Mr. **DONALD ROSS**, consultant surgeon, National Heart Hospital, and Mr. **DEREK RAY**, research engineer, British Heart Foundation, write: Having successfully used the Rygg bag in over 140 human perfusions, we felt that we had not fully taken advantage of the low prime of this oxygenator, for we were employing a separate heat exchanger the large volume of which often made it necessary to use blood in the prime. The low prime of the Rygg bag with the coil described makes it possible to use a clear fluid prime.

The advantage of disposability is lost if difficult-to-clean multi-tube stainless-steel heat exchangers have to be used. Disposable stainless-steel heat exchangers were found to be satisfactory, but they had a considerable resistance to flow and were prohibitively expensive. Accordingly, we investigated other techniques for maintaining temperature while on perfusion. Since we have used hypothermia below 34.5° C. only once in the last hundred bypass cases, a high-thermal-capacity heat exchanger was not thought necessary.

Microwave heating of the blood was rejected because of its complexity. Radiant heat was also rejected because of the risk that it would dry the blood film left on the sides of the bag as the levels changed. Therefore the simple device for immersion in the blood in the bag was designed (Fig. 1). The two collecting-chambers on the arterial side of the bag are slit with a sterile knife on the connector side of the bag, and the autoclaved coils* are then threaded carefully through these slits, avoiding contamination against the outside of the bag. A thermometer is placed in the fluid entering the coils from the heat reservoirs, so that the critical upper limit of temperature of 42° C. is never exceeded. Slitting of the bag is not a disadvantage, for, although it increases the prime slightly, this increase is nullified by the immersed volume of the coils.

Even if the coils are not used, we routinely pierce the bag for blood sampling and never proceed to perfusion without venting all three chambers of the bag. Venting of these chambers avoids the possible risk of embolism, which could result if both inlets to the defoaming chamber were blocked by drip nozzles.

The prototype coil itself was made from standard ¼-in. (6-mm.) 16-gauge copper tube, hand-formed with loosely wound coils. These coils were chromed before they were compressed to their final form. Experimentally we have shown that with a blood flow of three litres, a gradient of 10° C., and a fluid flow of 0.75 litre the heat transfer is 6,000 calories/minute. The performance of these coils is shown in the cooling curve for a 63-kg. patient with a 3.8 l./minute flow (Fig. 2). This was the one patient in whom hypothermia was instituted; the rate of cooling is shown with the coil perfused with ethylene glycol, starting at +2° C. and ending at +18° C. as the cold reservoir warmed. The room temperature was 22° C. If cooling is instituted by using the coil in this way it is necessary to have a brief circulatory arrest while a conventional heat exchanger is added to the circuit to assist rewarming.

This device is commercially available in stainless steel; we think it will be a worthwhile adjunct to the use of this excellent oxygenator until such time as Polystan Ltd. can produce a four-layered bag with heat-exchange surfaces on both sides of the blood compartment.

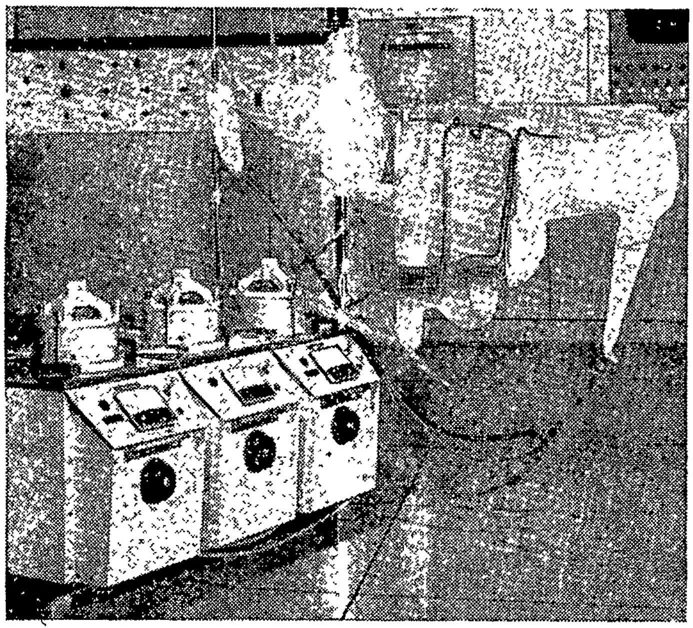


FIG. 1.—Cooling coils are shown against the Rygg bag in the position they would occupy. The pumps are National Heart Hospital pattern—Belmedical driven roller pumps, adjustable for occlusiveness with split heads for immediate tube-changing. The trolley is made from speed frame Dexion.

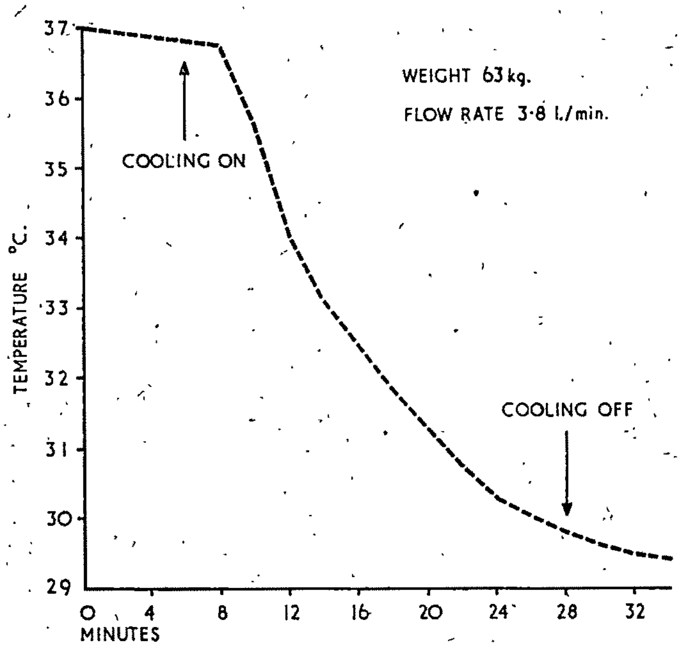


FIG. 2

---

* These coils are commercially available from Belmedical, Farnham Road, Slough, Bucks.

Book Reviews

Medical Care in Developing Countries

Medical Care in Developing Countries. Edited by Maurice King, M.A.(Cantab.), M.R.C.P. (Lond.). (30 chapters+appendix ; illustrated. 30s.) London : Oxford University Press. 1966.

In this book, which embodies contributions to a symposium on the subject held in Makerere, Uganda, the problems of medical care in emergent countries are considered in a very practical manner by authors skilled in the field and culled from university, health authorities, and lay specialists. Despite this diversity of talent, the book is homogeneous and represents a collaboration between academic and practical points of view which is unique.

There are 30 chapters, including an excellent hard-hitting introduction by the editor, Dr. Maurice King, who defines medical care as "the study of how the fundamental knowledge embodied in medicine and public health can best be applied to the benefit of a community." He enunciates three major propositions on which the book is based. Medical care in developing countries differs sharply from medical care in industrial ones ; its main determinant is poverty rather than a warm climate ; it is a subject of major importance, and it is possible to gather together enough knowledge to determine how to deal with the challenge it creates. The 12 axioms which follow from these propositions should form the philosophical and practical basis for those concerned in planning medical care, whose aim, as Professor Macdonald points out in his foreword, must be to "hasten the advancement of health, which is a universal object of all developing countries."

The second chapter deals with the fundamental question, How in rural areas in particular can preventive and curative services be planned to provide the maximum return in human welfare from limited resources of money and skill ? The ideal peripheral unit in a health service may not always be the so-called "health centre," particularly if it is built for occupation by a doctor in countries where doctors are few and in great demand, and are usually unwilling, short of compulsion, to work in rural areas. Well-trained auxiliaries may provide a temporary solution. Rex Fendall, from his own vast experience, offers a more realistic approach to the health centre, which he defines as "a unit which provides a family with all the health services it requires other than that which can only be provided in a hospital." Such a centre can be adjusted to the particular needs of a given locality, allowing for variables such as population density and the availability of trained staff, medical supplies, and visiting specialists.

Other chapters are concerned with the importance of collecting and interpreting epidemiological data, and with "community diagnosis," which implies knowledge of the ecology of particular diseases in relevant geographical areas, in turn demanding some understanding of the interplay between the infective agent and genetic, nutritional, cultural, agricultural, and other factors. The significance and importance of health education is pointed out with authority by Dr. Bennett, who writes with much practical experience. The training of auxiliaries and the relation between them and medically qualified personnel are discussed in detail. Medical schools in developing countries must be more closely associated with such teaching.

Chapters on administration and teaching, progressive patient care, and architecture of hospitals and health centres are followed by a description of the "sorting" systems in common use in outpatient clinics in the tropics. The importance of separating adults and children is stressed. Professor Jelliffe points out the very high proportion of children in tropical populations and discusses the diagnosis and management of his "top ten" diseases of childhood as seen in Makerere : pneumonia, ancylostomiasis, measles, pertussis, pyogenic and tuberculous meningitis, prematurity, sickle-cell disease, poliomyelitis, neonatal sepsis and septicaemia, and neonatal tetanus. There are very interesting and authoritative discussions of protein calorie malnutrition, kwashiorkor, and diarrhoeas in childhood. Dr. Morley contributes an excellent account of the philosophy, methods, and results of his "under-fives" clinic in Ilesha, Western Nigeria. Immunization campaigns are discussed by Dr. Stanfield in a practical and extremely useful manner.

The book also covers family planning, maternity care and the use and training of midwives, psychiatric problems, tuberculosis, blood transfusion, various hospital, laboratory, and training techniques (including medical records and teaching aids), and an account of supporting services such as the laundry and the workshop. Useful appendices follow, designed for the direct use of the doctor and the health planner in the tropics.

When the next edition of this remarkable book appears, as it must, it is to be hoped that it will include discussions on mass vaccination campaigns, the importance of medical field units for surveys of endemic disease, and the health problems engendered by the socio-economic developments which are the hallmark of the developing country and which are adding problems of population movement and interchange of infections to the already almost intolerable load the health services of these countries are expected to carry.

Everyone interested in the medical problems of developing countries should read this book. So should those concerned with general practice in the sophisticated world, in which so many problems are similar and where the idea of "community diagnosis" is certainly not academic.

BRIAN MAEGRAITH.

Bicentenary of Leeds Infirmary

The General Infirmary at Leeds. Vol. 1. The First Hundred Years. 1767–1869. By S. T. Anning. (Pp. 107+xii ; illustrated. 30s.) Edinburgh and London : E. & S. Livingstone. 1963.

The General Infirmary at Leeds. Vol. 2. The Second Hundred Years. 1869–1965. By S. T. Anning. (Pp. 188+xii ; illustrated. 42s.) Edinburgh and London : E. & S. Livingstone. 1966.

This month the General Infirmary at Leeds celebrates the bicentenary of its foundation. Fortunately the infirmary records since its inception have been preserved, thereby enabling the author to produce two books which constitute a well-written historical account.

The first volume covers the period from 1767 to 1869. The infirmary was located first in Kirkgate. Its foundation was not so much a result of the citizens' social conscience but rather as an economic necessity for providing medical care for the town, which was at that time rapidly developing its cloth and woollen industries. The first infirmary was, indeed, a conversion of Mr. Andrew Wilson's house, but it was soon necessary to move to a site near the Mixed Cloth Hall. In the late 1850s, even with 128 beds, the infirmary was so pressed for facilities that a move to larger premises was inevitable. The move took place in 1869, to the present site of the infirmary.

The second volume covers the period from 1869 to 1965. From the weekly records, reports, portraits, and plans the author has produced not just a catalogue of historical events but an absorbing account of the infirmary, its people, founders, committee members, staff—lay, medical, nursing, and ancillary—its buildings and departments, its work, and also the medical school. The founders obviously had good business acumen, which ensured the development of the infirmary.

Institutions become great because they are served by great people. There is no doubt that Leeds certainly had its share of great men. The period from 1866 saw rapid advances in surgery. There is a full description of life in the infirmary during this time, and of how the methods of antisepsis were introduced and how they were abandoned in 1880 with a recognition of the need for aseptic procedures. The change was largely accepted as a result of Moynihan's great influence.

There was an awareness, even in early times in this great provincial centre, of the need of forward planning. As early as 1860 the affiliation and amalgamation of science and medicine were appreciated. For the future the leaders of the infirmary see the necessity of locating their new medical centre in proximity to the university. The infirmary authorities also recognized in the early 1800s the need for a high standard of nursing. In

1889 the infirmary received Miss Nightingale's commendation, and with the Leeds University in 1921 the first Diploma of Nursing in Europe was established.

These two volumes, excellently written and illustrated, will not only be of interest to those who have worked in the infirmary but also to those interested in the history of hospitals and social services of the past 200 years.

JOHN REVANS.

Reflections on the Development of Medicine in America

Medicine in America. Historical Essays. By Richard Harrison Shryock. (Pp. 346 +xviii. 60s.) London: Oxford University Press. 1967.

Professor Shryock is known for his thoughtful writings on the social, cultural, and scientific aspects of medical history. In this volume he has gathered together a selection of his essays and added a preliminary chapter containing a "pilot study" of American medical history; though this synopsis is useful medical readers will note a few important gaps.

The essays are grouped under five headings—period pieces, personal and public hygiene, the medical profession, medical thoughts and research, and historiography. There is, unavoidably, a certain amount of overlapping. The author is a philosophic historian and states that his writing "to avoid distortion, must be largely impersonal, rarely dramatic, and never glamorous." Fortunately it is very difficult to be strictly impersonal in writing medical history, so that in the chapters dealing with medical thought we find an interesting account of Cotton Mather's advocacy of inoculation against smallpox, and are told about the remarkable anticipation of part of Darwin's hypothesis by that strange genius William Charles Wells (who incidentally spent most of his professional life in London). In the same group of essays will be found a very judicial estimate of Benjamin Rush's influence upon American medicine.

In the group of "period pieces" will be found an unusually interesting account of "Medical Care in the Old South" in which readers may be surprised to learn that mortality was greater among the free than among the slave negroes. The account of the muddled medical services during the early part of the American Civil War is depressing, though it was not worse than occurred in the Crimean War.

The chapters on popular and public health movements, and the campaign against tuberculosis in America, remind one of very similar movements in Britain. In the chapter on "Women in American Medicine" I was surprised to find that the proportion of women graduates in medicine in the United States is less than it is in Britain and other European countries. The author's view "that American opposition to the entrance of women into medicine was the fact that it was associated with a strong feminist movement" does not seem a sufficient reason.

Under the section of "historiography" the author gives useful advice on some little known or insufficiently used medical sources, and urges that historians should study more closely the history of science in America. The final chapter discusses the interplay of social and internal factors in modern medicine; most medical historians make this interplay obvious, but few have discussed the matter so philosophically.

ZACHARY COPE.

Do Delinquents "Grow Out of It"?

Deviant Children Grown Up. By Lee N. Robins, Ph.D. (Pp. 351+xiv. 68s.) Edinburgh: E. & S. Livingstone. 1966.

This is an important book which reports a 30-year follow-up of deviant children. A team of doctors and social workers under the guidance of Professor Lee N. Robins, Ph.D., Professor of Sociology in Psychiatry, Washington School of Medicine, carried out this research over a period of eight years. It consisted of locating and interviewing 624 men and women, 524 of whom had been referred 30 years previously as children or adolescents to the St. Louis Municipal Psychiatric Clinic in Missouri.

This research is almost unique owing to the fact that 90% of the adults were located after 30 years and 82% were interviewed. The social records of 98% were scrutinized, which involved searching national service and veteran, welfare, and hospital records, credit bureaux, and driving licence registers, police and prison files. The author points out that they were extremely fortunate in being able to cross-check with so many social sources, as often these records are not made available to research workers.

The prime aim of the study was to determine the adult performance of the 406 antisocial children and the 118 who had been referred for other reasons. 100 controls of similar age, I.Q., and social status were added.

Over a six-year period all children who were referred were studied, omitting those with I.Q.s under 80, negroes, and those who, at the time of referral, were over the age of 18. 28% received psychiatric treatment in the clinic. 50% were later institutionalized following appearance in juvenile courts, as against only 6% of the controls. When located, 71% of the adults had at some time or other been arrested. 86% admitted sufficient facts for psychiatrists to deem them sociopathic, only 7% denied all offences.

It was possible to correlate other forms of psychiatric illness in the adults with the symptoms that had been noted at the time of referral. Both alcoholics and hysterics had, in childhood, shown antisocial symptoms; this was also true of those who later developed schizophrenia. Children who were fearful and withdrawn were no more likely to develop psychiatric illness than the controls. There were no characteristic findings in childhood for those who later developed manic-depressive illness or anxiety neurosis.

For the sociopath the main predicting factor was the number of offences before referral and acts of aggression. Of the non-antisocial symptoms slovenliness and enuresis over the age of 6 were commonly associated with a later development of sociopathy. Having a delinquent father was the only childhood variable which correlated with persistent antisocial trends despite increasing age. Parental rejection and overly strict parents did not, in this study, predict sociopathy.

Child guidance clinics tend to attract referrals according to the preoccupations of the staff, so that not all clinics have the same proportion of antisocial children. The present fluidity of the American cultural background is not universal nor are the legal proceedings, so that it cannot be assumed that the findings of this group will necessarily be repeated elsewhere. This does not, however, detract from a remarkably fine piece of research.

This book is highly commended to all concerned with delinquents, adult and juvenile, and in particular to those sociologists and psychiatrists who are concerned with the prevention of crime.

R. F. BARBOUR.

Books Received

Review is not precluded by notice here of books recently received.

Equipment for the Disabled. An Index of Equipment, Aids and Ideas for the Disabled. 2nd edition. Edited by Margaret Agerholm, M.A., B.M., B.Ch.Oxon. (4 loose-leaf volumes; illustrated. £7 7s.) London: National Fund for Research into Crippling Diseases. 1967.

Plumbismo Cronico Ocupacional en Nuestro Medio. By Dr. Guillermo del Carpio. (Pp. 135. No price given.) Lima, Peru: Medicina del Trabajo. 1966.

Olfaction and Taste 2. Edited by T. Hayashi. (Pp. 835+viii; illustrated. £10.) Oxford: Pergamon. 1967.

Scientific Foundations of Surgery. Edited by Charles Wells, C.B.E., S.Pk., F.R.C.S., Hon. LL.D., and James Kyle, M.Ch., M.B., F.R.C.S., F.R.C.S.I. (Pp. 629+xix; illustrated. £6 6s.) London: William Heinemann. 1967.

The Unquiet Mind. The Autobiography of a Physician in Psychological Medicine. By William Sargant. (Pp. 240+xvi; illustrated. 30s.) London: William Heinemann. 1967.

Le Indicazioni Extraneurologiche Dell'elettromiografia. By Carlo Serra. (Pp. 544; illustrated. 12,000 lire.) Naples: Acta Neurologica. 1966.

The Prevention of Cancer. Edited by Ronald W. Raven, O.B.E., T.D., F.R.C.S., and Francis J. C. Roe, D.M., D.Sc., M.C.Path. (Pp. 397+xiv. £6.) London: Butterworth. 1967.

Hamilton Bailey's Demonstrations of Physical Signs in Clinical Surgery. 14th edition. Edited by Allan Clain, M.B.(Cape), F.R.C.S.(Eng.). (Pp. 627+x; illustrated. 75s.) Bristol: John Wright. 1967.

Vitamins and Hormones. Advances in Research and Applications. Vol. 24. Edited by Robert S. Harris, Ira G. Wool, and John A. Loraine. (Pp. 746+xviii; illustrated. £6 8s.) New York and London: Academic Press. 1967.

Neurological Problems. Edited by Jerzy Chorobski. (Pp. 444+xi; illustrated. 80s.) Oxford: Pergamon. 1967.

Clinical Orthopaedics and Related Research. No. 47. Edited by Anthony F. DePalma. (Pp. 256+x; illustrated. 60s.) London: Pitman. 1967.

Middle Articles

IS THERE AN ALTERNATIVE?

One of the main recommendations of the Porritt Report[1] was the creation of area health boards—authorities which would be responsible for the administration and co-ordination of all the medical services in any one area. In the report's view, " the preventive and personal health services can only be effectively integrated with the family doctor and hospital services by transferring them (services and staff) to the area health boards." At present a Royal Commission is considering the future structure of local government in England, while the Seebohm Committee is considering the future of some of the local authority services. In her article Miss Elizabeth Burney considers the possible relevance of changes in local government to some suggested changes in the health services.

Local Government Reform and the Health Services

ELIZABETH BURNEY, M.A., B.LITT.*

Brit. med. J., 1967, 3, 41–42

By the end of 1968 a Royal Commission will have published its blueprint for modernizing the structure and functions of local government in England (a separate commission sits for Scotland; Wales, for rather inadequate reasons, has been excluded). By the mid-1970's there is every chance that a profoundly reformed system will be in operation. Naturally the size and utility of the local authority health department is being reviewed along with everything else. But, still more important for the health services as a whole, the new structure could provide the long-discussed but little-sought opportunity for unifying the three branches comprising hospitals, general practice, and the community health services. The key point is that this could now take place under local authority leadership, instead of local government merely running the third branch, as it does at present.

This may at first seem far removed from local government reform, which is concerned in the first place with the optimum size of the elected unit. But size is meaningless unless related to functions; indeed, one very obvious difficulty is that each separate function of local government might ideally operate under slightly different circumstances, so that every solution is something of a compromise. But the pattern that is expected to emerge is likely to be similar to that already established in Greater London (also excluded from the current review). Large "first tier" authorities will probably deal with such things as town planning, transport, education, and possibly housebuilding. Within these areas smaller "second tier" authorities would deal with more localized community services, such as welfare, parks, and refuse collection.

"Regional" Units

What size would these new authorities be likely to be? It is fashionable to talk of the largest units as "regional," but this word means different things to different people. Some people (including myself) would prefer these to be as large as possible, so that they would not be many more in number than the present economic planning regions—perhaps only a dozen in the whole of England and Scotland. Others (including officials at the Ministry of Housing and Local Government) have been encouraging the Royal Commission to think in terms of the largest unit being keyed to the major cities and their hinterlands, in a scheme which might eventually produce outside London 20 to 30 "city regions," each averaging over two million people. In any case the actual population size in relation to area is likely to vary widely in different parts of the country. The second-tier authorities are also bound to vary in size, but it is likely to be agreed that for effective contact with their populations they will have to be considerably smaller than the 200,000-population London boroughs. In country areas ease of communications rather than numbers of people served might be the governing factor.

The purpose of all this is not only to increase efficiency but to strengthen local democracy by creating local councils which can be seen to be functioning in a way that is relevant to the needs of modern society. This must mean, among other things, that local authorities regain some of their independence from trivial administrative control from Whitehall (though not from effective quality control), together with the financial means to exercise that independence. For example, it has been argued that petrol tax should be levied by local rather than central government, or that local authorities should levy a sales tax. All this and much more becomes credible once the mass of dead wood hampering the present system has been hacked away.

The relevance to the health services becomes more obvious once one starts to look at the kind of functional and organizational changes which the Royal Commission is likely to consider. Already another committee (like the Royal Commission, under the chairmanship of Sir John Maud) has reported on the "management" of local authorities. It has recommended the abolition of government by departmental committee in favour of a single management committee for determining the main lines of policy in all fields, to be advised by specialist committees. Once this was achieved (and it could take place with or without any structural changes in the authorities as a whole) the traditional career structure of the "professional" local government officers within specialist departments would become less rigid. For, though specialists would still be greatly needed, they would not need to be organized to fit the particular group of jobs allotted to a policy committee, but could be more sensibly grouped according to functions or skills.

---

* Staff writer, *The Economist*

Seebohm Committee

As an example of this—and one which directly affects the health services—yet another committee (the Seebohm Committee) is currently considering the future of the local authority "personal and allied services." It is likely to recommend that social workers, whose skills are in demand in many different fields but whose clients may often be the same people with different "problems," should form a separate social work department within the local authority, servicing other departments where necessary. Once this possibility is admitted there is no particular reason why hospital social workers should not also be part of the same or a related organization.

Similarly, housing is a subject which at present involves several different departments: the housing department itself, and the departments dealing with health, architecture, and planning. Yet no one could seriously claim that public health, in the Victorian sense, any longer has a major role in deciding which house should be demolished. Far better concentrate the whole process of building and redevelopment in a single department, which should probably be part of the first-tier authority (there is a good case for making the allocation and management of housing into a second-tier function).

In the course of reorganization, therefore, it looks as if the medical officer of health could lose his responsibility both for housing and for social workers, including the entire welfare set-up. Why indeed should the few remaining traditional responsibilities of the medical officer of health—midwives, health visitors, and a hodge-podge of sanitary and statistical responsibilities—remain as they are? If the health department as we know it disappeared the way would be open for a much more realistic allocation of professional, technical, and administrative responsibility in the health and allied services as a whole.

Area Health Boards

Radical reorganization is no new idea. Back in 1962 the committee appointed by the medical profession to review the medical services (the Porritt Committee)[1] strongly recommended unified control of the three branches of the health service. They proposed that the existing structure should be replaced by area health boards, to which all doctors and health employees should be contracted. Subsidiary professional committees, they suggested, should be responsible for general medical services, for hospitals, and for preventive and social health services. They envisaged that the only bodies that would remain outside (though linked to) the system would be the teaching hospitals. But, because no new health role was suggested for the local authority itself, the committee had to propose a rather awkward solution for the medical officer of health. He should, they said, become the head of a hospital department of social health staffed by health visitors, social workers, and midwives, and be responsible to the area health board. Nevertheless, he should remain responsible to the local authority for "environmental health and hygiene."

There was a great deal of sense in these proposals, but one noticeable omission. Rightly anxious to free the area health services from petty Whitehall interference, nothing in the way of democratic control was proposed to take its place, other than a vague reference to "capable and public-spirited individuals" on the area health boards. Inevitably the impression was given of a system proposed by doctors for doctors. Yet there can be no doubt that health is properly a subject of both local and national democracy. For one thing, a great many decisions concern a choice of public investment—should not a community have a say in whether to build a health centre or provide more kidney machines? Or whether to build more houses, or to provide more maternity beds for people living in poor conditions? An elected body may respond much more readily than a hospital or an independent board to demands from the community itself—for instance, local government has on the whole been much readier than the hospital service to provide child guidance clinics.

It should not in fact be difficult to fit a unified health service directly into the reformed local government structure, substituting for the vaguely autonomous area health boards of the Porritt proposals direct control by the local authorities themselves. The likelihood of a two- (or even three-) tier structure of local government should make this easier—for instance, the major hospitals (including the teaching hospitals, since there is no good reason to exclude them) could be controlled by regional units of local government instead of by the present regional hospital boards. Small local hospitals might fit better into the second-tier functions of local government. At all levels community and medical services could be better linked—thus general practice could suitably become a branch of the lower-tier authorities, the basic unit for all the personal health and welfare services. Public investment could be channelled into group practices, health centres, or Porritt-type departments of social health in hospitals according to the needs of the areas concerned.

More scope could be given to professional administrators to obtain top jobs in the community health services for which the medical profession is not necessarily more suited than any other. Much more scope could be given to doctors, particularly general practitioners, to develop new forms of community care with the full backing of the local authority's hospitals, social workers, and elected representatives. Whether there would still be anybody called the medical officer of health, or what his status would be, matters very little. What does matter is that the system should give doctors every opportunity to develop all branches of the health services in response to real needs, as well as developing the means of finding out what those needs may be. Local government reform could surely provide the opportunity for a better distribution of resources and better support to doctors and their patients.

REFERENCE

[1] *A Review of the Medical Services in Great Britain,* 1962. London.

CONFERENCES AND MEETINGS

Thoracic Medicine

[FROM A SPECIAL CORRESPONDENT]

A conference on various aspects of thoracic medicine was held at the Royal College of Physicians of London on 15 and 16 June. At the first session—under the chairmanship of Professor R. R. A. COOMBS, F.R.S. (University of Cambridge), and devoted to immunology—Professor J. G. SCADDING (Institute of Diseases of the Chest, London) reviewed the conditions in which antigen-antibody reactions were concerned. Classifying the four known types of hypersensitivity reaction, he said that only two of these were commonly associated with bronchopulmonary disease. Type I, the anaphylactic type with immediate weal and flare reactions, was a familial tendency seen in such conditions as hay-fever, perennial vasomotor rhinitis, and infantile eczema. Type III reactions were of the delayed, Arthus type present in farmer's lung. The other forms of hypersensitivity—the cytolytic or cytotoxic Type II—seen in haemolytic anaemia—and the tuberculin Type IV were of less importance in chest disease.

Professor Scadding went on to describe some of the features of aspergillosis—in which allergy to aspergillus infection caused asthma—and farmer's lung, which was an alveolitis due to inhalation of the spores of thermophilic actinomyces released from mouldy hay. There were similarities between the changes seen in the extrinsic asthma of aspergillosis and the alveolitis of farmer's lung which suggested a parallel with intrinsic asthma and cryptogenetic fibrosing alveolitis, and provided a line for future research, since some as yet unknown type of reaction might underlie the latter conditions.

Inhaled Organic Antigens

Concentrating on hypersensitivity to inhaled organic antigens, Dr. J. PEPYS (Brompton Hospital, London) said that Type I hypersensitivity reactions took place in atopic persons, who made up about 10% of the population. They had a constitutional predisposition to sensitization by ordinary, everyday substances, to which they produced reactions of rapid onset and short duration. Delayed hypersensitivity reactions of Type III were seen mainly among non-atopic individuals sensitized by intensive exposure. These reactions were slower in onset, more tissue-damaging, and more prolonged than those of Type I. Inhalation tests had shown that extrinsic asthma could be of either type alone, or mixed. Allergic alveolitis was of Type III and included a number of conditions resembling farmer's lung. These were all caused by fine organic dusts with particles small enough (about 1 μ diameter), to lodge in the alveoli—and included bagassosis, mushroom picker's lung, wheat weevil disease, bird fancier's lung, pituitary snuff-taker's lung, and suberosis caused by inhalation of cork or oak bark dust.

Dr. Pepys concluded by emphasizing that treatment for allergic conditions should always be directed to the patient as a whole and not confined to the immunological findings.

Describing recent work on autoallergic aspects of respiratory disease, Dr. MARGARET TURNER-WARWICK (Elizabeth Garrett Anderson Hospital, London) outlined studies which had demonstrated pulmonary autoimmune reactions of several distinct types. There was, as yet, no direct evidence of a causal connexion between autoantibodies and pulmonary disease.

Surveying the part played by immune reactions in coal-workers' pneumoconiosis, Dr. J. C. WAGNER (Llandough Hospital, Penarth) said that 1% of all coal miners still developed pneumoconiosis, while in Wales the figure was 4%. Evidence for an immunological factor in the aetiology was provided by the presence of a raised titre of rheumatoid factor in many patients with complicated pneumoconiosis. Thus the rheumatoid factor was found in the serum of only 7 out of 35 patients with simple pneumoconiosis, compared with 8 out of 10 with the Caplan type and 10 out of 15 with progressive massive fibrosis and vasculitis; there was often no joint disease in the patients with a raised titre. In the discussion Professor Coombs pointed out that nobody yet knew whether the rheumatoid factor played any part in the pathogenesis of rheumatoid arthritis.

Immunity-deficiency Syndromes

Dr. J. F. SOOTHILL (Hospital for Sick Children, London) discussed immunity-deficiency syndromes, which included functional and quantitative deficiencies in both humoral and cellular immunity. Thus circulating antibodies could be immunologically deficient, though present in normal quantities, or reduced in quantity—as in hypogammaglobulinaemia. Similarly, cellular immunity was deficient functionally in sarcoidosis and quantitatively in lymphopenia. Cellular immunity tended to be neglected because—compared with antibodies—it was hard to measure. Primary antibody deficiency occurred in several familial forms and in the "acquired congenital" hypogammaglobulinaemia of congenital rubella, while secondary deficiencies ranged from physiological low levels in infancy and childhood, to myelomatosis and toxic effects of drugs or neoplasia. As a method of clinical testing, electrophoresis was being superseded by direct immunological studies.

Surgical and medical aspects of scoliosis were the subject of the first morning session, at which Sir HERBERT SEDDON (Royal National Orthopaedic Hospital, London) took the chair. Mr. C. W. S. F. MANNING (Royal National Orthopaedic Hospital) classified scoliosis as postural—which tended to straighten on bending forward—and structural—in which there was fixed rotation and little alteration on bending. Progressive scoliosis was of the structural type and became more severe during growth, especially in early adolescence. Though vertebral, neuromuscular, and thoracic causes accounted for 44% of cases of structural scoliosis, the aetiology was unknown in 56% of 2,000 patients included in a survey, and over two-thirds of these "idiopathic" cases had been adolescents of 11 or over. Treatment consisted of support in a plaster cast or Milwaukee brace, designed to extend the spine without restricting the chest, or operation for spinal fusion.

Effects of Scoliosis

Turning to the medical effects of scoliosis, Dr. P. A. ZORAB (Brompton Hospital) said that breathlessness was associated with peripheral lung deficiency in addition to mechanical causes. Reduction in pulmonary vascular marking noted radiographically was most severe in congenital cases, and post-mortem pulmonary angiograms had demonstrated a definite reduction in peripheral vascularity. There were wide variations in exercise potential. Severe scoliosis could be compatible with full exertion, while mild scoliosis might be associated with severe dyspnoea and disability. On the other hand, pregnant patients generally had normal deliveries even if respiration was impaired.

Continuing, Dr. Zorab said that scoliosis did not cause heart murmurs and had little effect on the electrocardiograph, since the heart's electrical axis was not much changed. Cardiorespiratory failure in middle-aged scoliosis was best treated in much the same way as emphysema—with bronchodilators, antibiotics, and drugs which acted on the heart.

Virus Infections

At the second morning session the chairman, Sir CHRISTOPHER ANDREWES, F.R.S., introduced Dr. D. A. J. TYRRELL (Common Cold Research Unit, Salisbury), who outlined the types of virus known to cause respiratory infection in man. Many of these were very selective in their choice of host cells, and their study had been simplified by the introduction of respiratory epithelium tissue cultures obtained from man or apes. Dr. Tyrrell went on to classify respiratory viruses. The myxovirus group included the viruses of influenza, causing mainly influenza, bronchitis, and bronchopneumonia; parainfluenza 1 and 2, causing bronchiolitis; and parainfluenza 3 and the respiratory syncytial virus, which were both responsible for infections at each end of the age spectrum—bronchiolitis and bronchopneumonia—and also for colds.

Among other types, the rhinovirus caused upper respiratory tract infections, and the Coxsackie and adenoviruses mainly sore throats or feverish colds. By contrast, croup, tracheitis, and sore throats were often due to streptococcal infection. Respiratory viruses could live independently for short periods only and spread most commonly by coughing and sneezing, but hardly at all during speech or normal breathing.

Dr. N. C. **Oswald** (St. Bartholomew's Hospital, London), describing virus infection from the clinician's standpoint, regretted that clinical virology was virtually non-existent. Delays in obtaining a virological diagnosis by culture or immunological methods often meant that the treatment was settled and the patient out of hospital before a result was received from the virus laboratory. Electron microscopy, which could give very rapid results, was useful only for identification of the smallpox virus and the assignment of other viruses to particular groups.

Continuing, Dr. Oswald said that single complement-fixation tests had been performed on 100 consecutive patients admitted to the Brompton Hospital to try to obtain earlier diagnosis of virus infections, but this was only a beginning. More bridges would be needed between hospitals and the laboratory strongholds of the virologists if clinicians were to make intelligent use of antiviral agents when these became available.

Sir **Christopher Andrewes** concluded the session by questioning whether sneezes were necessarily the only means by which respiratory viruses spread. Simultaneous, widespread outbreaks suggested the likelihood of long-term virus latency.

Surface-active Agents

The afternoon session—under the chairmanship of Dr. K. **Robson** (St. George's Hospital, London)—was devoted to surface-active agents in the lungs, and Dr. R. E. **Pattle** (Chemical Defence Experimental Establishment, Porton) described some of the properties of normal alveolar lining fluid, which had a very low surface tension. He demonstrated that lungs in which the surface tension was increased by damage to the alveolar lining collapsed into an airless, liver-like state when deflated.

The importance of low alveolar surface tension in the newborn was emphasized by Dr. L. B. **Strang** (University College Hospital, London). Normal babies needed a pressure of about 18 cm. water for initial inflation of the lungs, followed by much lower pressures for subsequent breaths, whereas the lungs of immature infants required repeated high inflation pressures for each successive breath—because the alveolar surface tension was high and the lungs became airless on expiration. The ability to retain alveolar air and clear alveolar fluid via the lymphatics after birth depended on low surface tension, which probably developed in the human foetus at about 32 weeks.

Describing conditions in which alveolar surface tension was raised, Dr. C. M. **Ogilvie** (Liverpool Royal Infirmary) said that these were of two types: firstly, those in which the mean alveolar size was restricted by shallow respiration of any cause, pulmonary congestion, asthma, or emphysema ; and, secondly, those in which the lining film was abnormal, such as hyaline membrane disease, pulmonary oedema, postoperative atelectasis, respirator syndrome, pulmonary artery occlusion, bilateral vagotomy, and following oxygen or detergent inhalations.

Professor C. H. **Stuart-Harris** (United Sheffield Hospitals) was in the chair at the second afternoon session and introduced Dr. **Lynne Reid** (Brompton Hospital), who emphasized that hypersecretion from the bronchial tree was the fundamental disability in chronic bronchitis. Studies in the rat had shown that it was possible by inhalation of sulphur dioxide under sterile conditions to produce progressive changes closely resembling those of chronic bronchitis, but in which infection played no part.

Further, Dr. Reid had found it possible to compare in the rat carcinogenic with the chronic-bronchitis-inducing effects of inhalation of sulphur dioxide, cigar, or cigarette smoke. All three agents increased the flow of mucus, while cigarette smoke induced numbers of mitoses many times greater than those following inhalation of cigar smoke or sulphur dioxide.

Studies on Chronic Bronchitis

Describing the results obtained so far in prospective studies of chronic bronchitis, Dr. C. M. **Fletcher** (Royal Postgraduate Medical School, London) said that there was now considerable doubt whether infection governed the course of chronic bronchitis, except in the later stages. The most highly significant factors found were the initial level of the forced expiratory volume (F.E.V.)—which was related to the rate of decline—and cigarette smoking. No significant relationship had been found between the course of chronic bronchitis and such factors as episodes of infection, purulence of sputum, or sputum volume.

Though these studies had shown what appeared to be susceptible groups—with low initial F.E.V.—they had left us almost wholly ignorant of the pathogenesis of chronic obstructive bronchitis.

Dr. Fletcher also suggested that in future the histamine-inhalation test might help to distinguish asthmatic from bronchitic patients.

Advances in assisted respiration were the subject of the final session under the chairmanship of Professor Sir **Max Rosenheim**, P.R.C.P. (University College Hospital). The use of controlled oxygen supplements was described by Professor A. **Crampton-Smith** (Radcliffe Infirmary, Oxford) with special reference to intermittent positive-pressure respiration via endotracheal or tracheostomy tubes in the treatment of 52 patients with obstructive lung disease. A small group of patients in status asthmaticus had responded well without tracheostomy and with no deaths ; twenty-four hours of intermittent positive-pressure respiration was usually sufficient if treatment was started early enough.

Among patients with exacerbations of bronchitis, tracheostomy had been performed at twenty-four hours if continued positive-pressure respiration was necessary. There were twelve deaths—all in this group. Dr. J. M. K. **Spalding** (Radcliffe Infirmary, Oxford) concluded the meeting by describing the changes in circulation, renal function, and acid-base balance resulting from increased intrathoracic pressure.

TOMORROW'S BUILDINGS

New Teaching Hospital at Oxford

At a press conference in Oxford on 14 June details were announced of the new regional hospital planned for Oxford. The hospital will be built on a 69-acre site south-east of the city centre, part of which is occupied by the Osler and Sunnyside Hospitals. It is intended to serve two main functions—firstly, that of a community hospital, and, secondly, that of a major centre for medical research providing comprehensive teaching facilities at both undergraduate and postgraduate level.

Building on Phase I of the hospital is planned to start early next year. This will comprise a 167-bed maternity unit, the Nuffield Institute (a research laboratory), and residential accommodation for 147 staff. The maternity unit will be on seven floors, with an acute floor (including admission and delivery suites ; operating-theatres ; special nursing, medical care, and baby care units ; and the University Department of Neonatal Medicine) at ground level. The third floor will house the University Department of Obstetrics, while on the fourth, fifth, and sixth floors there will be wards containing a total of 141 beds. The seventh floor will house a 10-bed isolation unit with its delivery room together with a 10-bed private patients' unit.

It is hoped that building on the next stage of the development—Phase 2A—will start immediately after Phase I has been completed, possibly in 1971. This will contain a new accident and emergency department, beds for 450 patients, a new children's ward, and further residential accommodation. The University Grants Committee has approved the provision of a large research building to support the various clinical departments. In addition, there will also be a new headquarters for the undergraduate medical school with a central medical library, lecture theatres, and seminar rooms, and a demonstration hall. In this way it is intended to create an academic centre open to students, teachers, general practitioners, and local-health-authority staff alike.

The consultant architects for the new hospital are Yorke Rosenberg and Mardall.

WITHOUT PREJUDICE

I should like to begin this page once more with Mr. Desmond Donnelly's contribution to the debate in the House of Commons on 9 June, the debate in which other Labour M.P.s also had the courage to challenge outmoded concepts of running the N.H.S. "At root," Mr. Donnelly said, "what I am concerned about is the humanity of the State towards the individual. What I am representing, really, is a radical reaction on behalf of the individual against the State." That declaration of faith brings him straight into my political category of "progressive reactionary." He reacts and wants to progress.

Mr. Donnelly was concerned with the size of the human unit for doing certain jobs. We have moved, he said, from the city State to the nation State, and are now moving to the super-State. A nation of 50 million people is too small for certain purposes of defence and commerce. At least that is the argument. And now the super-State is, or is supposed to be, under the governance of the World State or United Nations. All this dwarfs the individual. He feels desperately insecure and frightened. The size of the machine and its omnipresence make the individual doubt even his own identity.

It is when the State descends to the particulars of a case that the individual feels deprived of his stature as an adult. It is at this point that doctor and patient both suffer when subject to remote decision and control. The nation State is the right unit for managing certain movements of health and disease. It must have an overall plan. It has to protect the ports and frontiers from invasion by germs. But it attempts to do too much when it tries to direct the work of the individual doctor or prescribe too closely the way of life of the individual patient.

* * *

The machine of Government gets clogged with the small bits and pieces of social and political life. This is worrying many people. "The only way," Mr. Donnelly said, "in which we can get this logjam of decision-taking broken up is by devolving from this House a large number of matters which come before it now." He called for wider groupings of local authorities: "We have to devolve a large number of what one might call the incidence of government to regional, elected authorities or parliaments." Mr. James Griffiths would hand over some of the planning functions to elected regional councils and entrust them with the administration of the hospital service.

I fear, however, that as a nation we may have reached the stage of administrative rigidity which makes radical reform or adaptation to new conditions impossible. As Mr. Donnelly puts it, even when administrators themselves admit the need for reform, "change can be prevented by bureaucratic complexity and by the disorientation of motive and lack of adaptability and initiative among the very class of men necessary to implement that change."

It seems, from a statement by the Government spokesman, Mr. Niall MacDermot, that the Government is likely to favour less radical proposals than those put forward. The general conception, according to him, "is that one would get a region comprising what at the moment would be one county, or perhaps two, and a city which would be a centre to that region. It would be a transformation of the present county level, I think, with one other level of local government below it." But he doubted whether this kind of change would speed up the making of decisions or result in any reduction in the size of the public service. It depended on whether a great deal of the power to make decisions was going to be transferred to a lower level. "This is where the crux of the problem arises as to what are the functions that one envisages should be devolved."

I hope that the Government will not be long in staging a full-scale debate on the matters brought to the surface on 9 June. As Mr. Houghton said then, "we have probably provided the agenda for another occasion." The worst possible thing that could happen is the slow and almost imperceptible deterioration of the N.H.S. accompanied by the silent but continuous protest shown by the rising figure for emigration.

* * *

I look forward to the first Henry Miller report, and hope he will beat the politicians to the post. But he won't if he thinks he is going to get another £500 million out of taxation. As Mr. Donnelly said in the Commons debate in reference to this, "If there is any honourable Member who knows how we can raise £500 million next year for this purpose let him stand up. It cannot be done." But I feel sure that with substantial devolution of power and responsibility—the two must go together—to the periphery local efforts to raise money will succeed. Region South-west will be determined to show a thing or two to Region South-centre. Local people will be eager to raise extra funds for *their* hospitals, for *their* kidney centre, for *their* health clinics. Their enthusiasm might even carry them to the extreme of being willing to pay for their ordinary drugs and even to spare the odd obol for their ordinary doctors. They must have a focus for pride and enthusiasm.

* * *

Support for devolution comes from quite a different quarter, I am delighted to see, in the article by the distinguished economist Colin Clark in his contribution to the *B.M.J.* on 27 May. "What I do want to say, as emphatically as possible," he said, "is that if there have to be public authorities providing medical service they should be local or regional, not national. There are strong objections to unduly large-scale organizations, in this as in other fields." But he is equally emphatic in his view that there will be genuine devolution of responsibility for running hospital and medical services only if the regional authorities spend their own funds raised from taxes or fees from the inhabitants in the region.

In this matter he too, like Mr. Donnelly, is concerned with the optimum size of an organization. How large is too large? He quotes Professor Florence as saying that "no man ought to be required to be responsible for supervising in the direct line of command more than five subordinates. . . ." Another authority has said that when the principal officials of an organization spend more time in committees than in getting on with their jobs the organization is too big. And Colin Clark quotes an eminent civil servant thus: "The bigger an organization grows the more readily it falls a victim to the disease of bigness—indecision, apathy, routine and red tape, personal intrigue, confusion of counsel and responsibility . . . duplication of effort, waste of time in establishing responsibility, elaborate consultation, petty sabotage." We have been warned.

Mammoth organizations and Government departments will go the way of all mammoths and plesiosaurs and such-like creatures if they overgrow their strength and therefore capacity to survive. As Colin Clark observes, it has all happened before. And he joins with Desmond Donnelly in pointing a warning finger to ancient Rome in the period of her decline and fall.

All this has to do with the health of the ordinary citizen and his relation with the hospitals in his neighbourhood and with the doctors and nurses and other health workers. The N.H.S. will have to be moulded afresh with the help of new minds determined to give it a secure local habitation within the national framework.

Or are we just to sit passively and watch the progressive decline of Britain as if it was a show on the television screen?

PERTINAX

Correspondence

Letters to the Editor should not exceed 500 words.

Casualty Department—or G.P. Service?

SIR,—A survey of patients was undertaken at this hospital to determine the way the casualty department was used. Each year about 11,500 new patients are seen, and there is a total attendance of 25,000. Eighty per cent. of the new patients and all re-attendances are seen by the casualty officers between the hours of 9 a.m. and 9 p.m. The remainder of the new patients presenting during the night are seen by the resident house-officers.

An analysis of all new patients attending over the three-month period from October 1966 to January 1967 was made. They were divided into four main groups.[1]

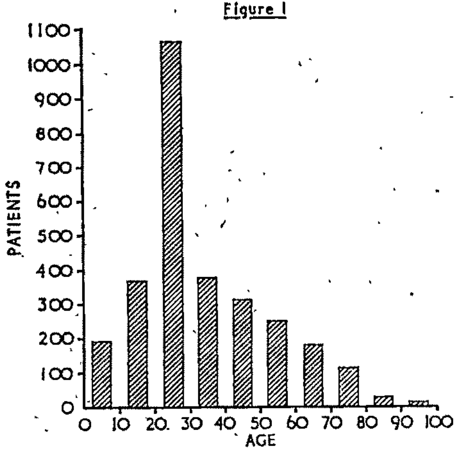
(1) Accidents.
(2) Medical emergencies.
(3) Surgical emergencies.
(4) Casual attenders.

All were then considered in relation to age. The reason why patients in Group 4, the casual attenders, came to hospital was also examined.[1-4] The survey was completed by correlating the cases with the population and type of area which the hospital serves.

Accident cases account for 52% of the patients seen, medical emergencies 9%, surgical emergencies 11%, and casual attenders 28%. These figures represent the average for all age groups, but there was no marked variation when each decade was considered separately.

A most striking feature which emerged was that nearly 40% of all new patients attending the department were between 20 and 29 years (Fig. 1).

Figure 1



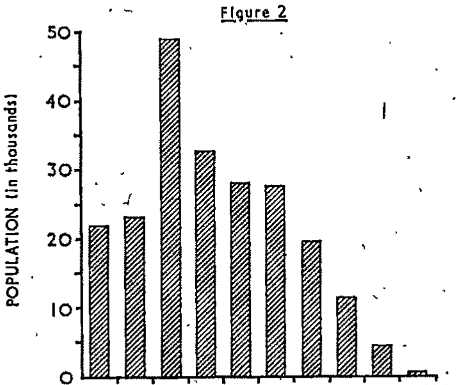
The reasons given by casual attenders for their call on the hospital service were:

(1) The patient had no general practitioner in this area—37%.
(2) It was more convenient to come to the hospital than to see or call their own doctor—27%.
(3) The patient's own doctor had no surgery that day or was not available—15%.
(4) Patient was a visitor to London—8%.
(5) The patient was under the care of the hospital for some complaint and therefore felt he or she should always be seen at the hospital—7%.
(6) The patient wanted a second opinion—6%.

The hospital serves mainly the Kensington and Chelsea districts—that is, the following London regions, W.8, S.W.5, S.W.7, and part of W.14. It is a densely populated area with heavy urban traffic, many hotels, but very little industry. All social classes are represented; there is a high student population and many young people living in "bed-sitters" and flats.

The number of young patients attending the casualty department is high, and this is probably typical of most casualty and accident departments.[1,3,5] It also conforms to the age distribution of the local population (Fig. 2).

Figure 2



There is a high percentage of casual attenders, but the department is still called "casualty" rather than an "accident and emergency department." We feel that a change to the latter would not cause a significant drop in the number of casual attenders because:

(1) A certain number of people will always present themselves at a hospital demanding attention.
(2) Type of area served: the department sees visitors to London if they are taken ill in this area.
(3) The shortage of general practitioners.

This last factor seems significant. Nearly 40% of the casual attenders are not registered with a general practitioner in this locality, and of these nearly a quarter had tried to register with one or more doctors before seeking the aid of the casualty department. We assume that if the other three-quarters of the casual attenders with no local doctor attempted to register they would meet with the same problem. Of our casual attenders 10% are registered with a practitioner in another area. About 25% of all our patients resident in this area (as opposed to visitors and those in transit) have no local general practitioner. It has been stated that there is no need for hospitals to provide a general-practitioner service.[2,5] Our experience suggests that if this hospital did not maintain its "open door" policy many people in this locality who required medical attention would receive none.—We are, etc.,

W. A. D. GRIFFITHS.
P. A. KING.
B. J. PRESTON.

St. Mary Abbots Hospital,
London W.8.

REFERENCES

[1] Garden, R. S., *Lancet*, 1965, 1, 901.
[2] Fry, L., ibid., 1960, 1, 163.
[3] Lowden, T. G., ibid., 1956, 1, 955.
[4] Mestits, P., *Brit. med. J.*, 1957, 2, 1108.
[5] Report of the Subcommittee on Accident and Emergency Services, Ministry of Health Standing Medical Advisory Committee, Central Health Services Council, 1962. H.M.S.O.

Endotracheal Tubes

SIR,—Reviewing the changing pattern of anaesthesia in a general hospital, Professor W. W. Mushin and his colleagues note that the greatest number of operations in any one year of life occurred in children up to 1 year.[1] It is probable that there is an increased use of endotracheal anaesthesia in infancy.

In 1962 experts from the Admiralty, War Office, Air Ministry, and others assisted the British Standards Institution to draw up a specification for endotracheal tubes.[2] Tubes to this standard are now marked according to the internal diameter. They are available from 2.5 mm. to 11 mm. in 0.5-mm. steps with an allowed tolerance of ±0.2 mm. The thickness of the wall in the first five tubes is identical—namely, 0.6 mm., with a tolerance of +0.2 mm. or −0.1 mm. A 4.5-mm. tube has a wall thickness of 0.6 mm., but a 5.5-mm. tube has a wall twice as thick—1.2 mm. Thus what at first sight appears to be an even grading results in considerable differences in external diameters. Also the limits of tolerance allowed the manufacturers permits quite a large variation.

The area of the air passage at the level of the cricoid ring of the newborn is approximately 14 sq. mm.,[2] and 1 mm. of oedema will reduce this area by 65%.[3] Familiarity with the Hagen-Poiseuille law may tempt junior anaesthetists to use too large a tube for an infant, especially if relying on a formula to calculate the correct size. If tubes were available with a more even progression in their external diameters this law might be more safely and less traumatically applied.—I am, etc.,

W. F. O'M. DOHERTY.

North Middlesex Hospital,
London N.18.

REFERENCES

[1] Mushin, W. W., Campbell, H., and Shang Ng, W., *Brit. J. Anaesth.*, 1967, 39, 323.
[2] *British Standards Institution Specification B.S. 3487*, 1962, p. 11.
[3] Wilton, T. N. P., and Wilson, F., *Neonatal Anaesthesia and Allied Problems*, 1965, p. 3., Oxford.

Heavy Uterine Bleeding

SIR,—In reply to a question (20 May, p. 494) your expert says that for practical purposes the only haemorrhagic disease associated with heavy uterine bleeding as a direct effect of the disease is idiopathic thrombocytopenic purpura. It is certainly the most important disease in this respect, but I think there are others which, although they are rare, should be remembered.

Buxton,[1] in reviewing 108 cases of purpura haemorrhagica, aplastic anaemia, and leukaemia, showed that in no fewer than 10 of these patients the initial and chief complaint was menorrhagia, and they were first seen at a gynaecological clinic. Hysterectomy was performed on one of them. The uterus revealed no pathology, and the patient died from aplastic anaemia. A second case of aplastic anaemia and a third of acute lymphatic leukaemia were likewise fatal. The other seven cases were of purpura haemorrhagica. Wheaton[2] reported three cases of leukaemia which presented as gynaecological emergencies. I have seen three fatal cases in which heavy uterine bleeding was the first sign of a blood disease. All three were admitted as gynaecological emergencies. One was a case of subacute lymphatic leukaemia and the other two were examples of agranulocytosis due to toxic drugs.

In my opinion abnormal uterine bleeding may be an important symptom of the following diseases of the blood: aplastic anaemia; agranulocytosis; the leukaemias; the purpuras; splenic anaemia; and secondary thrombocytopenia due to *x* rays or toxic drugs.—I am, etc.,

Bloxham,
Oxfordshire.

J. M. GATE.

REFERENCES

[1] Buxton, C. L., *Amer. J. Obstet. Gynec.*, 1941, 42, 502.
[2] Wheaton, C. E. W., *Brit. med. J.*, 1952, 1, 30.

Prevention of Rh Haemolytic Disease

SIR,—Recent reports[1-4] have demonstrated clearly the value of anti-D gammaglobulin in preventing the stimulation of Rhesus (D) antibodies by transplacental leakage of foetal red cells. Because of the shortage of anti-D gammaglobulin much attention has been devoted to the dose necessary to provide protection in routine use. As none of the series yet published has been able to include a case of massive transplacental haemorrhage so treated, the following case may be of interest.

A 21-year-old primigravida, blood group A Rh (D) negative with no antibodies detectable in the 34th week of pregnancy, was admitted in labour at 41 weeks to Portwey Hospital under the care of Mr. S. H. Riterband in September 1966. After a labour lasting 54½ hours, assisted breech delivery of a living male child weighing 8 lb. 5 oz. (3.78 kg.) took place. The condition of the infant initially appeared satisfactory but later deteriorated, and after 24 hours he was noted to be extremely pale. Haemoglobin was 8 g./100 ml., blood group A Rh (D) positive, direct Coombs test negative, serum not icteric. Examination of maternal blood at this stage revealed by the acid elution test[5] that a massive transplacental haemorrhage had occurred. Approximately 3,400 foetal cells were present in 50 low-power fields; equivalent to about 170 ml. of foetal blood. Precisely when the haemorrhage took place is not clear, but examination of the foetal heart record indicates that it was not more than twelve hours before delivery.

Anti-D gammaglobulin (5 ml.) was very kindly supplied by the Department of Medicine, University of Liverpool. The strength of this preparation was probably of the order of 700 μg./ml.[6] Owing to delay in diagnosis and transport difficulties the time interval between delivery and intramuscular administration of the gammaglobulin was just over 72 hours. The injection evoked no reaction in the patient.

Thirty-six hours after the injection the volume of foetal blood in the maternal circulation was reduced to about 80 ml., and these remaining cells gave a positive direct Coombs test. Free antibody was demonstrable in the serum at a titre of 1 in 4 by indirect Coombs test against R_1R_2 cells. On the tenth day after gammaglobulin less than 0.25 ml. of foetal blood was present and free antibody was still detectable to a titre of 1 in 4.

At three months and seven months after delivery maternal blood was examined for the presence of immune anti-D. None was detectable by saline, albumin, enzyme, or indirect Coombs techniques.

Whether the blocking of antigen sites on the foetal cells or the presence of free antibody is the determining factor, this case demonstrates that 5 ml. of anti-D gammaglobulin is sufficient on both counts against a foeto-maternal transfusion equivalent to more than half the blood volume of the baby. Absence of immune antibody, though not constituting absolute proof, suggests that immunization may have been prevented and that the proposed dose of 1 ml. for use in the cases more commonly found may well be sufficient.

I am indebted to numerous people, in particular to Professor C. A. Clarke, for assistance and to Mr. S. H. Riterband for permission to publish this case.

—I am, etc.,

County Laboratory,
Dorchester,
Dorset.

B. E. GILLIVER.

REFERENCES

[1] Woodrow, J. C., *et al.*, *Brit. med. J.*, 1965, 1, 279.
[2] Clarke, C. A., *et al.*, ibid., 1966, 1, 213.
[3] —— ibid., 1966, 2, 901.
[4] Gorman, J. G., Freda, V. J., and Pollack, W., *Lancet*, 1965, 2, 181.
[5] Kleihauer, E., and Betke, K., *Internist (Berl.)*, 1960, 1, 292.
[6] Clarke, C. A., personal communication.

Unusual Bone Abnormality in Congenital Rubella

SIR,—The radiographic changes in the skeleton which are considered to be pathognomonic of congenital rubella have been described in detail by Rudolph *et al.* and Singleton *et al.*[1-3] Briefly, these consist of poor mineralization with irregularity of the growth plate and altered trabecular pattern in the metaphyses of long bones. The distal ends of the femora are particularly affected. These usually heal spontaneously. Retardation of knee ossification centres also occurs. These bony abnormalities are more likely to occur in infants with multiple rubella defects. The lack of periosteal reaction has been stressed. Recently, Peters and Davis[4] have reported details of an infant with the congenital rubella syndrome in whom there was considerable periosteal new bone formation in several long bones, together with the usual features of rubella osteopathy. The infant had thrombocytopenic purpura and they postulated that the changes were the late results of subperiosteal haemorrhages.

An unusual bone lesion has recently been observed in a male infant with congenital rubella. The mother had rubella four weeks after her last menstrual period. The infant had bilateral cataracts and suffered from unexplained heart failure in early life. Rubella virus was recovered from the nasopharynx and the urine on admission at 3 weeks of age, and on several occasions up to 8 months. Platelet counts were normal. Psychomotor development at 12 months of age was delayed.

At 3 weeks of age a skeletal study showed mild but typical metaphysial lesions in the tibia and femora, and delayed development of the distal femoral and proximal tibial epiphyses. There was poor mineralization of the skull with ill-defined suture margins, but some irregular thickening was present in the frontal region. In the right clavicle an area of rarefaction was present towards the lateral end of the bone and lying centrally within it. In the next three months this lesion expanded and sclerosis and thickening due to periosteal new bone formation developed medially. At 7 months the medial and middle thirds of the bone were thickened but the lesion had not expanded further. At 1 year the right clavicle was of normal shape and structure.

This unusual clavicular lesion could represent a true osteitis due to rubella. Maternal rubella is known to have occurred in this case 28 days after the last menstrual period; thus foetal infection occurred at a very early stage in development. It is noteworthy that the clavicle is the first bone in the foetus to ossify. Ossification proceeds initially from two centres developing at about 5–6 weeks of intrauterine life. The time of the intrauterine infection may explain the localization and nature of the lesion in this case.—We are, etc.,

W. C. MARSHALL.
KATHLEEN HAYES.

Department of Virology,

A. R. CHRISPIN.

Department of Radiology,
The Hospital for Sick Children,
London W.C.1.

REFERENCES

[1] Rudolph, A. J., *et al.*, *J. Amer. med. Ass.*, 1965, **191**, 843.
[2] —— Singleton, E. B., Rosenberg, H. S., Singer, D. B., and Phillips, C. A., *Amer. J. Dis. Child.*, 1965, **110**, 428.
[3] Singleton, E. B., Rudolph, A. J., Rosenberg, H. S., and Singer, D. B., *Amer. J. Roentgenol.*, 1966, **97**, 82.
[4] Peters, E. R., and Davis, R. L., *Clin. Pediat. (Philad.)*, 1966, **5**, 743.

West Indian "Stomach"

SIR,—I was most interested to read Dr. K. A. Taylor's letter headed "West Indian Stomach" (3 June, p. 641). However, I was surprised that he did not find more conditions related to the chest.

I have recently returned from a spell of general practice in the West Indies, and when a patient complained of his "stomach" this usually referred to the chest or anything between the neck and epigastrium. The abdomen was usually referred to as the belly, and a fairly common presenting symptom would be "a cuttin' in the belly," "a cuttin'" meaning pain. The commonest complaint was of the "bad feels" and it was often very difficult to get any further than this. The word discharge did not seem to be used in any form and to ask if there was a vaginal discharge was of no avail, this being always referred to as "inflammation." One thing I did find most curious was that although the word " period " was not used, menses was clearly understood (and was an everyday word), although women were usually rather coy of mentioning having missed them and that they might be pregnant. It was often rewarding because of this to question any woman in her reproductive years about her menses if she came along with some other rather trivial complaint.

Hypertension was common to an extent that I often found myself considering whether the English idea of normality ought to apply. Strokes were common, a stroke being referred to as a " passover," but interestingly enough hypertensive left ventricular failure was infrequent, possibly because their coronary arteries are better able to deal with the muscular hypertrophy. It might be of interest to note here, for those interested in the aetiology of coronary artery disease, that although the sugar content of the diet was high (a sugar-producing country) there seemed to be very few cases of coronary artery disease in the practice. A common complaint was of " a beatin' in the head " and this was invariably associated with concern regarding their blood pressure, and it was always expected of the doctor to check their blood pressure if they came with this complaint. Often it was normal and they could go away happily reassured.

With further reference to the anatomy I found it helped a great deal when I learnt from my seniors that a complaint regarding the foot could apply to any part between the toes and the buttock, and a complaint regarding the hand to any part between the fingers and the shoulder; up till then I had found it a little confusing when the patient placed his hand on his hip and referred to a pain in the foot.

I must make it clear that the coloured section of the practice was principally drawn from agricultural workers on the sugar plantations together with a smattering from other occupations (hotels, etc.) and the observations I have made deal solely with my experience in this practice. The work was practical, interesting, and variable and if private general practice could be associated with a free national pharmaceutical service as well as a free hospital service it would seem to me the ideal way to practise medicine. Poverty was no barrier to proper medical care, abuse particularly with regard to visits was minimal, and the frivolous use of one's time was at a premium which the patient both expected and accepted.—I am, etc.,

NORMAN V. EDWARDS.

Stowmarket,
Suffolk.

" Izeised " English

SIR,—We feel that the editors of journals have a duty to protect the English language. You have just published an article entitled " Lymphocyte Transformation in Thymectomized and Nonthymectomized Patients with Myasthenia Gravis " (10 June, p. 679). Would not " The Influence of Thymectomy on Lymphocyte Transformation in Myasthenia Gravis " have been a better title?—We are, etc.,

J. R. BELCHER,
L. H. CAPEL,
Editors,
British Journal of Diseases of the Chest.
London E.2.

Pericarditis in the Tropics

SIR,—Dr. K. Somers's article " Pericarditis " (13 May, p. 423) makes many statements with which I agree entirely, but the following exception prompts me to write, lest a useful drug be discarded by some of your readers. Saying that " emetine usually has no effect on hepatic amoebiasis " is as far from the truth as making the same statement about penicillin G and beta-haemolytic streptococci. On occasion one may find chloroquine to be more effective in a specific case than emetine, but just as often the opposite may be found. The advantages of an oral versus an intramuscular medication should not be overemphasized when the patient is ill enough to be in hospital. The toxicity of both drugs makes it valuable to be able to choose between the two and not be forced to use only one.

Emetine has been effective for the treatment of hepatic amoebiasis since first reported by Rogers,[1] and it continues to be a most useful and life-saving drug. Our experience[2] would make us think that the batch of the alkaloid used by Dr. Somers must have come from an unreliable source before we would consider that the Ugandese variety of *Entamoeba histolytica* is emetine-resistant.—I am, etc.,

RODOLFO HERRERA LLERANDI.

University of San Carlos Medical School,
Guatemala, C.A.

REFERENCES.

[1] Rogers, L., *Brit. med. J.*, 1912, 1, 1424.
[2] Herrera-Llerandi, R., *J. Thorac. cardiovasc. Surg.*, 1966, 52, 361.

Infant-scalp Vein Needles

SIR,—Dr. C. F. P. Wharton's description about the use of infant-scalp vein needles (10 June, p. 702) has been quite interesting. I describe here a further use that these can be put to in adults, best illustrated by a brief case history:

> A 29-year-old man with acute fulminating ulcerative colitis had to have four operations in a period of three months. Repeated blood transfusions, continuous intravenous feeding, checks on haemoglobin, blood urea, electrolytes, etc., together with an extreme degree of wasting, had led to the blockage of almost all his superficial venous channels by thrombosis. These felt like thick cords under his skin. Nearing the end of his last operation for removal of the terminal colon and rectum his intravenous infusion stopped and intravenous cannulation became impossible. As the patient was slightly shocked, immediate cut-downs were made, first on both his cephalics, and then his saphenous, only to reveal thick cords without any lumen.
>
> In desperation a scalp vein needle was inserted into a small peripheral vein on the right wrist. To our surprise, in spite of all his superficial veins being blocked proximally, the flow through this was rapid and adequate, and 2 pints (1,080 ml.) of blood and 1 pint (540 ml.) of plasma could easily be pumped through this with the aid of a Martin's pump. Intravenous infusion was continued through the same needle for four days postoperatively, when it finally stopped. A similar one was put into a small vein on the other side and continued for a further four days.

Thus it seems that an infant-scalp vein needle can be used in shocked adults with collapsed veins where it may be difficult to get into a vein with a Branula, Intracath, or an ordinary " giving " set needle, especially when a cut-down has failed, as contrary to expectation one can easily pump blood, plasma, or fluid through it at great speed.—I am, etc.,

H. F. NAGAMIA.

Dorset County Hospital,
Dorchester.

Cephaloridine in Acute Pulmonary Infections

SIR,—Dr. P. Howard (27 May, p. 573) states that cephaloridine in a dose of 6 or 8 g. daily might be very effective in bronchial infections. This has been confirmed in a controlled trial in patients with severe and resistant, chronic, purulent bronchial infections.[1] Cephaloridine was compared in doses of 2, 4, and 6 g. daily to penicillin 6,000,000 units with streptomycin 1 g. daily. With the 2 g. dose of cephaloridine, penicillin and streptomycin was significantly more effective, with the 4 g. dose equal in effect, and with 6 g. definitely inferior both in short- and long-term clinical and sputum assessment. Unfortunately 6 g. daily of cephaloridine is associated with massive outpouring of hyaline casts.[2] Although this cast excretion is of uncertain and doubtful significance, 6 g. of cephaloridine daily should be given only when other antibiotics have failed and/or where the patient is very ill.—I am, etc.,

A. PINES.

Ware Park Hospital,
Ware,
Hertfordshire.

REFERENCES

[1] Pines, A., Raafat, H., Plucinski, K., Greenfield, J. S. B., and Linsell, W. D., *Brit. J. Dis. Chest*, 1967, 61, 101.
[2] Linsell, W. D., Pines, A., and Hayden, J. W., *J. clin. Path*, 1967. In press.

Banning of Heroin

SIR,—May I point out that the manufacture and distribution of heroin has been banned in Australia for a number of years (1 April, p. 53). This does not seem to have hindered the illegal trafficking of this drug, but merely to have pushed up the price on the black market. After using heroin in practice in England for a number of years I find its prohibition in Australia irksome to me, and an unnecessary injustice to an unfortunate few of my patients.

A letter on this subject published in the *Medical Journal of Australia* recently[1] produced no response at all from fellow practitioners. The greatest tragedy of this ban seems to be that we have a generation of doctors here that is unaware of the merits of this drug, but only the dangers they read of in the Sunday papers.—I am, etc.,

B. HEBER.

Mudgee,
New South Wales, Australia.

REFERENCE

[1] Heber, B., *Med. J. Aust.*, 1966, 1, 1091.

Drug Addiction

SIR,—In your leading article on " Drug Treatment Centres " (20 May, p. 455) you point out that we know little yet of the ecology of the different types of drug addiction, or of the social factors which encourage or precipitate it. While drug addiction is fortunately quite rare, a taste for pop music is almost universal among young people and pop singers are acknowledged leaders of fashion. It is therefore an alarming development that the worlds of pop and drugs are becoming more and more closely identified in peoples' minds. Not only are there widely publicized pronouncements by entertainment personalities regarding narcotics, but many popular lyrics carry thinly veiled references to drug-taking and the word "psychedelic," with all its associations, is freely used in press reviews of pop records.

Surely the image projected by popular entertainers is a powerful social factor which favours drug-taking.—I am, etc.,

J. TWOMEY.

Stourbridge,
Worcestershire.

Tremulous Iris

SIR,—We are interested in the syndromes associated with congenital non-traumatic ectopia lentis. In your recent leading article on tremulous iris (11 March, p. 585) you state that osteogenesis imperfecta has been recorded, accompanied by ectopia lentis, in a patient reported by Behr in 1913,[1] a citation also given by J. H. Stone[2] and V. A. McKusick.[3] This paper in fact described a 38-year-old widow who suffered progressive diminishment of visual acuity from the age of 12. Severe myopia with bilateral microcornea, keratoconus, and blue sclerotics were found on examination two years later. At the age of 19 years her hearing was noted to be poor and she became totally deaf in her early twenties. Her most troublesome complaints were due to recurrent spontaneous dislocations of the large joints; at first the left foot and knee joints and later a dislocation of the left shoulder joint occurred while the patient was "carrying a laundry-bag downstairs." She was observed in the University Eye Clinic in Kiel for 24 years and ectopia lentis was never recorded.

May we add that the title of Behr's paper was most misleading—"Keratoconus, blue sclera and chronic dislocation"?—We are, etc.,

MARTIN CAREY.
OLIVER FITZGERALD.

Department of Medicine
and Therapeutics,
University College, Dublin,
and St. Vincent's Hospital,
Dublin.

REFERENCES

[1] Behr, C., *Klin. Mbl. Augenheilk.*, 1913, **16**, 291.
[2] Stone, J. H., *Amer. Heart J.*, 1966, **72**, 466.
[3] McKusick, V. A., *Heritable Disorders of Connective Tissue*, 1966, 3rd ed., p. 246. St. Louis.

Inflatable Splints

SIR,—Dr. Heather Ashton's article on the danger of inflatable plastic splints (10 December 1966, p. 1427) has been received with disbelief by clinicians in this country who have used it. Controlled experiments by J. B. Spooner and colleagues (4 February, p. 297) showed that the indirect method of recording blood flow described in Dr. Ashton's article was inaccurate because the sensing device itself was subjected to the pressure of the splint. For some reason Dr. Ashton ignored publications dealing with the safety of the principle.

My interest in the clinical application of circumferential pneumatic compression dates back to the second world war, when I began to apply the principle of the aviation G-suit to prevent postural hypotension in patients operated upon in the sitting position.[1] Experience showed that if a wrap-around plastic G-suit was inflated with a patient supine its splinting effect would interfere with placing him in the sitting position. This suggested the idea of an inflatable splint, and an experimental model was developed at the Cleveland Clinic in 1952. In 1958[2] the effectiveness of this principle in controlling bleeding was reported. The manner in which circumferential pneumatic compression stops arterial bleeding without interrupting blood flow was described in 1966.[3-4]

When we first began to investigate the pneumatic splint we also thought it dangerous to employ pressures in excess of capillary pressure.[5] For this reason it was decided to study the problem in the laboratory. We began by employing a pressure we felt certain would cause gangrene in the dog's leg. Because the marked tapering of the hind leg caused the inflated splint to creep downward at high pressures, the foreleg was selected. The pressure in the splint was held at 180–200 mm. Hg for five hours. On recovery from anaesthesia the dog walked normally and with no apparent ill effects. In the next test a pressure of 300 mm. Hg was applied for six and a half hours. This dog exhibited only a wrist drop, which cleared within a week. In the next animal a pressure of 300 mm. Hg was applied continuously for ten hours. After the splint was removed the leg became extremely swollen. The oedema subsided in seven days, but a wrist drop persisted for five weeks. There was no loss of tissue nor other evidence of damage. These results suggest that circumferential pneumatic compression applied to a large area of a limb is safer than when applied to a small area, as by a blood-pressure cuff. Why this should be so is at present being investigated.

Angiographic studies employing time-lapse cinematography were done on the foreleg of a dog whose blood pressure was 170/110. With pressures in the splint above the systolic the flow of Hypaque in the brachial artery appeared to be completely arrested; despite which, within seconds, some of the medium appeared in veins below this level. At a pressure of 120 arterial flow was present during systole. At a pressure of 90 flow was maintained during diastole. These findings, admittedly at variance with the theory of the critical closing pressure of blood vessels, were not mentioned by Dr. Ashton.

Hartman[6] employed the inflatable plastic splint as a dressing after meniscectomy. He applied it from mid-thigh to a point above the ankle at 30 mm. Hg for 48–72 hours. It prevented oedema and effusion, and for some unexplained reason oedema of the protruding portion of the limb did not develop.

Dr. Ashton describes her splint in which two layers are sealed together at intervals to produce longitudinal, inflatable sections. She reaches the conclusion that pressures are applied only to sections of the limb beneath the inflated portions. We tried this principle and found that pressure on the limb under the uninflated strips was greater than that under the inflated portions. This is a demonstration of the law of Laplace. Since Dr. Ashton quotes A. C. Burton, with whom I have been in communication during my studies, obviously she is aware of the law of Laplace.

Dr. Ashton further states that "in all patients tested rhythmic contraction of the forearm muscles after inflation of the splint produced typical ischaemic muscular pain in the forearm after 10 to 20 contractions." This is at variance with some unpublished data from the Cleveland Clinic. A pneumatic splint was applied to the calf in six patients with intermittent claudication. In each case inflation to 30 mm. Hg (by actual measurement) resulted in no reduction in the claudication distance.

Unfortunately, Dr. Ashton's article has now been abstracted in *Modern Medicine*. The further dissemination of this publication is certain to deny to innumerable patients the benefits of this amazingly safe, therapeutic device.—I am, etc.,

W. JAMES GARDNER.

Cleveland, Ohio 44115,
U.S.A.

REFERENCES

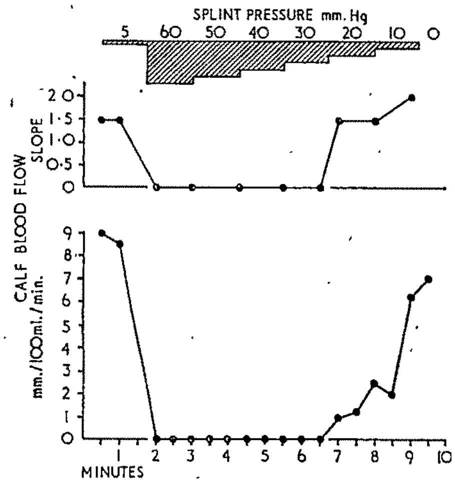
[1] Gardner, W. J., and Dohn, D. F., *J. Amer. med. Ass.*, 1956, **162**, 274.
[2] —— Taylor, H. P., and Dohn, D. F., ibid., 1958, **167**, 985.
[3] —— ibid., 1966, **196**, 491.
[4] —— and Storer, J., *Surg. Gynec. Obstet.*, 1966, **123**, 792.
[5] —— *Cleveland Clin. Quart.*, 1962, **29**, 54.
[6] Hartman, J. T., ibid., 1965, **32**, 1.

SIR,—I have been interested in the correspondence provoked in your columns by my paper (10 December 1966, p. 1427) in which it was reported that a plastic splint applied to a limb and inflated to a pressure of 30–40 mm. Hg may impair the underlying circulation. I am surprised by Dr. W. J. Gardner's statement above that my findings have been received with disbelief in the U.S.A., since a recent paper by Ginsberg *et al.*[1] from Fort Howard, Maryland, not only confirms my findings but also adds a warning that the effects on the blood flow in the enclosed limb should be taken into account by prospective users of the splint.

Both Dr. Gardner and Drs. J. B. Spooner, S. J. Corne, and R. J. Stephens (4 February, p. 297) are doubtful about the validity of the method used to assess blood flow, because the sensing device was subjected to the pressure of the splint. However, I also showed in my paper (Fig. 3) that the same results were obtained when blood flow was measured distal to a splint and the sensing device was not subjected to the splint pressure.

Moreover, my results are by no means isolated findings peculiar to the method employed. Many workers, using a variety of methods, have shown that the application of an external pressure to a limb or digit causes a reduction and sometimes a complete cessation of blood flow. For example, Burton and Yamada[2] with pressure plethysmography of the forearm, Roddie and Shepherd[3] with heat flow discs on the fingers, and Gaskell and Krisman[4] with microscopic observations of nailbed capillaries, all came to the same conclusion, and their results have been confirmed by other workers. In all these studies an external pressure of 40 mm. Hg was regularly observed to reduce blood flow considerably, and in a proportion of subjects flow was apparently reduced to zero.

In addition, studies with radioactive sodium injected into the calf or forearm muscle show that the clearance of this may cease altogether in some subjects when a splint is inflated around the limb to pressures around 40 mm. Hg (see Fig.). These studies are being carried out with Professor D. N. Walder, Department of Surgery, University of Newcastle upon Tyne. Non-clearance of radioactive sodium from an area of muscle can only mean that there is no blood flow through that area of muscle, and this observation thus supports the other evidence that inflation of a splint can on occasion stop the blood flow, at least through muscle.



Blood flow in the calf of a normal subject under a plastic splint enclosing the foot and leg from above the knee. Splint inflation pressure is indicated at the top of the Figure. Upper trace shows the rate of clearance of radioactive sodium injected into a portion of calf muscle (in arbitrary units representing the slope of disappearance of the isotope). Note that a horizontal slope indicates that there is no clearance. Lower trace shows blood flow in ml./100 ml./min. as measured simultaneously with a mercury-in-rubber strain gauge around the calf.

Thus at least five different methods for assessing blood flow have given results in similar circumstances. All these methods, as Dr. Gardner points out, are indirect, for there is no direct method for measuring blood flow through small vessels, such as arterioles, in intact human limbs subjected to external pressures. But there is direct evidence from microscopic examination of intact mammalian vessels that small vessels can and do suddenly close down when arterial transmural pressure is lowered.[5] A theoretical reason for this has been discussed by Burton,[6] and the presence of a flow cessation pressure in vascular beds,[7] whatever the mechanism by which it is caused, is generally accepted among circulatory physiologists.

Apparently conflicting evidence was reported by Dr. Gardner,[8] who found that in dogs with splints inflated around the forelimb the injection of 10 ml. of a radio-opaque medium into the subclavian artery is followed by visualization of the medium in the brachial artery and subsequently in the veins. He did not state, however, the pressure at which the radio-opaque material was injected. Yet this must have been above the systolic blood pressure, and the injection must therefore temporarily have raised the transmural arterial pressure. This would have the same effect as temporarily lowering the splint pressure and would allow an opening up of small vessels that were previously closed. Therefore his findings cannot be accepted as showing that under normal circumstances an appreciable blood flow continues through small vessels under an inflated splint. The main arteries are known to remain open, as evidenced by the fact that arterial pulsation in the part under the splint is undiminished, and it may be that a trickle of blood, confined to bone or interosseous vessels protected from receiving the full splint pressure, persists.

For similar reasons, the experiments of Drs. Spooner, Corne, and Stephens cannot be considered relevant to the usual situation under a splint, for in assessing blood flow they used a congesting cuff pressure greater than diastolic pressure. As noted by Greenfield[9] "too high a pressure in the collecting cuff may cause it to act as a valve, preventing diastolic reflux, and artificially elevating the mean arterial pressure downstream." Diastolic reflux of blood occurs in a variety of conditions[10] [11] and almost certainly occurs in the present case.[3]

The important practical question, of course, is not whether the blood flow can cease absolutely under a splint but whether a considerable reduction in blood flow might be harmful. Even apart from the evidence already referred to, most observers who have seen the blanched skin under a plastic splint, and the reactive hyperaemia on its removal, agree that the blood flow is at least reduced. My purpose in publishing my results was to warn users of such splints of their possible effect on the circulation. They may not have harmed the normal dogs referred to in Dr. Gardner's letter, but can one be sure, for example, that severe reduction in blood flow does not delay the healing of fractures ? Can one be certain that a tightly inflated splint will not precipitate gangrene in a diabetic with an already impaired peripheral circulation ?

Proper precautions, however, need not detract from the general usefulness of the splint. In some circumstances the reduction in blood flow resulting from splint inflation may be useful *per se*, for instance in controlling haemorrhage.[12] Dr. Welply (4 February, p. 297) also suggests that a reduction in blood flow might sometimes be desirable. Nevertheless, I would maintain that until further information is forthcoming it would be prudent to ensure that splints of the present design are not inflated to pressures exceeding 30 mm. Hg.—I am, etc.,

HEATHER ASHTON.

Department of
Pharmacology,
The Medical School,
Newcastle upon Tyne 1.

REFERENCES

[1] Ginsberg, M., Miller, J. M., and McElfatrick, G. C., *J. Amer. med. Ass.*, 1967, **200**, 180.
[2] Burton, A. C., and Yamada, S., *J. appl. Physiol.*, 1951, **4**, 329.
[3] Roddie, I. C., and Shepherd, J. T., *J. Physiol. (Lond.)*, 1957, **136**, 498.
[4] Gaskell, P., and Krisman, A. M., *Circulat. Res.*, 1958, **6**, 461.
[5] Lamport, H., and Baez, S., *Physiol. Rev.*, 1962, **42**, Suppl. No. 5, p. 328.
[6] Burton, A. C., *Amer. J. Physiol.*, 1951, **164**, 319.
[7] Ashton, H., *Clin. Sci.*, 1962, **22**, 79.
[8] Gardner, W. J., and Stoner, J., *J. Amer. med. Ass.*, 1966, **196**, 491.
[9] Greenfield, A. D. M., *Amer. J. Med.*, 1957, **23**, 675.
[10] Wilkins, R. W., and Bradley, S. E., *Amer. J. Physiol.*, 1946, **147**, 260.
[11] Holling, H. E., and Verel, D., *Clin. Sci.*, 1957, **16**, 197.
[12] Gardner, W. J., and Stoner, J., *Surg. Gynec. Obstet.*, 1966, **123**, 792.

Frozen Sections

SIR,—Your leading article "Frozen Section in Surgery" (18 March, p. 651) prompts us to remind you of our previous letter to you.[1] We do not agree that frozen section "remains unchallenged in the rapid diagnosis of lesions before their treatment by surgical means.". As reported previously, drill biopsy[2] [3] performed as an outpatient procedure provided a correct diagnosis in 96% of patients with lumps in the breast, and a report of the histology on a paraffin section could be obtained within 24 hours. The advantage of having a histological report in this way is that it enables the surgeon to plan the subsequent treatment with the patient's full knowledge and co-operation. In our experience drill biopsy causes little trauma to the breast and opens up fewer venous and lymphatic channels than does an open biopsy.—We are, etc.,

T. J. DEELEY.
IAN BURN.

Hammersmith Hospital
and Royal Postgraduate
Medical School,
London W.12.

REFERENCES

[1] Deeley, T. J., and Burn, I., *Brit. med. J.*, 1966, **2**, 235.
[2] —— *Acta Un. int. Cancer*, 1960, **16**, 338.
[3] —— and Pollock, D. J., *Brit. J. Cancer*, 1966, **20**, 442.

Colistin in Purulent Bronchial Infections

SIR,—I read the article of Dr. A. Pines and his colleagues (27 May, p. 543) with interest. I cannot agree, however, that colistin has no place in the treatment of purulent exacerbations of chronic bronchitis. At least 50% of the patients treated with colistin[1] by inhalation at this hospital were chronic bronchitics, with acute purulent exacerbations of their condition.

Since the winter of 1965–6 *Pseudomonas pyocyanea* infections have ceased to be a problem in this hospital.—I am, etc.,

N. P. HALLIDAY.

Queen Mary's Hospital,
Sidcup, Kent.

REFERENCE

[1] Halliday, N. P., *Clin. Trials J.*, 1967, in press.

Crush Injuries of the Chest

SIR,—We would like to reply to some of the points raised by Dr. J. M. Leigh in his letter (6 May, p. 374). Apart from the early cases in our series, we have measured Pa_{O_2} (or Sa_{O_2}) in all our patients, and the results obtained were invariably low when the patients were breathing air.

Referring to those patients who have a low Pa_{O_2} and a low P_{CO_2}, Dr. Leigh says, "Any beneficial effects of intermittent positive pressure respiration (I.P.P.V.) in such a patient are due to a lowering of V_{O_2} as a result of the abolition of respiratory effort and sedation produced by the drugs given, and also the alleviation, to a certain extent, of atelectasis by the positive pressure." From the point of view of blood gas results this is largely true, although reduction of any pulmonary oedema or congestion present will also raise the Pa_{O_2}.

However, we feel that the benefits of I.P.P.V. extend beyond the correction of abnormal blood gas values. I.P.P.V. affords greater patient comfort, both by preventing painful over-riding of fractured ribs and by permitting the use of adequate doses of analgesics. The early use of I.P.P.V. will tend to obviate the later development of the "wet-lung" syndrome. Furthermore, the use of I.P.P.V. by effecting the internal splinting of the fractured ribs prevents subsequent gross deformity of the thoracic cage.

Dr. Leigh also refers to the possible deleterious effects of I.P.P.V. on cardiac output and cerebral blood flow. Our usual practice is to use the minimum positive pressure commensurate with adequate ventilation. However, the pressure required depends on the state of the lungs, and if the compliance is low, high inflationary pressures are necessary. If severe hypotension does occur as the result of I.P.P.V., this is treated with vasoconstrictor drugs.—We are, etc.,

W. BARGH.
H. W. C. GRIFFITHS.
K. B. SLAWSON.

Department of Anaesthetics,
The Royal Infirmary,
Edinburgh 3.

Accident Services

SIR,—Mr. Daniel Lamont's letter (6 May, p. 374) raises questions which are of fundamental importance to ambulance services, to first-aid teaching, and to the need for hospital-based flying squads to give on-the-spot resuscitation. I have tried to get recent evidence of the causes of death in those brought in dead following road-traffic accidents in this county, and have failed to find hard facts which could be used to decide how many of these deaths could be averted by medical care subsequent to the injury.

Pathologists vary in their estimates of deaths from airway obstruction — some putting the figure as high as 25%; others, regarding agonal vomiting as a "normal" finding, give a lower percentage. Neurosurgeons cite pneumonia due to inhaled vomit or secretion as the commonest cause of death following head injuries in which the brain damage does not kill the patient. The number of deaths from airway obstruction and from the inhalation of vomit or secretions can be influenced by good first aid.

Some deaths may occur at the scene of an incident, and some casualties could not be saved by any techniques available today. What percentage of the total do these cases represent? What is the role of airway obstruction, bleeding, and other causes in such deaths? And, out of those found alive at the scene of an incident, how many could be kept alive by a combination of first aid and resuscitation? What are the causes of death during the ambulance ride? What percentage of these deaths is preventable? And what action is required to improve the existing situation?—I am, etc.,

A. WARD GARDNER.

Esso Refinery,
Southampton.

Unexpected Foreign Body

SIR,—I wonder what percentage of dentures are made with radio-opaque material?

This week a patient presented himself at the surgery with a persistent cough present for about four months. Four months ago he had an accident at the pit during which he was knocked unconscious. He missed his dentures at the time but did not think it worth mentioning to me. Since then he has been in and out of the surgery with a cough, purulent sputum, etc. An *x*-ray of the chest six weeks ago was negative. Yesterday during a most violent paroxysm of coughing he coughed up his dentures, which measured about 2 in.×½ in. (5.08 cm.×1.27 cm.) and came, presumably, from his trachea.

He has since then had a repeat chest *x*-ray, once more negative, and also an *x*-ray of his dentures, which were not opaque. Surely this is dangerous and such dentures should not be allowed to be made.—I am, etc.,

G. STEIN.

Sutton-in-Ashfield,
Nottinghamshire.

Intrauterine Contraceptive Devices

SIR,—I have read with interest the article on intrauterine contraceptive devices in the "Current Practice" series, written by Dr. J. Frampton and Mr. D. Mathews (10 June, p. 683). Since they mention the Saf-T Coil but have no figures available yet, I think this is a good time to mention to you the preliminary findings of a series I am doing.

The patients are drawn from the Oldchurch Hospital gynaecological department and the Westminster Branch of the Family Planning Association.

During the year June 1966 to May 1967 162 patients were fitted with a Saf-T Coil 33S. This is the device with the double spiral and two nylon threads in the cervical canal. A total of 694 woman months have been recorded. The expulsion rate and removal rate compare very favourably with the published figures of other devices. Two devices have been expelled, both two months after insertion during a menstrual period.

Seven devices have been removed: one after nine months as a further pregnancy was desired; one after one month for sepsis (this device was inserted early in the puerperium); five for menorrhagia (three of these were noted to have menorrhagia before).

Of this series, 12 patients had already expelled Lippes Loops C. Four of these had expelled them on two occasions. Two other patients had already tried Lippes Loop C but the device had been removed for menorrhagia. Two patients had tried Birnberg bows, but these were removed for menorrhagia. Thus in this series a total of 16 patients had already found other devices unsatisfactory.

As many of the patients wished for maximum protection from pregnancy they were offered the opportunity of using Emko foam as well, but it was discovered that most of these discontinued the foam after the first two months. A total of 33 patients elected to use the foam. One patient in this series has become pregnant.

A total of 497 woman months have been observed where the Saf-T Coil alone was the only method of contraception. This compares very favourably with the pregnancy rate of other devices. It is interesting that the two expulsions and the pregnancy occurred in patients who were fitted with their devices in the months of January, February, and March this year when the fixed red marker on the introducer had been changed to an adjustable one. I feel that these three devices may well have been inserted too low into the uterus, and since this technique has been adjusted no further expulsions have occurred.

This preliminary report suggests that the Saf-T Coil may well have a lower pregnancy rate and expulsion rate than other devices so far reported.—I am, etc.,

KATHLEEN FRITH.

Oldchurch Hospital,
Romford, Essex.

SIR,—May I add our experience with the Saf-T-Coil 33-S to your very helpful article on intrauterine contraceptive devices by Dr. John Frampton and Mr. Dudley Mathews (10 June, p. 683).

In this practice I have now inserted 50 Saf-T-Coils, covering a period of approximately 200 woman months, and have been more than favourably impressed by:

(1) The ease of insertion; there have been no failures to introduce the coil.

(2) No cervical dilatation has been found to be necessary in any case.

(3) None have been expelled.

(4) Patient acceptability. There have been no requests to remove the coil.

(5) The advantage of a complete unit in a pre-sterilized pack, which means there is no need to sterilize any other instrument.

(6) Last, but not least, no pregnancies to date.—I am, etc.,

J. STUART BROWN.

West Malling,
Kent.

Hypophysitis and Hypopituitarism

SIR,—The description of the case of hypophysitis and hypopituitarism by Drs. R. Hume and G. Hefin Roberts (27 May, p. 548) certainly suggests an autoimmune basis for the disease. A number of patients with hypopituitarism for which no cause has been found have been studied at Charing Cross Hospital. Sera have been sent to my colleagues with the suggestion that pituitary antibodies might be present. Preliminary investigations only have so far been made, but clearly pituitary antibodies should be sought in patients with idiopathic hypopituitarism. —I am, etc.,

P. B. S. FOWLER.

London W.1.

"Cruachan"

SIR,—The article on "Cruachan" (17 June, p. 758) was of great interest to me. In London a hostel for diabetic children, now at Palingswick House, Hammersmith, has long experience of the problems mentioned in the article and has been dealing with them, since its foundation, originally at Hutton during the war (1939–45), when the need presented itself for special arrangements for diabetic children in the evacuation period.

It is the experience of this Inner London Education Authority hostel that an increasing number of the children needing such provision show, in addition to the diabetes, various disorders of behaviour and very frequently a social problem also.

Only a small proportion of diabetic children need hostel accommodation, and for differing lengths of time, but for those who do there can be little doubt that it is a valuable measure, and most of them learn quickly to manage their own diabetic life.—I am, etc.,

A. B. STEWART,
Medical Adviser,
Inner London Education Authority.

County Hall,
London S.E.1.

A Matter of Principle

SIR,—The recent Conference of Local Medical Committees (24 June, *Supplement*, p. 177) has gone down in history as officially recording an overwhelming vote against the "principle" of payment for special experience and service. This must surely, without doubt, be the most incredible and shameful decision ever taken by a conference of learned professional men living in a democracy. I am glad that my name was recorded as voting against it. There were a few of us there who felt that this was an extremely serious matter of principle, and unfortunately the conference saw fit to allow none of us to put any opposing view forward. Presumably the profession will now ask the Government to cease paying any vocational training allowances, as these allowances are entirely payment in recognition of special experience. Presumably, also, we shall now ask that doctors on the obstetric list will be paid at the same rate as doctors not on the obstetric list.

That this shameful state has arisen is, I am sure, entirely the fault of members of the General Medical Services Committee who phrased the wording of the referendum. I sincerely believe that the vast majority of people who voted in the referendum do not really disbelieve in the principle of rewarding merit, and that they were answering an entirely different question. The question which they answered, and which I believe is the question which should have been put, is, "Do you believe that it is possible to devise a completely fair scheme for distributing merit awards in a way suggested by the Working Party?" Had this been the question put, I am sure that there would have been an almost 100% answer of "No."

I wonder what will be the feelings and thoughts of any young doctor about entering a branch of the profession which has stated overwhelmingly it does not believe in the rewarding of merit? I believe, and I know that I am not alone, that if the conference had been willing even to consider—which it was not—a scheme for the direct and automatic reward for the possession of certain criteria it might have been possible to persuade the Government to give favourable consideration to using the £2½m. This is already done in the armed Forces and public health services by the payment of extra money for the possession of diplomas. Once the Ministry and the profession had agreed what attributes they would like to see the general practitioners possessing I do not see how any Government could fail at least very carefully to consider the rewarding of these attributes directly. Now that the fear that a scheme involving selection and secrecy might be imposed on the profession has been removed, I hope and trust that every general practitioner will spare a few minutes seriously to consider the real implications of this appallingly bad decision taken at the recent conference. Then perhaps pressure can be brought through the local medical committees to see to it that, while rejecting the Working Party's proposal, it again becomes the policy of family doctors that as a matter of principle whenever possible and practicable merit shall be rewarded.—I am, etc.,

Talgarth, Brecs. J. M. LONDON.

B.M.A. Action

SIR,—My motion that modern techniques of sampling public opinion should be used by the B.M.A. to find out whether the public thinks enough money is being spent on the N.H.S. was carried without a dissenting vote by the Junior Members Forum.[1] As Dr. J. F. Pigott said, nothing would be gained from this if Mr. Enoch Powell was right in saying[2] that present expenditure reflects electoral opinion. But Mr. Powell's argument that the constancy of N.H.S. expenditure must reflect electoral opinion is a *non sequitur*. If both major political parties have the same policy on this the electorate is gagged. Their real opinions can be brought to light only by research. A trace of action here would achieve more than years of talk. Since the Ministry (if it agrees with Mr. Powell) has the onus of proof and the B.M.A. that of disproof, they should co-operate in the experiment.

If raising the N.H.S. budget were electorally popular would not one or both parties have included it in their platform? That presupposes an infallible clairvoyance by politicians that has sometimes failed them in the past. The N.H.S. is assumed to be good enough if the public makes few complaints. The answer is put the public in the picture first and then ask if the N.H.S. budget is adequate. The taxpayers have to judge whether the N.H.S. should have priority over other claims on the revenue. We do not know for sure what their verdict would be. But if they supported the B.M.A.'s view that more money should be spent on the N.H.S. the profession would have a vastly more powerful weapon than it had ever had, since public opinion is the dynamite that moves Governments.

Many doctors think the extra money urgently needed by the N.H.S. should come from direct payments by patients. But it is generally thought that the majority of the electorate believe that medicine should be financed out of taxes, not by direct payment. Would not the future of medicine be far brighter if doctors and patients were united on this? The last Tory Minister of Health dismissed direct payment in one sentence. Do we seriously think Mr. Kenneth Robinson will be more amenable?—I am, etc.,

Bristol Royal Infirmary,
Bristol.
R. S. CORMACK.

REFERENCES

[1] *Brit. med. J. Suppl.*, 1967, **2**, 115.
[2] *Brit. med. J.*, 1967, **1**, 556.

Recognizing Experience

SIR,—Much has been heard recently about efforts to reverse the "brain drain" of doctors. My present predicament highlights one reason why these are unlikely to be successful.

In New Zealand I held a registrar appointment for nine months and was for three months a senior house-officer at the Postgraduate School of Obstetrics and Gynaecology in the University of Auckland, a post which is recognized by the College in this country. On my return I took an appointment as senior house-officer, necessary for approved training purposes, and applied for protection of salary through my regional board. The reply they received from the Ministry stated that there are no provisions for reckoning experience outside the hospital service in this country for incremental purposes.

It seems strange to find that in a so-called "national" service a colleague from the same hospital in Auckland, when he first came to work in this country, was allowed full credit for his experience.

I wonder how many others have had such preferential treatment and how many like myself have had experience shunned, perhaps because they have had the misfortune to work for one of the less sympathetic regional boards.

Obviously you must choose your regional board carefully, and those lured from overseas to return to the N.H.S. should be aware that the experience thus obtained, unless under the auspices of the Ministry of Overseas Development, is of no value to the N.H.S. and they would be well advised to stay where it is appreciated.—I am, etc.,

Luton and Dunstable Hospital,
Luton, Beds.
R. H. T. WARD.

Is There a Shortage?

SIR,—One year ago the Seventh Report of the Review Body on Doctors' and Dentists' Remuneration[1] contained the observation (paragraph 59, iii): "There is no sign . . . that there is any difficulty in filling (consultant) appointments."

However, the Joint First Report on the Negotiations with N.H.S. Hospital Doctors and Dentists (*Supplement*, 27 May, p. 135) includes the following: "The Department pointed out that some existing consultant posts were difficult to fill. . . . They undertook to invite . . . all boards to re-advertise vacant posts."

There seems to be an inconsistency here which calls for an explanation from the Ministry.—I am, etc.,

ROBERT J. EVANS.

North West Surrey Group Laboratory,
St. Peter's Hospital,
Chertsey, Surrey.

REFERENCE

[1] *Review Body on Doctors' and Dentists' Remuneration, Seventh Report*, 1966, Cmnd. 2992. H.M.S.O.

Merit Awards to Hospital Staff

SIR,—The attitude of hospital staff towards merit awards is at present being assessed by a postal ballot conducted by the British Medical Association, and the position concerning these awards has also been dealt with by letters in the *Daily Telegraph* of 16 June *et seq.*

If merit awards are to continue, and there may be a case for this, it is clear that it is generally felt that the present secrecy which surrounds them should be abolished, and they should be fair and seen to be fair, and that all senior hospital staff wherever employed and all regions should be treated equally. These standards can be achieved in two ways:

(1) By "paying the rate for the job." For example, a professorial chair of surgery would presumably be paid at a higher rate of salary than other surgical appointments. Further, this higher rate would apply equally in London, Bristol, or Aberdeen Universities, or others.

(2) Each consultant, S.H.M.O., and registrar, and perhaps administrative medical officers in the hospital service, should have a "personal merit rating" and the markings, as officially laid down on this rating, should be known to him. The marking could be made on the following sort of basis:

(*a*) Research or development work carried out. This assessment to be made by an award council in the specialty concerned.
(*b*) Teaching commitments.
(*c*) Clinical or administrative responsibility.
(*d*) Seniority and experience in the specialty.
(*e*) Higher professional qualifications.
(*f*) Committee services. Assessments to be by regional boards.

If such a system were adopted many of the present anomalies would be overcome and every man would benefit according to the merit rating to which he was entitled. The ethical objections to the secrecy of the present system and the patronage which it of necessity brings in its train would be resolved.—I am, etc.,

Winchester, Hants. C. REMINGTON-HOBBS.

New Constitution

SIR,—Much has been written and said by many for years now on the matter of a new constitution. The Memorandum by the East Yorkshire Branch (*Supplement*, 3 June, p. 143), in the opening paragraph referring to the Revised Report on the Constitution, states: "It should be viewed as a battle in the 100 years' war between the centre and the periphery for power." This surely is what the whole thing is all about. As long as we are all fighting among ourselves our real opponents will continue laughing. We have a great need to foster understanding and to effectively co-operate all along the line, so that members see justice done by a fully effective fighting force, with representation and representatives and leaders in whom we can all have confidence. Surely only by proportional representation, as far as practically possible, can we even have that power of overwhelming membership which would come when the profession with unity speaks with one voice. A strong organization would automatically attract members to it. The new constitution seeks to do this. I firmly believe that at this stage the memorandum by East Yorkshire can only hope to cause further delay in what is long overdue. Further delay must be dangerous.

East Yorkshire fears that power will be taken from the periphery. I hope that East Yorkshire will carefully consider Motion 340 by City of Aberdeen: "That the Scottish representatives on the Representative Body should be nominated by the Scottish Council." There are obviously differing problems in different areas, otherwise there would not be such a wide range of opinions.

Idealists and realists who will not settle their differences often end up with revolution. Revolution within the Association might have undesirable, unforeseeable, and uncontrollable effects. The solution to this particular problem must surely be something that tries to balance the swinging pendulum of opinion.—I am, etc.,

C. C. LUTTON,
Honorary Secretary,
East and Midlothian Division,
British Medical Association.

Musselburgh, Midlothian.

Invasion of Privacy

SIR,—In due course I shall be forced under section (5), paragraph 7, part I, schedule I, *Statutory Instruments*, 1966, No. 1210, to accept entry of a local doctor to inspect my practice premises, which are in my private home.

My wife and I have always regarded this term of service as an invasion of personal privacy and ethically and morally wrong. Surely it is about time this term of service was deleted in just the same way as the "test prescription" term of service was deleted on moral and ethical grounds.—I am, etc.,

Southampton, Hants. J. G. TEES.

General Practice

SIR,—As a principal in general practice who finds himself ten years qualified this month, I have been reflecting on the matters which perplexed and distressed me during my progress towards becoming established. On qualifying M.B., Ch.B. I little realized how ill-prepared I was for general practice. My Alma Mater had provided me with no special tuition for this branch of my profession. I didn't know an E.C.10 from an O.S.C.1, and was ready to be exploited by public and patient alike.

I was quite naive about my obligations and rights as an assistant or principal. The legal aspects of partnership or assistantship agreements, despite their importance, were a complete mystery to me. At that time, of course, there was unemployment among doctors, and written agreements were often overlooked. An assistant often had to accept without question a dangerously high proportion of the work of the practice without adequate training or experience. The salary was £800 per annum and you provided and ran your own car out of it. Rotas were unheard of, and four hundred applicants for a practice vacancy was not uncommon.

During the last ten years I have waited in vain for the establishment to produce a mandatory basic contract or agreement for assistants and junior partners; to guarantee a minimum stipend for assistants and a minimum proportion of partnership profits for junior partners; to guarantee that a junior partner reaches parity with his fellow partners within a reasonable length of time; to guarantee that all junior partners receive a written agreement; and to outlaw once and for all the concealed sale of goodwill. These guarantees would make general practice a much more attractive calling for the young man who wants to settle down and make a career of it. But the G.M.S.C. have refused to take definite action on the grounds that the affairs within a partnership are only the concern of the partners themselves, and beyond the terms of reference of that committee. What a fatuous position to adopt on such a fundamental issue involving the careers of so many general practitioners.

Apart from the organization of refresher courses, the Royal College of Practitioners has made no impression on me at all during my ten years since graduation. Yet this is the very body which one would have thought would have pioneered a career structure for young general practitioners in this country, just as the other Royal Colleges have done in their own fields. I am forced to assume, therefore, that the College is happy with the *status quo*.

I am bound to agree that most of my criticisms would be answered by the introduction of a salaried service, yet I myself have many reservations about this, as I feel that my status would be reduced to that of a local authority medical officer. If, however, there were guarantees that my position and clinical freedom remained as at present, and if I were assured that the G.M.S.C., the Council of the B.M.A., the Annual Conference of Local Medical Committees, the Royal College of General Practitioners, and the Ministry of Health would all be abolished, and that general practice would be run as an independent corporation along the lines of B.O.A.C. or the Electricity Board, beyond the influence of the politicians, then I would agree to a salaried service. Then I would feel that the next ten years, for a man graduating in 1967, would present a much more stable and attractive career than the last decade presented to me.—I am, etc.,

Glasgow S.3. DUNCAN STRANG.

Ice-cream Van Accidents

SIR,—In our experience here a not uncommon cause of head injury in young children has been the acute suppression of caution and road drill by the prospect of ice-cream. They have usually been hit by passing vehicles when, at the sound of the bell, they rush blindly to the van to purchase, or as they run back home to consume.

We should be interested to hear from your readers whether this special type of accident is widespread throughout the country. If it is, some publicity might encourage its prevention.—We are, etc.,

M. BRIGGS.
JOHN M. POTTER.

Accident Service,
Radcliffe Infirmary,
Oxford.

"Intimations of Immortality?"

SIR,—Graduates of this university must have felt a glow of pride to see Lister's original paper of 1867 reprinted in the *B.M.J.* (1 April, p. 9). Less gratifying have been the continuing requests for reprints that have subsequently come here addressed to Dr. Joseph Lister, University of Glasgow, Glasgow, Scotland. Your readers may wish to ask themselves whether this mode of address should be regarded as a subtle and graceful compliment to Lister's immortality, or merely points a moral to both those who issue and those who receive requests for reprints.—I am, etc.,

The University, Glasgow. C. M. FLEMING.

Obituary Notices

J. ST. GEORGE WILSON, M.C., M.B., CH.M., F.R.C.S., F.R.C.O.G.

Mr. J. St. George Wilson, formerly a consultant obstetrician and gynaecologist in Liverpool, died on 4 June, at the age of 76.

John St. George Wilson was born in China on 8 April 1891, and received his medical education at Liverpool University, graduating M.B., Ch.B. in 1914, and taking the Conjoint diploma in the same year. He served in the Army during the first world war, and after demobilization began training as an obstetrician and gynaecologist. He held resident and registrar appointments successively at the Liverpool Royal Infirmary and the Shaw Street Hospital for Women, and studied for a time in Vienna. In 1921 he was admitted Fellow of the Royal College of Surgeons of England and was awarded a mastership in surgery by his own university. His ability and industry were such that by 1925 he held appointments as honorary assistant obstetrical and gynaecological surgeon at the Liverpool Royal Infirmary, and honorary assistant surgeon at the Liverpool Maternity Hospital. Later he was appointed consultant obstetrician at Walton Hospital, and also joined the consultant staff of the Hoylake and West Kirby Cottage Hospital. He was a foundation member of the Royal College of Obstetricians and Gynaecologists and was elected to the Fellowship in 1933. During the nineteen-twenties onwards he was one of the outstanding obstetricians and gynaecologists in the north-west, and well known throughout the country. He was a member of the Gynaecological Club, and rarely missed a meeting of the North of England Obstetrical and Gynaecological Society.

T. N. A. J. writes: The North of England Obstetrical and Gynaecological Society was always lively, and never more so than when St. George Wilson was present. His quick brain and ready wit made him a master of repartee if not debate. His views were always definite, and he never hesitated to express them in forthright if few words. In him courage overruled discretion; this earned him a Military Cross during the first world war, but, combined as it was with brusqueness, often made him enemies later.

Despite this St. George Wilson was a great man, having vision as well as knowledge, and being a first-rate clinician and surgeon with an extensive experience. His gifts were such that he could have achieved anything that he wanted, anything from a large practice to positions of administrative importance in the profession. But he did not want such things. St. George Wilson found it impossible to conform; he liked to be different for the sake of being different, to disagree even when he subconsciously agreed. He enjoyed being a lone wolf and he was pre-eminently a "no" man. It was these characteristics which made him in August 1948 retire from his hospital appointments long before his time had expired. He could not stomach working under the conditions of a National Health Service. Yet before he went he took care to arrange matters so that the newly created university whole-time team could take over his unit at the Liverpool Royal Infirmary. It was such magnanimous actions, and care for the interests of his juniors, as well as his extraordinary ability, which endeared him to those who knew him best, and this despite his foibles.

After leaving his professional activities St. George Wilson became a farmer or market-gardener, but his restlessness persisted. At no time in his life, it is said, did he live in the same house for more than three years at a time. For one short period he lived in South Africa. His disappearance from the scene during the last twenty years resulted in the fact that few of the present generation of obstetricians and gynaecologists know his name, and extremely few realize what they, and obstetrics as a whole, owe to him. It was St. George Wilson who led the way in the revolution in obstetric practice which was a feature of the 1920–40 period. Brought up in the old school, he adopted and created new approaches. He tried out every new management of toxaemia as it was introduced. He was a leader in antenatal care, conducting each one of his clinics personally. His book *Prenatal and Postnatal Management*, which appeared in 1937, even included all details of antenatal as well as postnatal exercises.

St. George Wilson's greatest contribution to the literature was his article "Lower Uterine Segment Caesarean Section," which appeared in the *Journal of Obstetrics and Gynaecology* in 1931. In this he described fifty consecutive operations carried out personally since 1926 using the transverse incision in the lower segment. These operations were carried out late in labour in neglected cases, often infected, and long before sulphonamides or antibiotics were discovered. Only one patient died. The lower segment operation had been carried out previously in three or four isolated cases in Britain, and more frequently in other countries, but his was the first series of operations to be performed in this country. Moreover, he perfected his technique to such an extent that he was prepared to treat patients by trial of labour rather than by elective section, to employ the operation for conditions such as prolapsed cord and placenta praevia, and to make it take the place of difficult vaginal delivery and the then traditional obstetric manœuvres. The introduction of lower segment caesarean section into Britain is often credited to the late Charles Marshall. This is incorrect. Marshall, and all the other younger obstetricians working in Liverpool in the early 1930's, learned the operation from St. George Wilson and followed his teaching implicitly. The gospel spread across the north of England, and ultimately pervaded the whole country. As a result it can be claimed that St. George Wilson more than any other individual was the father of modern obstetric practice, at least as it applies to Britain. As a gynaecologist, too, St. George Wilson was among the best. Technical skill alone was not enough for him; he paid attention to medical gynaecology, and especially to pathology. Indeed, he never accepted a pathologist's report on tissues removed without examining each section himself.

That this man, who contributed so much to obstetrics, should of his own volition disappear into obscurity for the last twenty years of his life was tragic. Yet it is typical of him. Indeed, if he were alive today he would forbid any tribute or any mention of his achievements. To those of us who knew and admired the man despite all his quirks it is important to place on record his greatness, if only to make modern obstetricians realize to whom they owe their present good fortune of practising obstetrics in a relatively easy and safe way. We should remember him, as well as his wife, his daughter, and three sons, who survive him. One of his sons is a member of the medical profession.

E. H. T. CUMMINGS, C.B.E., D.C.L. M.D., D.P.H., D.T.M.

Dr. E. H. T. Cummings, a former senior medical officer in the Colonial Government of Sierra Leone, died suddenly on 17 June in Freetown, Sierra Leone. He was 76.

Eustace Henry Taylor Cummings was born in Freetown in 1890. He came to Britain in 1912, and was one of the first Africans to read medicine at the University of Liverpool, where he qualified with the Conjoint diploma in 1917, graduating M.B., Ch.B. in 1918 and taking the D.P.H. in the same year. He had a distinguished academic career, and was awarded the John Garrett international fellowship in bacteriology for 1918–19 and the M.D. was conferred on him for his thesis in that year, when he also took the D.T.M. After serving house appointments, including the post of additional police surgeon in Birmingham, he was appointed by the Secretary of State in 1920 as medical officer, Sierra Leone. In 1941 he was appointed M.B.E. In 1944 he was made a member of the Elliot Commission on higher education in the Colonies, and whose report and recommendations resulted in the establishment of the Universities of Ibadan and of Ghana. He and the late Arthur Creech-Jones, M.P., played an active part in insisting that Fourah Bay College, now the University of Sierra Leone, and the oldest institution of higher learning in West Africa, should be retained as a university college of Durham University and developed into an autonomous university.

This has now been accomplished. After retiring from the Colonial Medical Service he served on the council of Fourah Bay College, and his services were recognized by the conferment of the honorary D.C.L. of Durham University in 1960. He was in active professional practice up to the day of his death.

Dr. Cummings served for five successive years as Mayor of Freetown, and in 1952 was appointed C.B.E. for public service. He was president of the Sierra Leone Branch of the British Medical Association in 1955.

Until recent years Dr. Cummings was a frequent visitor to Britain, and was a well-known figure in both London and Liverpool. He is survived by his wife, Janet, and by a son and daughter.—I. G. C.

F. G. L. BARNES, M.B., B.S., D.P.M.

Dr. F. G. L. Barnes, a former senior medical officer for mental health under the Ministry of Health and Local Government of Northern Ireland, died at his home in Cultra, County Down, on 17 June. He was 76.

Francis Gregory Lawson Barnes was born in Clarborough, near Retford, Notts, on 12 March 1891, and received his medical education at St. Bartholomew's Hospital, London, qualifying with the Conjoint diploma in 1921. He had a distinguished academic career, and was gold medallist of his year. Early in his career he evinced an interest in psychiatry, and took the D.P.M. in 1924. He graduated M.B., B.S. in 1930. After appointments as physician in charge of the psychiatry department at Poplar Hospital, and psychiatric consultant in St. Andrew's Hospital, Bow, he was appointed physician superintendent of Long Grove Mental Hospital, Epsom, in 1934, from which post he retired in 1951. At that time he was invited to become senior medical officer (mental health) to the Ministry of Health and Local Government, Northern Ireland, and served in that capacity from 1951 until 1958. Although at that time he was almost 67 years of age, he enjoyed excellent health and continued to give valuable service in a part-time capacity as a specialist in mental health to the Ministry's regional medical service and was able to continue in this work until some months ago.

Dr. Barnes was an excellent clinician and right up until his illness his reports, whether on clinical matters or on mental health policy, were of the highest order. He settled down happily in Northern Ireland, and was held in affectionate regard by all his colleagues. Although confined to the house for several months, he bore his illness with patience and fortitude. The deepest sympathy of his many friends and colleagues will be extended to his devoted wife and son.—F. F. M.

W. D. N. writes: Freddie Barnes, as he was affectionately called in the L.C.C. Mental Hospital Service, has been a friend of mine since 1913 when we were in "digs" together as medical students at St. Bartholomew's. He was three years my senior, and should have qualified at the beginning of the first world war. However, the financial stringencies of the medical student prompted him to take the Certificate B in the O.T.C., to which was attached a handsome gratuity in those far-off days. The result was that Barnes joined the Army Reserve and was commissioned in the King's Own (Liverpool) Regiment. He was quickly sent overseas and was very severely wounded in the battle of the Marne. He saw no further active service but spent the rest of the war in an infantry training depot at Plymouth. It was not till after the armistice that he returned to Bart's to complete his medical education. I again came into close contact with him as a medical colleague and he was my first deputy at Horton Hospital, and after three years he was promoted to succeed David Ogilvy in charge of Long Grove Hospital. Barnes was a competent psychiatrist and a good administrator. Though a strict disciplinarian, he was popular with both patients and staff. He was a delightful colleague and one of the most loyal one could wish for.

R. S. REID, M.B.E., M.B., CH.B.

Dr. R. S. Reid, formerly in general practice in Bath, died in hospital on 10 May. He was 77.

Robert Scott Reid was born on 8 May 1890, and was educated at Glasgow High School and University. At the university he was a contemporary of Walter Elliot and Osborne Mavor (James Bridie). He played rugger for the university first fifteen, and had an international trial for Scotland. Versatile as he was, even in his young days, he also played soccer for Queen's Park. His studies were interrupted by the first world war, and after demobilization with the rank of lieutenant he returned to the university, graduating M.B., Ch.B. in 1920. The following year he set up in practice at Bath, where he remained for 46 years. He was honorary surgeon to the Bath Rugby Club for that time and president of the club on two separate occasions. He was also medical officer to the Bath Football Club, medical officer to the Bath Red Cross, and divisional surgeon of the St. John Ambulance Brigade. During the second world war he was medical officer to the Admiralty at Bath. In 1947 he was appointed M.B.E., and in 1962 was invested as commander of the Hospital of St. John of Jerusalem.

C. R. G. writes: The doyen of the medical profession in Bath, Bob Scott Reid was the perfect example of "the real old family doctor." In 1921 Bob came to practise in Bath, and it was there that his real versatility was given the opportunity to flourish. He was an exceptionally able general practitioner, an outstandingly good obstetrician, and a doctor who gave the utmost confidence to all his patients. He was small in stature, but a giant in heart and mind. He was gentle and reassuring to the old and "a genial uncle" to the young. In both these spheres he earned his niche as medical officer to the old people's homes, and medical officer to the children's homes.

Despite his large practice and his constant devotion to his patients, Scott Reid found time for many activities in sport and in first aid. This he did at the expense of his own leisure time. He hardly ever had what might be regarded—and expected—as "a decent holiday." He was known throughout the West Country as an outstanding bowler. He represented Somerset County for many years, and played in international bowling trials in 1935 and 1936. He was president of the Somerset County Bowling Association and of the Bath Bowling Association. In the field of first aid Scott Reid had the highest reputation.

Bob had a host of friends in Bath, and they will miss him very greatly. His keen sense of humour and his amazing fund of stories would cheer up any of us on the cloudiest of days. His immense courage could not be daunted even by the serious illness and suffering of the past months. He would not give in, and was visiting patients up to three days before he died.

He is survived by his wife, Gertrude, and by a son and daughter, to whom we extend our deepest sympathy.

R. B. McCOLL, M.C., M.B., CH.B.

Dr. R. B. McColl, a general practitioner at Hanmer, Flintshire, died suddenly at his home on 26 April. He was 71.

Robert Balderston McColl was born in Paisley, Renfrewshire, on 26 January 1896, and received his medical education at Glasgow University, graduating M.B., Ch.B. in 1924. He started practice in Hanmer in 1926, first in partnership with the late Dr. Clark, and subsequently he was in partnership with his brother, the late Dr. Hugh Ernest McColl, O.B.E., from 1947 until 1964. He was still actively engaged in medical practice at his death. During the first world war Dr. McColl held a commission in the Highland Light Infantry. He was awarded the 1914–18 Star, and was subsequently awarded the Military Cross in France for his gallantry and distinguished service in action. He saw service both in France and at Gallipoli. After demobilization with the rank of captain he returned to general practice. During the second world war he gave much of his time to lecturing for the Red Cross. He took an active interest in the British Legion's activities and was a past vice-president. Dr. McColl held several local appointments, and was visiting physician to the Ellesmere Cottage Hospital. He was secretary and treasurer of the Denbigh and Flint Division of the British Medical Association from 1949 to 1954, and chairman of the Division in 1948–9 and again in 1960–1. He was also a member of the Wrexham Clinical Society and of the Chester and North Wales Medical Society.

Dr. Robert McColl was a well-known figure throughout north-west Shropshire, and his death will be mourned by many hundreds of patients and friends alike. He devoted a considerable amount of his time towards raising funds for the restoration of his local church. He maintained the highest standards of medical practice, and was not only an excellent physician but a respected and kindly friend to all his patients.

He is survived by his wife, Julie, and his two sons, Anthony and Colin, to whom all his friends and colleagues offer their deepest sympathy.—H. G.-T.

News and Notes

EPIDEMIOLOGY

Lead Poisoning at Bradford

Two sisters aged 3 years and 2 years were admitted to Bradford Children's Hospital on 11 June 1967 suffering from convulsions. There was no history of epilepsy, and five other siblings were well. There were no findings to support a specific diagnosis. A clinical suspicion of poisoning was reinforced by the history that a number of animals in the neighbourhood had recently died with convulsive symptoms. This was reported to the Medical Officer of Health for investigation.

The home and its surroundings were visited on 13 June. In the back yard there were remnants of burnt battery casings and ash. The weather was warm, and it was stated that no burning of battery cases had occurred for two to three weeks, but that there had been previous burning for a period of approximately three months. A house-to-house visit revealed several properties where burning had taken place, substantial quantities of remnants and ash being widespread. At the same time an inquiry was made into illnesses of the occupiers and their pets. Subsequently the people were invited for clinical and haematological examination. Radiological investigation is proceeding. The major source of the battery casings was in a disused scrap yard with access through a broken fence. In the succeeding days three smaller dumps were found scattered through the industrial parts of the area.

Investigation of the two children showed punctate basophilia and characteristic lead lines on *x*-ray examination. The children, whose fits were initially controlled with paraldehyde, had further convulsions, and despite treatment with an infusion containing calcium disodium versenate (30 mg./kg. body weight) on 14 June both died in the early hours of 15 June.

Clinical Findings

As a result of the initial examination of 60 residents in houses where it was admitted that batteries had been used for fuel, five children and two adults thought to have evidence of lead poisoning were admitted to hospital.

Case 1.—Girl aged 2 years. Anorexia during previous week. Vomiting on day of examination. No clinical abnormality, haemoglobin level of 9.6 g. per 100 ml. Marked stippling, reticulocytosis, and late normoblasts. *X*-ray of long bones showed dense zones at metaphyses consistent with heavy metal poisoning.

Case 2.—Girl aged 2 years. Asymptomatic except for incoordination of eye movements. Basophilic stippling. *X*-ray examination showed dense zones at the knee regions approximately 2 mm. thick and at the wrists about 1 mm. thick.

Case 3.—Girl aged 3 years. Clinically well, but haemoglobin level was 9.5 g. per 100 ml. Marked basophilic stippling and reticulocytosis. On *x*-ray examination there were zones of increased density at the growing ends of long bones.

Case 4.—Girl aged 10 years. No clinical abnormality. Basophilic stipple cells, and on *x*-ray examination zones of increased density were present.

Case 5.—Girl aged 5 years. Admitted to hospital because of abdominal pain and vomiting. Blood films did not show evidence of toxicity but zones of increased density were present on *x*-ray of long bones.

Case 6.—Woman aged 39, who continued to burn batteries despite a warning two days earlier, developed acute abdominal pain, paraesthesia, and ataxia on 17 June.

Case 7.—Boy aged 14 years. Developed acute abdominal colic and paraesthesia in his hands on 16 June.

In addition three adults were admitted as doubtful cases, with presenting symptoms of jaundice (Case 8), neurological symptoms (Case 9), and mental illness (Case 10). There is no confirmation that lead poisoning is contributory. A further 160 people in the area, free from symptoms but with a history of occasional use of battery cases, are being examined; several positive *x*-ray findings are known, but detailed findings are not yet completed.

Comments

This incident confirms the dangers arising from the burning of battery cases. The plastic case is probably non-toxic, but substantial quantities of lead salts are adherent to the case. In 1955 J. A. Gillet[1] reported on an outbreak of lead poisoning at Rotherham. Our initial investigation agrees with his that the most likely vehicle of poisoning is the toxic ash remaining after burning, the ash being probably ingested and possibly inhaled. An unusual number of deaths in domestic pets had occurred in the weeks preceding the outbreak.

The danger could be averted by proper disposal of battery casings as a matter of normal commercial practice, and indiscriminate dumping would be amenable to legislative control. All these cases occurred in an area where difficult social and economic problems exist.

W. TURNER,
Medical Officer of Health.
F. N. BAMFORD,
Principal Medical Officer, Child Health.
J. S. DODGE,
Senior Medical Officer, Epidemiology.

Health Department,
Bradford.

REFERENCE

[1] Gillet, J. A., *Lancet*, 1955, 1, 1118.

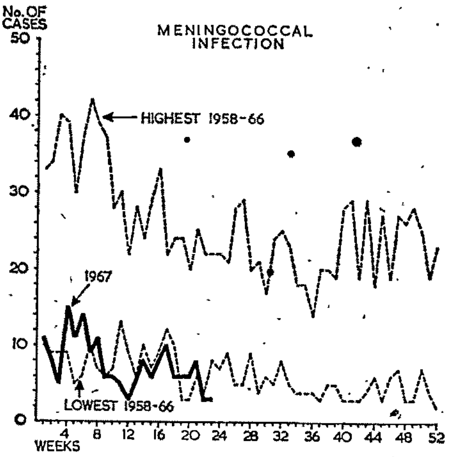
Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available.

	Week Ending	
Dysentery	9 June	**16 June**
Gloucestershire	37	**25**
Bristol C.B.	33	**25**
Greater London	93	**70**
Greenwich	3	**13**
Islington	20	**12**
Lambeth	0	**11**
Southwark	5	**10**
Lancashire	192	**107**
Liverpool C.B.	10	**10**
Oldham C.B.	5	**10**
Preston C.B.	4	**11**
Denton U.D.	5	**10**
Thornton Cleveleys	113	**13**
Northumberland	9	**15**
Ashington U.D.	8	**13**
Warwickshire	60	**49**
Birmingham C.B.	17	**13**
Coventry C.B.	27	**19**
Yorkshire West Riding	70	**74**
Edinburgh	37	**40**
Glasgow	35	**32**
Wigtown County	0	**11**
Measles		
Lancashire	537	**446**
Liverpool C.B.	130	**110**
Leicestershire	431	**316**
Leicester C.B.	185	**170**
Nottinghamshire	317	**280**
Nottingham C.B.	128	**133**
Warwickshire	457	**352**
Birmingham C.B.	146	**180**

Graphs of Infectious Diseases

The graph below shows the uncorrected number of cases of meningococcal infection in England and Wales. Figures for 1967 are compared with the highest and lowest figures for each week in the previous years shown.



PARLIAMENT

Powers of Search to Control Drug Peddling

[FROM OUR PARLIAMENTARY CORRESPONDENT]

Two changes are to be made in the Dangerous Drugs Bill during its progress through the House of Lords, where it was given a second reading on 20 June.

The first relates to the safe keeping of drugs, and the second to the powers of search. On the first, LORD STONHAM, Under Secretary to the Home Office, said the Home Secretary had recently consulted the representative bodies of the pharmaceutical industry and pharmacists with a view to strengthening his powers of requiring the safe keeping, record keeping, and packaging of "hard" and "soft" drugs. The representative bodies had fully endorsed the principle of his proposals for wider enabling powers to impose or modify controls as the situation developed. The detailed requirements would be discussed with the interests affected.

On the second proposed amendment he pointed out that the police had been hampered in detecting unauthorized possession by the present limits on their power to search on suspicion. The Government therefore proposed to give the police power to stop and search without warrant any person suspected of being in unlawful possession of a drug controlled under the 1964 and 1965 Acts. They intended to stop the "pushers" and pedlars of drugs by all means in their power.

Notification of Addicts

The Bill was an enabling measure, concerned solely with drugs scheduled under the Dangerous Drugs Act, 1965. It extended to Scotland and Northern Ireland. Under the powers it conferred the Home Secretary would be able to make regulations to require the notification of addicts by doctors and to prohibit doctors, except under licence, from providing addicts with specified drugs—initially heroin and cocaine. As regards notification the regulations would have to define addiction, state the circumstances in which notification would be required, specify the central authority (the Chief Medical Officer of the Home Department), and prescribe the procedure for notification. Lord Stonham emphasized that notification would have no legal consequences of any kind for the addict. It would not give the patient any continuing status as an addict as if he had been registered. The central records of notification would simply enable the inquiring doctor to be put in touch with any doctor who had previously notified that patient. Information provided by doctors would be safeguarded under the Official Secrets Act.

The intention was that in selected Health Service hospitals the doctors who received licences would be consultant psychiatrists in charge of the treatment of persons addicted to heroin and cocaine, and certain medical staff under their supervision. The criteria to be aplied for licensing doctors in approved centres outside the Health Service were under consideration.

Response of Hospitals

LORD SANDFORD, speaking for the Opposition, offered the opinion that doctors would come to regret their decision to do other than the Brain Committee had recommended and keep control of the disciplinary procedures, in this case by the General Medical Council. It was not a decision of the Government, or the wish of the Opposition, but a decision of the medical profession that would bring down on them all the paraphernalia of tribunals referred to in clauses 2 and 3 and in the schedule.

The object of the Bill was to shift the treatment of addicts into centres to be established, primarily in the London and Metropolitan hospitals. The Minister of Health had set out what he wanted of the hospitals in a memorandum of 7 March. What response had there been? His own information—admittedly incomplete—was that the hospitals were far from satisfied: they had been given no extra money; they were not clear how the centres were to operate; and they were far from ready to make the provisions without which the Bill could not operate.

(*Continued overleaf*)

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **10 June** (No. 23) and corresponding week **1966**.

Figures of *cases* are for the countries shown and for Greater London. Figures of *deaths* and *births* are for the whole of England and Wales (London included), Greater London, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0		1	0	0	0	
Dysentery ..	628	628	101	18	1	502	87	59	13	2
Encephalitis, acute ..	1	0	0			3	0	0	0	
Enteric fever:										
Typhoid ..	4	0	0	0		5	2	0	0	
Paratyphoid	2	0	0	0		3	0	0	0	
Food-poisoning	79	13	7	170		128	32	8	3	
Infective enteritis or diarrhoea under 2 years				22	31				23	26
Measles* ..	9,144	652	105	162	118	6,990	609	68	125	95
Meningococcal infection ..	3	1	0	0		7	3	2	0	
Ophthalmia neonatorum	5	0	0	0		4	2	1		
Pneumonia† ..	114	20	66	13	1	109	12	54	0	
Poliomyelitis, acute:										
Paralytic ..	1	0	0	0		0	0	0	0	
Non-paralytic	0	0	0			0	0	0	0	
Puerperal fever§	86	33	1	0		87	27	8		
Scarlet fever ..	334	56	21	12	6	306	44	27	12	8
Tuberculosis:										
Respiratory ..	230	51	31	11		298	67	41	7	
Non-respiratory ..	38	11	7	4		3	0	13	3	
Whooping-cough	548	64	79	17	26	270	36	33	9	6

DEATHS	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0		0	0	0	0	0	0	0	0
Dysentery ..	3	0		0		2	0		0	
Encephalitis, acute ..					0					0
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	7	0	0	0	0	5	1	1	0	0
Influenza ..	3	0	0	0		2	0	0	0	
Measles ..			0	0	0		0	0	0	0
Meningococcal infection ..			0					0		
Pneumonia ..	586	78	11	15	8	551	97	29	15	8
Poliomyelitis, acute ..		0	0	0	0	0	0	0	0	0
Scarlet fever ..	0		0	0	0		0	0	0	0
Tuberculosis:										
Respiratory ..	41	9	2	0	2	41	7	2	0	0
Non-respiratory ..				0	0		1		0	0
Whooping-cough	1	0	0	0	0	0	0	0	0	0
Deaths 0–1 year	270	52	20	5	8	255	42	21	8	22
Deaths (excluding stillbirths)	9,797	1551	528	99	141	9,240	1415	517	93	185
LIVE BIRTHS	17,431	2885	912	264	574	16,944	2835	943	292	504
STILLBIRTHS	234	34	12			245	41	13		

* Measles not notifiaole in Scotland, whence returns are approximate. † Includes primary and influenzal pneumonia. § Includes puerperal pyrexia.

Established Machinery

Lord Amulree sought an assurance that the old machinery, such as it was, would not be taken away before the new machinery was ready; that the general practitioner would not be banned from prescribing drugs to addicts until the network of treatment centres was working properly; and that extra money would be found for the establishment of clinics and staff, and premises if necessary.

Lord Segal thought the most welcome part was the provision that regular prescribing of dangerous drugs should be taken out of the hands of the general practitioner and devolve on licensed consultants who would be able to keep a strict control over the patient. It was highly important that the element of financial gain to the general practitioner by his prescribing of dangerous drugs to an addict should be entirely removed.

Government's Reply to Debate

Lady Phillips, answering the debate for the Government, told Lord Sandford that the Minister of Health felt that the hospitals, after full discussion of the March memorandum, were "quite happy about the proposals," and that their response had, in fact, been most satisfactory. Additional funds needed by some teaching hospitals would be forthcoming. Some hospitals had particular problems, such as additional staff, and these were being examined.

Heroin was regarded as the best drug for some cases of intractable pain, and it was certain that the medical profession would not accept a prohibition on the prescription of heroin for the treatment of new patients.

She assured Lord Amulree that the old machinery would not be removed before the new was established.

All hospital boards were given additional money each year for development, and in general the Minister expected them to be able to finance the treatment centres from this money. It might be more difficult for the teaching hospitals, whose budgets were smaller than those of the regional boards, but the Minister had said that if necessary extra money would be made available from a small contingency fund.

The **Home Secretary** stated in answer to a question on 22 June that the Minister of Health and he hoped that the notification regulations under the Dangerous Drugs Bill could be brought into operation in the autumn and the prescribing regulations in the new year; but until consultations with the medical profession and other interests were further advanced he could not say when these regulations would be published.

Homosexual Law Reform Bill

Opponents of the Sexual Offences (No. 2) Bill marshalled their forces against its further progress on the report stage in the House of Commons on 23 June, and successfully prevented its being completed. According to the rules of the private members' legislation the Bill has now failed, since the time allotted to back-bench legislation has run out before it has completed its passage through the House. There appears to be some expectation among its supporters that the Government will come to their rescue by giving it additional time.

Questions in the Commons

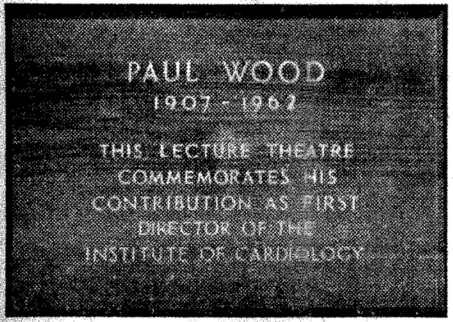
Health Check Weeks

Mr. **Julian Snow**, Parliamentary Secretary to the Ministry of Health, explaining the Ministry's attitude to health checks on 14 June, said that screening of the general public should be undertaken only for conditions that could be clearly and accurately diagnosed. Except in these circumstances it could do harm and was, in any case, a wasteful use of resources both local and national. For that reason he was not convinced on present evidence that this method of detecting disease should be recommended to health authorities generally. The Ministry, however, was most interested in the work that was being done by local authorities in this field and was following it closely.

Safety Order for Tractors

The Commons on 21 June approved an order requiring tractors to be fitted with a safety cab or frame. The regulations would apply to new tractors in three years' time. For used tractors bought before 1 September 1970 the obligation on farmers to provide cabs for them would not apply for a further seven years.

MEDICAL NEWS



Paul Wood Memorial Tablet

A plaque to the memory of Dr. **Paul Wood**, the first director of the Institute of Cardiology, was unveiled on 23 June by Sir **John McMichael**, F.R.S., director of the British Postgraduate Federation.

The ceremony was held in the Institute's lecture theatre at the National Heart Hospital in the presence of Mrs. Wood and members of the family. In his tribute Sir John referred to the great part Dr. Wood played in the development of the Institute and to the inspiring influence he had on his staff.

About 80 members of staff, past and present, attended the unveiling.

Appointments to Professorships

Dr. **Ian MacDonald**, reader in physiology at Guy's Hospital Medical School, has had the title of professor of applied physiology conferred on him in respect of his post at Guy's. Dr. Macdonald graduated at Guy's Hospital in 1944 and after holding several house appointments and serving in the R.A.M.C., mainly in the Middle East, he joined the physiology department at Guy's. He proceeded to the Ph.D. in 1953, and M.D. in 1959, and the D.Sc. in 1966. In 1958 he was a lecturer in physiology at the University of Witwatersrand and in 1961 a visiting research worker in the department of medicine, University of Cape Town, where he studied lipid metabolism in kwashiorkor. Dr. Macdonald has published several papers on the metabolic effects of dietary carbohydrates. He has served as a member of the council of the Nutrition Society.

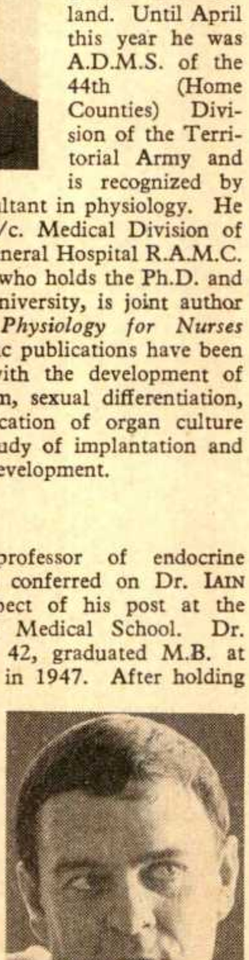
Dr. T. C. N. **Gibbens**, reader in forensic psychiatry at London University, has been appointed titular professor with effect from 1 October. Dr. Gibbens was educated at Westminster School, Emmanuel College, Cambridge, and St. Thomas's Hospital, and graduated in 1939. He served throughout the war in the R.A.M.C., from 1940 to 1945 in a P.O.W. hospital in Germany. After a year as house-physician at the Postgraduate Medical School at Hammersmith he became registrar at the Maudsley Hospital. From 1948 to 1950 he held a Nuffield fellowship in psychological medicine, and studied at the Institute of Psychiatry in New York and Sing-Sing prison psychiatric unit. On return to this country he became senior lecturer in forensic psychiatry and was appointed reader in 1964. During this period he was also psychiatrist to the L.C.C. remand home for girls, and served on the Streatfield Committee and on the Royal Commission on the penal

[Barr

system. He is a member of the Advisory Council for Probation and Aftercare, and of the research subcommittee of the Advisory Council on the Penal System. This year he is president of the British Academy of Forensic Sciences and of the International Society of Criminology. His publications include *Shoplifting* (1962), *Psychiatric Studies of Borstal Lads* (1963), and *Cultural Factors in Delinquency* (1966).

Dr. FRANCIS O'GRADY, reader in bacteriology at St. Bartholomew's Hospital, London, has had the title of professor of bacteriology conferred on him in respect of his post. Dr. O'Grady, who is 41, entered the Middlesex Hospital Medical School as a Scholar in 1945 and after obtaining first-class honours in the London Special B.Sc., Physiology, graduated M.B., B.S. with honours in 1950. After house - physician appointments at the Middlesex and North Middlesex Hospitals he began his career in pathology at the Bland-Sutton Institute. There he worked with the late F. R. SELBIE on experimental tuberculosis and hypersensitivity. He continued this work, with studies on the human tuberculin reaction, while pathologist to the Army Chest Centre, and this formed the basis of the thesis for which he was awarded the M.Sc. in 1956 and the M.D. in 1957. After the Army he returned to the Bland-Sutton Institute, where he worked on the pathogenesis and treatment of mouse thigh candidosis. In 1950 he was invited to join R. L. RILEY and the late W. F. WELLS in the experiment they were conducting in Baltimore to demonstrate the mechanism of airborne transmission of human pulmonary tuberculosis. The results of this and other epidemiological studies were embodied in a book with R. L. RILEY, *Airborne Infection: Transmission and Control* (see *B.M.J.*, 24 November, 1962, p. 1374). Relinquishing his appointment as assistant professor of environmental medicine at Johns Hopkins, he returned to this country, and in 1962 he was appointed to his present post, vacated by R. A. SHOOTER when he became head of the department. Dr. O'Grady's recent investigations have been into the mechanisms and management of urinary tract infection.

Dr. T. W. GLENISTER, vice-dean and reader in anatomy at Charing Cross Hospital Medical School, has had the title of professor of embryology conferred on him in respect of his post at the school. Dr. Glenister, who is 43, graduated from St. Bartholomew's Hospital Medical College in 1947. After house appointments at St. Bartholomew's Hospital and St. Andrew's Hospital, Dollis Hill, he served for two years in the R.A.M.C. In 1950 he was appointed demonstrator in anatomy at Charing Cross Hospital Medical School, where he was promoted lecturer in 1952, senior lecturer in 1954, and reader in anatomy in the University of London in 1957. In 1954 he was a member of the first international team undertaking embryological research at the Hubrecht Laboratory, Utrecht, and he visited various centres in the United States in 1963. He served as programme secretary and assistant secretary of the Anatomical Society of Great Britain and Ireland. Until April this year he was A.D.M.S. of the 44th (Home Counties) Division of the Territorial Army and is recognized by the Army as a consultant in physiology. He now serves as O. i/c. Medical Division of the 217 (Eastern) General Hospital R.A.M.C. (V). Dr. Glenister, who holds the Ph.D. and D.Sc. of London University, is joint author of *Anatomy and Physiology for Nurses* (1965). His scientific publications have been concerned mainly with the development of the urogenital system, sexual differentiation, and with the application of organ culture techniques to the study of implantation and early mammalian development.



The title of professor of endocrine chemistry has been conferred on Dr. IAIN MACINTYRE in respect of his post at the Royal Postgraduate Medical School. Dr. MacIntyre, who is 42, graduated M.B. at Glasgow University in 1947. After holding house appointments at Stobhill Hospital, Glasgow, and Peterborough Memorial Hospital he became assistant chemical pathologist at the Royal Hospital, Sheffield, and demonstrator in the university department of biochemistry under Professor Sir HANS KREBS. In 1952 he was appointed registrar in chemical pathology under Professor EARL J. KING at the then Postgraduate Medical School of London, and was awarded the first Drummond Fellowship in 1954. He became assistant lecturer in 1956, lecturer and consultant in 1959, and reader in 1963. He holds the Ph.D. and is a founder member of the College of Pathologists. Dr. MacIntyre was visiting scientist at the National Institutes of Health, Bethesda, Maryland, during 1961 and visiting professor of medicine in the University of California at San Francisco in 1964. He will be joint director with Professor RUSSELL FRASER of the new endocrine unit at the Royal Postgraduate Medical School. His published work includes papers on renal function, total body composition, magnesium metabolism, and on the origin, chemistry, and physiology of thyrocalcitonin.

Butterworth Gold Medal

The subject of this year's essay for the Royal College of General Practitioners' Gold Medal is "The Manifestations and Management of Senility," and for 1968 "The Promotion of Health After Leaving School." Essays for 1967 should be identified by motto only, with the author's name and address in a sealed envelope, and should not exceed 10,000 words. They should be submitted to the chairman of the awards committee, Royal College of General Practitioners, 14 Princes Gate, London S.W.7, by 31 August.

Royal College of General Practitioners

On 23 June Mr. DAVID BRUCE, the United States Ambassador, unveiled a plaque to the memory of President KENNEDY at the Royal College of General Practitioners, Hyde Park. Mr. Kennedy lived in the building when his father was Ambassador to Britain. Dr. ANNIS GILLIE, president of the College, and Dr. H. N. LEVITT, chairman of the Council, also participated in the ceremony. The unveiling was followed by a reception.

People in the News

▶ Dr. JOHN APLEY, lecturer in child health at Bristol University, is to succeed Dr. PHILIP EVANS as leader of the British paediatric team in Saigon (see *B.M.J.*, 2 July, 1966, p. 61).

▶ Dr. EDWARD COOPER, of the Chester Beatty Research Institute, London University, has been appointed head of the department of experimental pathology and cancer research at Leeds University.

▶ D. V. PARKE, Ph.D., reader in biochemistry at St. Mary's Hospital Medical School, London, has been appointed to the chair of biochemistry at the University of Surrey.

▶ Dr. TREVOR WESTON has been appointed editor for Family Doctor Publications.

Coming Events

West London Medico-Chirurgical Society.—Annual dinner, 6 July, 8 p.m. for 8.30 p.m., Mitre Hotel, Hampton Court. Tickets £2 2s. Applications to Honorary Secretaries, West London Medico-Chirurgical Society, West London Hospital, Hammersmith, London W.6.

King Edward's Hospital Fund for London.—Meeting on management services and information systems, 18 July, Hospital Centre, 24 Nutford Place, London W.1.

British Association for the Advancement of Science.—Annual meeting, 30 August to 6 September, Leeds.

Third Malaysian Congress of Medicine.—11–13 August, Kuala Lumpur. Details from the Secretary, Dr. S. T. PAI, Department of Surgery, University of Malaya, Pantai Valley, Kuala Lumpur, Malaysia.

Association des Médecins de Langue Française.—Congrès Français de Médecine, 26–30 September, Montreal. Details from Secretariat, 13 rue Molière, Paris 1.

Vth World Congress of Gynaecology and Obstetrics.—23–30 September 1967, Sydney. Details from Secretary-General, G.P.O. Box 4139, Sydney, Australia.

Societies and Lectures

For attending lectures marked ● a fee is charged or a ticket is required. Applications should be made first to the institution concerned.

Monday, 3 July

Institute of Diseases of the Chest.—6.15 p.m., Dr. B. E. Andrews: The Virologist and Lung Disease.

Tuesday, 4 July

Institute of Dermatology.—4.30 p.m., Mr. R. R. Phillips: Uses and Methods of Photography in Dermatology.

London University.—At Charing Cross Hospital Medical School, 5 p.m., special university lecture in medicine by Professor D. W. Seldin (Texas): Pathogenesis and Treatment of Oedema.

St. Charles's Hospital Medical Centre.—8.45 p.m., clinicopathological conference: A Case of Diabetes with Complications.

West Suffolk Hospitals Postgraduate Centre.—At Drummond Hall, West Suffolk General Hospital, 1.15 p.m., Dr. J. Wedgwood: Use and Abuse of Antibiotics.

Wednesday, 5 July

Royal Free Hospital.—5.15 p.m., Dr. J. Waldenström (Malmo, Sweden): Disorders of Protein Metabolism.

Royal Postgraduate Medical School.—2 p.m., urology seminar. (2) 5 p.m., Professor J. Kirklin (Baltimore, U.S.A.): Problems of Interest in the Surgical Treatment of Acquired Valvular Heart Disease.

Stoke Mandeville Hospital.—(1) 12.15 p.m., Dr. M. S. Good: Clinical cases. (2) 6 p.m., Dr. M. Kinsbourne: Brain Stem Syndromes.

West Middlesex Hospital.—At Lecture Theatre, 5 p.m., postgraduate lecture by Dr. D. M. L. Doran: Gout.

Thursday, 6 July

Royal Postgraduate Medical School.—4 p.m., Mr. P. McKelvie: Laryngeal and Pharyngeal Neoplasms.

Friday, 7 July

Royal Postgraduate Medical School.—(1) 10.15 p.m., Mr. M. Hobsley: Influence of Acid/Base Balance on Gastric Secretion; (2) 11.30 a.m., Mr. A. Cox: Clinicopathological conference.

Sunday, 9 July

Clwyd and Deeside Board of Postgraduate Studies.—At Royal Alexandra Hospital, Rhyl, 10 a.m., symposium: Malignant Disease.

Royal Northern Hospital, London.—10 a.m., Dr. D. Geraint James: clinical conference.

New Issues of Specialist Journals

Obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London W.C.1.

ANNALS OF THE RHEUMATIC DISEASES

Contents of the May issue are as follows:

Heberden Oration, 1966: Categorization of Medicine: A Survey of Still's Disease. E. G. L. Bywaters.
The Joint Disease of Sarcoidosis. J. M. Gumpel, C. J. Johns, and L. E. Shulman.
Fibrin Promotion and Lysis in Arthritic Joints. M. I. Barnhart, J. M. Riddle, G. B. Bluhm, and C. Quintana.
Significance of the Occurrence of Transparent Skin: A Study of Histological Characteristics and Biosynthesis of Dermal Collagen. B. McConkey, K. W. Walton, S. A. Carney, J. C. Lawrence, and C. R. Ricketts
Carpal Tunnel Syndrome in Rheumatoid Arthritis. C. G. Barnes and H. L. F. Currey.
Relative Roles of Genetic and Environmental Factors in the Control of Serum Uric Acid Levels in Normouricaemic Subjects. J. A. Boyle, W. R. Greig, M. K. Jasani, A. Duncan, M. Diver, and W. Watson Buchanan
Jaccoud's Arthritis. E. Beausang, E. V. Barnett, and S. Goldstein.
Phenolsulphonphthalein Clearance from the Knee Joint in Normal and Pathological States. R. Nakamura, H. Asai, H. Sonozaki, and M. Nagano.
Ferritin Formation by Synovial Cells Exposed to Haemoglobin in vitro. K. D. Muirden, J. R. E. Fraser, and B. Clarris.
Topical Fluocinolone in Rheumatoid Arthritis. L. Hall and the late N. R. Banerjee.
Heberden Society. Book Review. New Zealand Rheumatism Association. Abstracts.

Volume 26, No. 3. Yearly subscription (6 numbers) £4 4s., abroad £4 15s.

BRITISH JOURNAL OF OPHTHALMOLOGY

Contents of the June issue are as follows:

Retinal Vasculitis Associated with Anterior Uveitis. J. Nolan and J. F. Cullen.
Volume Changes in Indentation Tonometry. U. Majzoub.
Retrocorneal Membranes. I. Their Origin and Structure. E. S. Sherrard and P. V. Rycroft.
Retrocorneal Membranes. II. Factors Influencing Their Growth. S. S. Sherrard and P. V. Rycroft.
Vascular Abnormalities in Disciform Degeneration of the Macula Lutea Demonstrated with Fluorescein. L. Lemke and A. Jütte.
Effects of Prednisolone Eye Drops. T. G. Ramsell, W. Trillwood, and G. Draper.
Fibromyxosarcoma of the Eyelid. I. M. Shukla and S. Agrawal.
Invasion of the Orbit by Maggots. S. P. Mathur and J. M. Makhija.
Microsurgery in Ophthalmology. M. J. Roper-Hall.
A Simple Cryosurgical Instrument and its Application in Ethiopia. J. Edwards, L. L. Woodget, F. O. Mueller, and R. Ludek.
A Sterile Disposable Cryoextractor (Cryophake). Jack W. Passmore and Robert P. Hughes.
New Iris Retractor for Use in Cryosurgery. G. M. Maclure.
Ophthalmological Synopses. Review. Obituary. Notes.

Volume 51, No. 6. Yearly subscription (12 numbers) inland £8 8s., overseas £9. With *Ophthalmic Literature* and Index (7 numbers) inland £15, overseas £16.

BRITISH JOURNAL OF MEDICAL EDUCATION

Contents of the June issue are as follows:

List of Contributors.
Editorial.
Educational Science and Education for Medicine. George E. Miller.
Individual Study and Educational Technology. C. E. Engel.
Programmed Instruction in Medical Education: Comparison of Teaching-machine and Programmed Textbook. T. B. Stretton, R. Hall, and S. G. Owen.
Medical Students' Sudy: Time and Place. Nicolas Malleson.
The Students' Health and Welfare Centre (SHAWCO), University of Cape Town, South Africa. David Katz.
Neglected Fundamentals in Undergraduate Psychiatric Education. A. C. Woodmansey.
Role of Genetics in Medical Education in North America. R. J. F. Withers.
Marking Multiple-choice Examinations. Bernard Lennox.
Guessing in Multiple-choice Tests. B. Cooper and J. M. Foy.
Closed-circuit Television and Videotape Recording in Teaching Pharmacology. J. D. Gasking, J. P. Quilliam, and K. E. Wiggins.
Projectors. N. C. Manley-Cooper.
Medical Research Council Support for the Training of Research Workers. Joan Faulkner.
Book Reviews. News and Notices.

Volume 1, No. 3. Yearly subscription (4 numbers) £3 3s., abroad £3 10s.

Universities and Colleges

CAMBRIDGE

Appointment.—Dr. M. J. Mitchinson (university lecturer, pathology).

The M.D. Committee have awarded the Raymond Horton-Smith prize for 1965–6 to Dr. G. R. Fraser for a thesis entitled The Causes of Blindness in Childhood.

The M.D. Committee have awarded the Sir Lionel Whitby medal for 1965–6 to Dr. D. A. Hopkinson for a thesis on Genetical and Biochemical Studies on Human Red Cell Acid Phosphatase in Health and Disease.

M.D.—D. A. Chamberlain, A. M. Fisher, J. E. Stark, P. J. Crosland-Taylor, R. E. Kendell, R. Carlisle, L. J. Chalstrey.

M.Chir.—*E. C. Ashby, *R. H. Whitaker, H. B. Stallard, M. Spiro, D. E. Elgar.

M.B.—P. J. Black, *C. B. Bentley Phillips, M. A. Hutson, P. E. M. Jarrett, Cecilia A. Lindsay-MacDougall.

* By proxy.

ABERDEEN

Appointments.—Dr. N. Edwood (lecturer, medicine); Dr. C. Murray (chief medical officer, Student Health Service); Dr. C. H. Baxter (terminable lecturer, chemical pathology); Dr. P. N. Bennett (terminable lecturer, medicine); Dr. J. S. Legge, Dr. R. F. Scott (terminable lecturers, pathology); Dr. P. A. Slater, Dr. Julie C. Carter (lecturers, pathology).

EDINBURGH

Appointments.—Dr. D. W. Straughan (senior lecturer, Department of Pharmacology); Dr. Catherine M. U. Maclean (lecturer, Department of Social Medicine); Dr. Elizabeth Fender (lecturer, Department of Anatomy); Dr. A. G. Fraser (lecturer, Department of Bacteriology); Dr. H. J. K. Mamattah (temporary lecturer, Department of Bacteriology).

BIRMINGHAM

Appointments.—Dr. J. M. Wilson (research fellow, Department of Theology); Dr. G. Harris (lecturer, Department of Experimental Pathology); Dr. M. J. Andrews, Dr. J. E. D. MacLaren, Dr. M. J. McMahon (temporary lecturers, Department of Anatomy).

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At a meeting of the Council held on 8 June, with Professor (now Sir) Hedley Atkins in the chair, the Sir Arthur Keith medal was presented to Professor A. J. Harding Rains.

The Begley prize was presented to Dr. R. A. Lucas (St. Mary's Hospital).

Professor R. B. Duthie, the Nuffield professor of orthopaedic surgery, Oxford, was elected to the Fellowship *ad eundem*.

The following were co-opted to the council for the year 1967–8, representing various branches of practice: Anaesthetics, Dr. Derek Wylie; Dental Surgery, Mr. Terence Ward (re-election); General Practice, Dr. A. J. Whitaker; Gynaecology and Obstetrics, Mr. J. A. Stallworthy (re-election); Ophthalmology, Mr. A. G. Cross (re-election); Otolaryngology, Mr. D. Ranger; Radiology, Dr Thomas Lodge (re-election).

A diploma of membership was granted to D. E. MacFarlane.

After the meeting the Gordon-Taylor lecture was delivered by Sir Eric Riches, on "The Gordon-Taylor Tradition in the Surgery of Cancer."

All communications with regard to editorial business should be addressed to The Editor, British Medical Journal, B.M.A. House, Tavistock Square, London W.C.1. Telephone: 01-387 4499. Telegrams: *Aitiology, London W.C.1.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs.

ADVERTISEMENT AND SUBSCRIPTION ORDERS should be addressed to The Manager at B.M.A. House, London, or at 415 Bourke Street, Melbourne, Victoria, Australia.

MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the British Medical Association, B.M.A. House, London, or to the Scottish Secretary, B.M.A., Scottish Office, Drumsheugh Gardens, Edinburgh.

BRITISH MEDICAL JOURNAL

LONDON SATURDAY 8 JULY 1967

Pointers

Post-concussional Sequelae: Patients may have organic lesions in the brain which are as yet insufficiently studied, according to Mr. A. R. Taylor (p. 67). Leader this page.

Significance of Systolic Clicks: Dr. Mary Stannard and colleagues, from Melbourne, Australia, confirmed prolapse of posterior leaflet of mitral valve and the incidence was familial in 13 patients (p. 71).

New Semisynthetic Penicillin: Carbenicillin reported active agent against *Ps. pyocyanea* by Dr. E. T. Knudsen and colleagues (p. 75). Drs. R. J. Jones and E. J. L. Lowbury found that combined with gentamicin it protected burned mice against *Ps. aeruginosa* (p. 78).

Urinary White Cell Excretion: Dr. R. M. Lindsay and colleagues found significant rise in females but not in males after surgery (p. 83).

Convulsive Status Epilepticus: Drs. M. J. Parsonage and J. W. Norris used intravenous diazepam for effective control (p. 85). Leader at p. 63.

Intermittent Haemodialysis: Mr. G. J. A. Clunie and colleagues describe satisfactory experiences with Silastic-Teflon arteriovenous cannula system (p. 88).

Prevention of Urinary Infection: Professor W. A. Gillespie and colleagues report use of sterile disposable plastic drainage bags satisfactory for closed drainage (p. 90).

Case Reports: Methaqualone addiction and delirium tremens (p. 92). Successful treatment of thrombocytopenic purpura (p. 93).

Today's Drugs: Radioiodine therapy (p. 95).

New Look at Postgraduate Training: Mr. P. W. R. M. Alberti advocates formal postgraduate training programmes to replace present haphazard schemes (p. 101).

Accidents in Childhood: A memorandum of the British Paediatric Association (p. 103).

Research in Progress: M.R.C. Rheumatism Research Unit (p. 105).

Contact Lenses: Description of suction holder (p. 106).

Pertinax: Without Prejudice (p. 107).

Common Market and Medicine: Letter from Italy (p. 108).

Proceedings of Council: Approval given to reorganization of representative machinery for hospital junior staff, *Supplement,* p. 15.

G.M.S. Committee: Dr. J. C. Cameron reelected chairman and negotiating team appointed, *Supplement,* p. 18.

Post-concussional Syndrome

The pathogenesis and management of the sequelae of closed head injury have been matters of dispute for more than a century. As Mr. A. R. Taylor points out in his paper at page 67 of the *B.M.J.* this week, there are two principal schools of thought on the aetiology of the post-concussional syndrome: some believe that symptoms after even minor head injury are the result of physical damage to the brain, while others equally firmly hold the view that the symptoms are mostly of psychogenic origin.

In his review of concussion, written in 1962, Sir Charles Symonds[1] stressed the pathological and experimental evidence that damage to neurones and white matter was a common sequel of closed head injury, and he favoured the organic view. But in 1966 Henry Miller,[2] after analysing his experience of many cases referred to him in connexion with claims for compensation, found it difficult to believe that the clinical features of this disorder could justify its speculative attribution to cellular damage. Now as evidence in support of the organic origin of post-concussional symptoms Taylor points out that in various conditions headaches, dizziness, lack of energy, and defects of memory and concentration may result from brain damage even when there are no accompanying physical signs. He refers to evidence[3] showing that the brain may be more severely damaged from a relatively minor blow to the head if the head is freely movable than by a blow severe enough to fracture the skull with the head immovable. While it is true that professional men often return to work more quickly after a head injury than do manual workers, many who did so within six months still had symptoms 18 months after the injury. Mr. Taylor incidentally mentions three doctors who suffered disabling symptoms long after injuries for which no compensation was claimed. Surveys of German soldiers suffering head injury in the first world war[4] and a study of Americans after the Korean war[5] showed that many had significant and persistent symptoms and had not been able to return to satisfactory employment. There is also neuropathological evidence that damage to axons and myelin sheaths and to nerve cells in the brain-stem and in the cerebral hemispheres may follow relatively minor injury, while special tests[6 7] have shown disorders of vestibular function and persisting, posturally induced nystagmus in many patients.

For these reasons Taylor discards the view that patients with head injury, if properly managed, socially adjusted, and carefully rehabilitated, will not have "neurotic symptoms." He suggests that minor difficulties in concentration and performance indicate that these people have suffered organic cerebral damage. Many of these patients are abnormally sensitive to alcohol and some undergo lasting changes of personality.

At first sight these arguments seem, as Taylor points out, to refute Miller's[8] conclusion that the severity and duration of post-concussional symptoms are inversely proportional to the severity of the head injury. In a clinical situation where exact methods of examination and investigation are rarely informative and in which pathological evidence is relatively

© British Medical Journal, 1967. All reproduction rights reserved.

scanty, opinions are bound to differ. However, it seems that in many respects Taylor and Miller are describing different syndromes. Most neurologists and neurosurgeons would accept that frontal and occipital headaches which are present on waking, throbbing in character, and accentuated by bending or coughing or sneezing are usually organically determined. Most would also accept that disorders of memory and concentration and transient vertigo ("dizzy bouts," with transitory staggering brought on often by change in posture) are common results of organic damage after closed head injury. Like post-traumatic epilepsy, commonly appearing in 6 to 18 months after a head injury sufficient to give post-traumatic amnesia of 24 hours or more, these symptoms must surely be accepted as organic. They may resolve slowly, but generally do so in the less severely injured patients in one to two years after the accident. By contrast, any neurologist who frequently examines patients for medico-legal purposes is familiar with the type of injury which has produced no more than a minor laceration of the scalp without impairment of consciousness, an injury which if experienced in a domestic environment or on a field of sport would have been forgotten within a few days of the wound's healing, but which has been followed by apparently prolonged and disabling sequelae. Such patients often complain of "terrible" or "severe" headache which is vertical in situation or described as like a tight band, a weight, or sense of pressure. These symptoms are characteristic of non-organic headache and are common also in anxious or depressed patients who have never experienced head injury. Many symptoms may be associated with headache, but the physician often finds a striking over-reaction during the examination, which is punctuated by sighs, groans, and protestations of pain, and voluntary contraction of the muscles of the neck often impairs passive movement of the head. No neurologist of experience will accept that this syndrome, whether attributed to "hysteria" or to malingering, could have an organic basis. One difficulty is to assess the apparently intense depression, tension, and anxiety often seen in such cases. There are certainly patients in whom lasting phobias, related perhaps to the place of work where the accident occurred, to working at heights, or to riding in motor vehicles, are seen. The fact that symptoms often clear up in a few months after settlement of a compensation claim certainly supports Miller's thesis[8] about the nature of this type of traumatic or "compensation" neurosis. The same may be true of some "blackouts." Attacks like those described by L. D. Osler and M. G. Fusillo[9] as "a peculiar type of post-concussive blackout" may follow head injury, fail to respond to anticonvulsant therapy, yet cease abruptly after a substantial financial settlement.

Thus it is difficult to draw any firm conclusions about the aetiology and management of the post-concussional syndrome. Morning headache of throbbing character accentuated by movement, and vertigo induced by change in posture, together with disturbance of memory and concentration, are common and undoubtedly organic sequelae of closed head injury. Occasionally they follow minor trauma. The most that can be done in these cases is to advise adequate rest and relaxation, to give symptomatic treatment, and to reassure the patient that almost certainly the symptoms will eventually resolve. But when florid neurotic or "hysterical" manifestations follow trivial head injury, early settlement of any outstanding compensation claim is the single most significant factor contributing to ultimate recovery.

---

[1] Symonds, C., *Lancet*, 1962, 1. 1.

[2] Miller, H., *Proc. roy. Soc. Med.*, 1966, 59, 257.

[3] Denny-Brown, D., and Russell, W. R., *Brain*, 1941, 64, 93.

[4] Goldstein, K., *After Effects of Brain Injuries in War*, 1942, p. 220. London.

[5] Caveness, W. F., in *Head Injury Conference Proceedings*, 1966, p. 209. edited by W. F. Caveness, and A. E. Walker. Philadelphia.

[6] Friedman, A. P., Brenner, C., and Denny-Brown, D., *J. Neurosurg.*, 1945, 2, 36.

[7] Houdart, R., Cathala, F., Pialoux, P., Raby, D., Fontelle, P., and Vollmer, D., *Presse méd.*, 1966, 74, 449.

[8] Miller, H., *Brit. med. J.*, 1961, 1, 919.

[9] Osler, L. D., and Fusillo, M. G., *J. Neurol. Neurosurg. Psychiat.*, 1965, 28, 344.

Asbestosis

The first case of asbestosis was described as "typical fibroid phthisis" by H. M. Murray in 1907,[1] but it was another 20 years before there was an official inquiry into conditions in asbestos factories.[2] Soon afterwards W. B. Wood and S. R. Gloyne[3] thought that the disease was getting under control, a view shared 15 years later by H. Wyers.[4] These authors were concerned only with asbestos processing and textile manufacture and their optimistic statements have not withstood the test of time and of the expanding use of asbestos. It is true that in those factories where the asbestos regulations of 1931[5] have been rigorously implemented the excess mortality has been considerably reduced,[6 7] but on a national scale annual "certifications" for asbestosis have been rising since 1950.[8]

Asbestos has been used for at least 4,000 years,[9] but it became an important industrial mineral only at the end of the last century. Since then its output has risen from about 500 tons to more than 3 million tons per annum.[10 11] It has innumerable uses in building, shipbuilding, insulating, refrigeration, paper, textile, engineering, plastics, and many other industries. At present tests are being made with asbestos–asphalt for road surfacing.[12 13] The labour force in many of these industries is highly mobile and distributed over a large number of small units. In addition there is a vast number of "do it yourself" enthusiasts who may be exposed intermittently to highly concentrated asbestos dust. The biological significance of pulmonary asbestos bodies is not yet clear,[14] but they have been found in large proportions of necropsies in widely separated areas.[15 16]

Preventive measures and legislation have lagged behind clinical and pathological evidence. The rising numbers of certifications for asbestosis contrast strongly with the declining trends of most other mineral dust pneumoconioses. Part of the increase is certainly due to a lower threshold of suspicion and more accurate diagnosis. Probably many cases of asbestosis were in the past classified as idiopathic pulmonary fibrosis, bronchitis, or Hamman–Rich syndrome. Significantly, not less than 58% of 315 newly diagnosed cases of asbestosis were found in unscheduled occupations such as laggers, brakeliners, and sprayers.[14]

The pulmonary fibrosis caused by asbestos is a disabling condition, but unlike disease produced by exposure to silica and coal dust asbestosis also carries a serious risk of malignant neoplasia of the bronchus and of the serous membranes, and possibly also of carcinoma of the gastrointestinal tract.[17]

The association between asbestosis and lung cancer was first described by K. M. Lynch and W. A. Smith in 1935,[18] and has since been confirmed by many investigators. The

Chief Inspector of Factories stressed the association in 1947[19] and R. S. Doll and his colleagues have published follow-up and cohort investigations[20 21] which suggest that in at least one factory the attack rates from bronchogenic cancer in men who entered the industry after 1933 are not higher than would be expected in the general population. But in the United States E. C. Hammond and his colleagues[22] reported 53 deaths from lung cancer in 300 consecutive necropsies of insulating workers, and found the death rates from pulmonary and pleural cancers seven times higher in asbestos workers than in American white males.

Since J. C. Wagner and his colleagues[23] first described the occurrence of pleural mesotheliomata in the crocidolite mining districts of South Africa many cases have come to light elsewhere. In Britain most cases have been discovered in London[24] and at the larger ports where much asbestos is handled in the shipbuilding industry.[12 25 26] Diffuse peritoneal tumours associated with asbestos exposure have been reported.[27] There seems to be little doubt that these tumours—which as recently as 1960 were regarded as " rare curiosities "[28]—are of occupational or environmental origin. Wagner[29 30] produced pleural neoplasms in animal experiments, and his findings have now been confirmed by other investigators.[31] The important question of whether only crocidolite or other types of fibres also, especially the widely used chrysolite, have carcinogenic properties has not yet been unequivocally answered.[14]

Two aspects of the asbestos–mesothelioma association are very disturbing. In some cases extremely short exposures have been reported.[12 24] There is also growing evidence that residents in asbestos mining or manufacturing districts and those at risk by the brushing and washing of contaminated working clothes can develop mesenchymal tumours or the bizarre pleural fibrosis and calcifications which seem to be associated with exposure to asbestos.[32 33]

The scope of the problems yet to be solved has been clearly set out by J. C. Gilson in his summing up of a symposium held in New York[34] and in the report of the subcommittee of the International Union against Cancer.[35] The most important of these problems are: the type of asbestos as a factor in the risk of asbestosis and malignancy; the excess risk of malignancy from asbestos in the absence of clinical, physiological, and radiological manifestations of asbestosis; the organization of prospective surveys to establish the risk to industrial and residential populations; agreement on the clinical, lung function, and the notoriously difficult radiological criteria for diagnosing asbestosis; agreement on the most accurate type of dust measurements; and the clinical significance of pleural plaques and of asbestos bodies.

In the meantime it is to be hoped that the promised revision of the 1931 Asbestos Regulations[36] will soon be put into effect and that they will cover all workers at risk, including those engaged in loading and transporting asbestos. Present evidence suggests that crocidolite is the most dangerous of asbestos fibres and it may be possible to find suitable substitutes for at least some of its uses. The uncontrolled dumping of asbestos waste[37] should not occur again. Finally, in view of the long induction period of asbestosis and malignancy the present restriction, that a worker claiming disability benefits for mesothelioma under the Industrial Injuries Act must have been employed after 4 July 1948,[38] seems to be entirely unrealistic and should be abolished.

[1] Murray, H. M., *Report Dept. Comm. on Compensation for Industrial Diseases*, 1907. H.M.S.O., London.
[2] Merewether, E. R. A., and Price, C. W., *Report on Effects of Asbestos Dust on the Lungs and Dust Suppression in Asbestos Industry*, 1930. H.M.S.O., London.
[3] Wood, W. B., and Gloyne, S. R., *Lancet*, 1934, **2**, 1383.
[4] Wyers, H., *Postgrad. med. J.*, 1949, **25**, 631.
[5] *Asbestos Industry Regulations, Statutory Rules and Orders*, 1931. H.M.S.O., London.
[6] Smither, W. J., *Proc. roy. Soc. Med.*, 1966, **59**, 57.
[7] Hill, I. D., Doll, R. S., and Knox, J. F., ibid., 1966, **59**, 59.
[8] McVittie, J. C., *Ann. N.Y. Acad. Sci.*, 1965, **132**, 128.
[9] Kiviluoto, R., ibid., 1965, **132**, 235.
[10] Hendry, N. W., ibid., 1965, **132**, 12.
[11] Hueper, W. C., ibid., 1965, **132**, 184.
[12] Gold, C., and Cuthbert, J., *Publ. Hlth (Lond.)*, 1966, **80**, 261.
[13] *Guardian*, 12 November 1966.
[14] Gilson, J. C., *Trans. Soc. occup. Med.*, 1966, **16**, 62.
[15] Thomson, J. G., *Ann. N.Y. Acad. Sci.*, 1965, **132**, 196.
[16] Cauna, D., Totten, R. S., and Gross, P., *J. Amer. med. Ass.*, 1965, **192**, 371.
[17] Selikoff, I. J., Churg, J., and Hammond, E. C., *New Engl. J. Med.*, 1965, **272**, 560.
[18] Lynch, K. M., and Smith, W. A., *Amer. J. Cancer*, 1935, **24**, 56.
[19] Merewether, E. R. A., *Ann. Report Chief Inspector of Factories for 1947*, 1947. H.M.S.O., London.
[20] Doll, R., *Brit. J. industr. Med.*, 1955, **12**, 81.
[21] Knox, J. F., Doll, R. S., and Hill, I. D., *Ann. N.Y. Acad. Sci.*, 1965, **132**, 526.
[22] Hammond, E. C., Selikoff, I. J., and Churg, J., ibid., 1965, **132**, 519.
[23] Wagner, J. C., Sleggs, C. A., and Marchand, P., *Brit. J. industr. Med.*, 1960, **17**, 260.
[24] Newhouse, M. L., and Thompson, H., ibid., 1965, **22**, 261.
[25] Owen, W. G., *Brit. med. J.*, 1964, **2**, 214.
[26] Elmes, P. C., and Wade, O. L., *Ann. N.Y. Acad. Sci.*, 1965, **132**, 549.
[27] Enticknap, J. B., and Smither, W. J., *Brit. J. industr. Med.*, 1964, **21**, 20.
[28] Willis, R. A., *Pathology of Tumours*, 1960, 3rd ed., Butterworth, London.
[29] Wagner, J. C., *Nature (Lond.)*, 1962, **196**, 180.
[30] —— *14th Intern. Congress on Occup. Hlth, Madrid Communication*, 1964, 1066.
[31] Smith, W. E., Miller, L., Elsasser, R. E., and Hubert, D. D., *Ann. N.Y. Acad. Sci.*, 1965, **132**, 456.
[32] Kiviluoto, R., *Acta radiol. (Stockh.), Suppl.*, 1960, No. 194.
[33] Hourihane, D. O'B., Lessof, L., and Richardson, P. C., *Brit. med. J.*, 1966, **1**, 1069.
[34] Gilson, J. C., *Ann. N.Y. Acad. Sci.*, 1965, **132**, 696.
[35] Report and Recommendations of the Working Group on Asbestos and Cancer, *Brit. J. industr. Med.*, 1965, **22**, 165.
[36] *Hansard*, 8 August 1966, Col. 237.
[37] *Lancet*, 1966, **2**, 219
[38] *Prescribed Diseases Regulations (1966) Statutory Instruments*, No. 987. H.M.S.O., London.

Status Epilepticus: A Medical Emergency

Despite modern treatment status epilepticus remains a dangerous condition carrying a high mortality. Its consequences remain largely uncharted because in most instances reports of treatment end with the control of the status or death. But, since there is evidence that the longer the status continues the greater the mortality, early treatment is important and status should be regarded as a medical emergency.

Status epilepticus is defined as the occurrence of grand mal convulsions without recovery of consciousness between fits. The recognition of fully developed status is easy enough: not only have fits been multiple and usually frequent, with persisting unconsciousness, but other signs of physiological stress —in the heart, lungs, kidneys, and in fluid and electrolyte balance—may have developed. A practical problem is to decide at what stage the patient needs transfer to hospital and to the sometimes very specialized management that may be required. Many patients in early status respond rapidly to a simple increase in the routine anticonvulsants they are already having. Moreover, when status supervenes in an established case of epilepsy there is often adequate warning in the form of increased frequency of fits, up to several a day, but with recovery of consciousness between—so-called serial epilepsy. In these circumstances a trial may be justified for a few hours—but no more—of the sort of measures that can be undertaken at home (paraldehyde intramuscularly in adequate dosage being a stand-by). But if status continues then admission to hospital should be arranged at once. When status occurs as the very first manifestation of epilepsy, as is not very uncommon when the causative focus is in the frontal region, the likelihood of an intractable form is much greater, and admission to hospital should certainly be arranged.

In established status the problem of management is threefold: to control the fits, to ensure an adequate airway and oxygenation, and to maintain the biochemical *milieu intérieur* as normal as possible. Monitoring of fluid balance, electrolytes, blood urea, blood pressure, and pulse will be required, and a simple airway may be needed. If status is long continued then tracheostomy with full curarization and assisted respiration may be necessary; in that case monitoring of blood $P\text{co}_2$ and $P\text{o}_2$ will also be called for. In some cases these measures are life-saving, and this makes the condition a matter for urgent admission to hospital.

The linchpin of treatment must remain the control of the fits, and the sooner this is achieved the less need there will be for other measures. If a substantial increase in routine anticonvulsants—given by injection rather than by mouth—does not abolish fits and allow return of consciousness within an hour or two, additional drugs must be used. The remedy most widely advocated is paraldehyde given intramuscularly or intravenously in glucose saline or plasma drip. The wide margin between anticonvulsant and serious toxic doses makes this a drug of choice. Other preparations—soluble barbiturates, soluble phenytoin, and inhalation anaesthetics—have been successfully used, but have not in general displaced paraldehyde. Recently, however, a new drug diazepam (Valium), introduced initially as a muscle relaxant and tranquillizer, has been found to give benefit in status. First reports on it came from French neurologists.[1] [2] Now Drs. M. J. Parsonage and J. W. Norris in this issue of the *B.M.J.* (page 85) give their experience of its use in nine cases of severe status. They gave it intravenously and in seven patients attained immediate control of seizures. The effect was rapid and obvious both on clinical seizures and on electroencephalographic discharges. Although in seven cases other methods of treatment were also used—including paraldehyde in four—there was no doubt that diazepam was a valuable and at times decisive therapeutic agent. Its rapidity of action and its absence of serious toxic effects must recommend it as one first choice in the treatment of persisting status. Initially it should be given intravenously, and Parsonage and Norris advise a saline drip (100 mg. per 500 ml.), though 10-mg. intravenous doses repeated may be given. Control may later be maintained by intramuscular injection. Once control is established a gradual return to the usual oral remedies should be undertaken. There is not yet any clear evidence that the drug is effective by mouth on its own, though it appears at times to be an effective adjuvant to others.

The addition of diazepam to the treatment of status does not reduce the seriousness of this condition. Parsonage and Norris's series contains two deaths, one patient with persisting severe dementia and one with residual hemiparesis. This morbidity is important and has been little considered heretofore. There is growing evidence that mental and neurological deficit may follow status. This reinforces the argument for rapid control of the condition, for careful attention to the biochemical milieu while it lasts, and for early and if possible preventive treatment.

---

[1] Naquet, R., Soulayrol, R., Dolce, G., Tassinari, C. A., Broughton, R., and Loeb, H., *Electroenceph. clin. Neurophysiol.*, 1965, 18, 427.

[2] Gastaut, H., Naquet, R., Poiré, R., and Tassinari, C. A., *Epilepsia (Amst.)*, 1965, 6, 167.

Safer Dental Anaesthesia

In July 1965 the Standing Medical and Dental Advisory Committees of the Central Health Services Council set up a Joint Subcommittee at the request of the Minister of Health with the following terms of reference:

> To consider the use of general anaesthetics in general dental practice and to advise:
>
> (1) How far the administration of general anaesthetics for conservative treatment can be justified, and
>
> (2) How far the administration of general anaesthetics for any purpose without the attendance of a second practitioner can be justified.

This report has now been published[1] and the members of the Joint Subcommittee must be congratulated on producing a document which not only will influence the future of dental anaesthesia but will also serve as a model of the way to present authoritative and exact information in a concise form.

The report classifies the main groups of patients whose clinical condition may justify general anaesthesia for conservative work in general dental practice as follows: (*a*) spastics or others who because of physical infirmity would be uncontrollable under local analgesia; (*b*) patients who are known to react adversely or to be resistant to local analgesics; (*c*) mentally subnormal patients; (*d*) those whose psychological attitude to dentistry is such that they would refuse from fear any form of dental treatment not performed under anaesthesia and who, in the opinion of the dental surgeon, are unsuitable for local analgesia. It can be inferred from the report that the Joint Subcommittee thought some dental practitioners were making too little use of local analgesia for conservative dentistry, for the introduction of lignocaine as an analgesic agent nearly twenty years ago has made the employment of local analgesia reliable and certain. For many years the average Briton had an ingrained fear of the dental surgeon and did not consult him until he could request him to take all his teeth out "with gas but not cocaine." Little wonder then that he prefers that such conservative dentistry as he will permit should be performed while he is asleep. In other countries, such as the U.S.A. and Scandinavia, where local analgesia has been the routine form of pain relief for all types of dental surgery, the use of general anaesthesia for conservative dentistry has not been so enthusiastically championed as in Great Britain.

The report is careful to point out that the relatively low mortality connected with dental anaesthesia in the past is related to the short time for which it is administered. However, if longer operations become more frequent, the mortality and morbidity must inevitably rise, especially if practitioners who are not properly trained administer general anaesthetics for them. The report states that the "administration of general anaesthesia and the performance of dental surgery require the undivided attention of anaesthetist and operator respectively and . . . cannot be combined without risk." This authoritative statement will surely receive general assent.

---

[1] *Dental Anaesthesia,* Report of a Joint Subcommittee of the Standing Medical and Dental Advisory Committees on Dental Anaesthesia. Ministry of Health. 1967. H.M.S.O.

[2] *Brit. med. J.*, 1967, 1, 447.

Indeed, when sending the report to hospitals the Ministry states in an accompanying circular, "When an anaesthetic for dental treatment is administered to a patient in hospital, it is important that there should be one person with a clearly defined responsibility for the patient's general condition and general health whilst in hospital." Clearly this implies that the anaesthetist is responsible both for the preoperative assessment of the patient and for immediate postoperative care and that this is a responsibility which cannot be delegated to the less skilled. There can be no doubt that when a patient is rendered unconscious for a considerable time it is in the interests of his safety for the same criteria to be followed even though the operative work is done as an outpatient either in hospital or in general practice. The report concedes that there would not be enough trained anaesthetists to make this possible in every case, but the section discussing undergraduate and postgraduate teaching of both medical and dental students is comprehensive and will give much food for thought to those concerned with this problem. In all, this report points the way to safer and better dental anaesthesia, some aspects of which were recently discussed in these columns,[2] and it should encourage the development of this branch of the specialty of anaesthesia.

A Year's Cancer Research

The Forty-fourth Annual Report of the British Empire Cancer Campaign for Research was published this week.[1] It is shorter than its immediate predecessors as a result of a decision to exclude accounts of incomplete or inconclusive work. The provision of author and subject indices is an improvement, though the latter is less valuable than the summary which introduced the report in previous years.

The first stage of cancer research is to define the problem, and this is the role both of cancer registries, such as those in Kampala, Jamaica, Fiji, and Neyyoor in South India, and of the special panels concerned with tumours of the testis, bone, and thymus. Some of the difficulties of this first stage are evident in the report from Neyyoor, where religious and health beliefs, shortages of pathologists, and language differences make it difficult to obtain a clear idea of the incidence of the disease. Nearer home epidemiological data are somewhat easier to obtain, and the calculation of death rates for cancers and other diseases for Scotland, Northern Ireland, and Eire will provide valuable basic information for future work. New tables produced by R. A. M. Case enable the calculation of the risk of cancer at particular sites during the period 1911–1960 in these countries.

Circumstantial evidence favouring a virus as the cause of Burkitt's lymphoma continues to accumulate, but direct proof remains elusive. Meanwhile a national survey of tumours of domestic animals in England has shown, as expected, a relatively high incidence of leukaemia in cattle, and efforts are being made to find a virus cause for both this disease and the lymphosarcoma of cats and dogs. Attempts to recover the mouse sarcoma virus from tumours induced by it in the hamster were unsuccessful, though Huebner and his colleagues are reported to have succeeded in doing so by growing the hamster tumour cells in vitro in the presence of a murine leukaemic virus. According to Professor M. G. P. Stoker the Kilham rat virus, an osteolytic virus isolated from transplanted tumours, is the first animal virus found to contain single-stranded D.N.A. An interesting observation is that the Friend virus depresses the immune response in mice; a similar effect has been observed in response to mouse thymic virus and to treatment with chemical carcinogens.

Under certain conditions immune reactivity may be enhanced by prior exposure to *x*-radiation. From Newcastle upon Tyne C. A. H. Trench, C. A. Green, and others report an increased response to sheep erythrocytes in both rabbits and rats irradiated two months earlier. This may be relevant to treatment of cancer by radiotherapy. In relation to causation, however, V. Wallis and P. C. Koller conclude that in mice there is no obvious relation between the level of immune responsiveness after radiation and the subsequent development of leukaemia.

A peculiar and apparently specific affinity between submesothelial tissues and asbestos is reported by F. J. C. Roe and his colleagues at the Institute of Cancer Research. This may explain the causal relationship between exposure to asbestos and mesothelioma. The relative risk of different types of asbestos remains uncertain, but it is of interest that A. and P. R. Peacock have seen malignant tumours in fowls at the site of injection of tremolite as well as of amosite and crocidolite. According to J. S. Harington and G. Macnab asbestos may be present in phagocytes both in phagosomes and free in the cytoplasm. In Belfast, where asbestos cancer occurs in relatively high incidence, the department of therapeutics of Queen's University organized a meeting of medical officers from the Northern Ireland Ministry of Health and Social Services, from the Medical Research Council, and from several large industrial firms, which resulted in a general agreement to abide by the "Code of Practice in Handling Asbestos" drawn up by the Asbestosis Research Council.[2]

It is tragically true that many elegant and sometimes costly diagnostic techniques reveal cancers for which no more than palliative treatment is likely to be available. Of particular interest, however, is the localization of tumours by various isotope techniques. Like previous years, 1966 did not see the introduction of an automated system for the examination of cervical smears, but the development by A. I. Spriggs and M. M. Boddington of a technique for collecting and fixing cervical cells in suspension so that the cells can subsequently be stuck on to plastic tape for automatic scanning may be an important step forward. Similarly, the formation of a library of classified cervical cells should prove invaluable in the development of an automatic cell-recognition device. In view of the known association between poor sexual hygiene and the risk of cancer of the cervix uteri, it is perhaps surprising that more attention has not been paid to women attending venereal-disease clinics. In a survey of patients attending such a clinic H. C. McLaren and his colleagues in Birmingham found precancerous lesions in a number of women under 30 and in two under 20 years of age. Several groups of workers have persisted in their search for a suitable biochemical screening test for cervical precancer. In this connexion it is difficult to believe that any further study of the enzyme 6-phosphogluconate dehydrogenase is justified, since in no case has a rise in its level proved as reliable a guide as cytological investigation. According to G. G. Muir the level of the enzyme reflects an inflammatory reaction rather than the presence of malignant cells.

---

[1] British Empire Cancer Campaign for Research, *Annual Report for 1966*, 1967. London.

[2] *Code of Practice in Handling Asbestos*, 1965. Internal Report drawn up by the Asbestosis Research Council.

[3] Report of United States Veteran Administration Cooperative Urological Research Group, *Surg. Gynec. Obstet.*, 1967, 124, 1011.

A method for predicting which form of endocrine ablation or hormone therapy is most appropriate to individual cases of breast cancer would constitute an important step forward. Unfortunately none of the many attempts to develop such a method has so far proved successful. Meanwhile A. P. M. Forrest and Helen J. Stewart express doubt whether pituitary implantation of yttrium-90 can always completely ablate the gland's function. A recent comparison of the results of different methods of treating carcinoma of the prostate[2] came to the disappointing conclusion that treatment with oestrogen did not result in a prolongation of life; in fact death from heart disease and cerebrovascular accidents was substantially more frequent in patients given 5 mg. oestrogen daily. Several centres are moving towards the use of computers in relation to radiotherapy dosimetry, while T. J. Deeley and M. A. Longy at the Hammersmith Hospital are working out methods for using computers in relation to the follow-up of cancer patients and assessment of treatment.

All those who helped the central organization and the three autonomous councils of the British Empire Cancer Campaign for Research to collect the record sum of £2m. deserve the highest praise, particularly as this has enabled the Campaign for the first time to guarantee its grants to major research centres for three consecutive years.

Intestinal Necrosis due to Digitalis

If digitalis had been introduced at the present time it is doubtful whether it would have passed the scrutiny of the Dunlop Committee. In spite of its immense value, the gap between therapeutic and toxic actions is narrow, especially in patients with chronic heart failure, in elderly patients, and when diuretics are given at the same time. Arrhythmias, such as ventricular extrasystoles and atrial tachycardia, are well-known indications of toxicity, and sudden death may result from cardiac arrest or ventricular fibrillation. J. L. C. Dall[1] has drawn attention to the dangerous situation in which refractory cardiac failure may be the result of treatment with digitalis. Various neuropsychiatric manifestations are easily overlooked, especially in the elderly; they include disturbances of vision, confusion, hallucinations, and depression.

Gastrointestinal symptoms are common. Anorexia, nausea, vomiting, and diarrhoea are well known, but the occurrence of abdominal pain is not sufficiently stressed, and its true nature may be mistaken for an intra-abdominal catastrophe. In some patients a syndrome of abdominal pain, diarrhoea, and melaena mimicking mesenteric occlusion has been attributed to digitalis.[2 3] In a recent report[4] three patients were encountered in a single year, and a further eight were discovered by reviewing post mortem records. All were elderly and had been taking digitalis for chronic heart failure. Many already had features of digitalis toxicity when they developed signs of ileus, with a tender, distended abdomen, coffee-ground vomiting, and melaena. The condition was invariably fatal within a few days of onset, and necropsy showed diffuse, haemorrhagic lesions throughout the mucosa of the stomach and intestines, most marked in the jejunum. The veins were engorged, but in no case was there evidence of mesenteric arterial occlusion. Digitalis has been shown to lower splanchnic blood flow and to increase splanchnic vascular resistance in patients with heart failure,[5] and such an effect may be critical when the mesenteric circulation is already compromised. It is possible that potassium depletion may also be a factor, since diuretics have commonly been given, and vomiting or diarrhoea will lead to further loss of potassium.

Such serious toxic effects deserve respect, and prevention is better than cure. The one indication for maintenance therapy with digitalis is atrial fibrillation, and the dose should seldom exceed the equivalent of 0.25 mg. digoxin twice daily, with a day's treatment omitted once a week. Patients with chronic heart failure may need less than this, and a careful watch should be kept for signs of toxicity or for a sudden change in tolerance to the drug. Any untoward symptom in a patient taking digitalis should raise the possibility of toxicity, and if in doubt the drug should be stopped. Early administration of potassium, chelating agents, or β-adrenergic blocking drugs may reverse the more serious toxic effects.

---

[1] Dall, J. L. C., *Lancet*, 1965, **1**, 194.
[2] Gazes, P. C., Holmes, C. R., Moseley, V., and Pratt-Thomas, H. R., *Circulation*, 1961, **23**, 358.
[3] Polansky, B. J., Berger, R. L., and Byrne, J. J., ibid., 1964, **30**, Suppl. No. 3, p. 141.
[4] Muggia, F. M., *Amer. J. med. Sci.*, 1967, **253**, 263.
[5] Ferrer, M. I., Bradley, S. E., Wheeler, H. O., Enson, Y., Preisig, R., and Harvey, R. M., *Circulation*, 1965, **32**, 524.

Therapeutic Misadventure

The numbers of deaths from therapeutic misadventure in England and Wales vary considerably from year to year. In 1959, for instance, they numbered 136. They then gradually rose to 220 in 1962, falling to 181 in 1963 and to 103 in 1964, the latest year for which figures have been published.[1] The present trend is therefore satisfactory, but the possibility that it is part of a largely chance fluctuation cannot yet be ruled out. Nor is the interpretation of the figures always entirely clear, because it is generally seriously ill patients who receive the most potent remedies, and in such circumstances the attribution of death to the effects of the treatment instead of to the disease can be problematical.

The latest report from the Registrar General[1] records 19 deaths from corticosteroids compared with 25 in 1963. This continues a downward trend from the total of 40 deaths in 1962. Similar substantial decreases in the numbers of deaths over the three years 1962–4 are recorded for those due to anticoagulants (21, 16, 9) and anti-cancer drugs (18, 16, 4). The number of deaths resulting from penicillin also dropped sharply, from 7 (plus 1 in conjunction with streptomycin) in 1963 to only 1 in 1964, and a considerable reduction is to be noted in deaths attributed to the results of radiotherapy, which fell from 46 to 32. In contrast two drugs previously known to cause death from therapeutic misadventure did not show much change—phenylbutazone, with 8 deaths in 1963 and 7 in 1964, and chloramphenicol with 6 and 4 respectively. Of the 74 deaths from surgical procedures it is notable that the operations of oesophagoscopy and dilatation of the oesophagus, together causing 12 deaths, stand out as much the largest group, as noted before in these columns.[2] The fatality in these cases followed on perforation of the oesophagus.

---

[1] *The Registrar General's Statistical Review of England and Wales for the Year 1964*, Part III, Commentary, 1967. H.M.S.O.
[2] *Brit. med. J.*, 1965, **1**, 1205.

Papers and Originals

Post-concussional Sequelae*

ALEX. R. TAYLOR,† M.A., F.R.C.S.

Brit. med. J., 1967, 3, 67–71

After a year in which several papers have appeared describing a quantitative relationship between the late symptoms of head injury and measurable deviations from physiological and psychological norms (Houdart *et al.*, 1966 ; Lishman, 1966 ; Taylor and Bell, 1966), it would seem to be an appropriate time to re-examine a one-hundred-year-old question about the aetiology of post-concussional sequelae.

The same argument has ranged back and forth almost unchanged over this hundred years. In 1866 Erichsen presented 63 cases of severe injury sustained mostly on American railroads. He was concerned with the severity of the symptoms in the absence of much evidence of external injury. He thought the symptoms were due to molecular derangement of the spinal cord. In 1879 Regler, who had noted a great increase in the severity of symptoms after the introduction of compensation awards in 1871, expressed the view that they were actuated by fright, long inactivity, and a desire for financial gain. He thought there was no evidence for molecular derangement. This was the so-called "railway spine" controversy.

In 1962 Symonds reviewed the aetiology of concussion, and stressed, inter alia, the finding of cellular and diffuse white-matter damage. In 1966 Miller, analysing his experience of many head-injured litigants, wrote: "I cannot believe that the clinical features of this disorder justify its speculative attribution to cellular damage." This was a judgement about the writer's beliefs and not about concussion, but there is a good historical precedent for this too. In 1863, rejecting the then current vascular theories, Hilton wrote: "I cannot conceive it possible that a long continuance of the symptoms of concussion can depend upon any temporary error of this kind." Or again, Strümpell (1888) wrote: "I cannot free myself from a feeling of uncertainty in these cases of head injury."

It is worth while noting that in the early days of the argument the symptoms of "spinal concussion" preceded the inauguration of compensation payments, and that they were the same before as after, though their severity apparently increased. Indeed, the difference of opinion about aetiology has been bedevilled for 100 years by the inability of physicians to disentangle the symptoms occurring after concussion from the symptoms that follow the initiation of a claim for compensation. I have yet to read an article on the subject of post-concussional sequelae in the British literature which does not contain the words "litigation" or "psychogenic" in the first dozen lines. Even a critical leading article about post-traumatic headache, written in April 1966, which concluded that treatment was not easy but was well worth while, contained the statement that in at least two-thirds of the patients there is a psychogenic element. This is certainly an advance on a similar leader of 1961, which said: "Above all, the general physician . . . should find it advisable to refer a patient to the psychiatrist as soon as possible . . . " and concluded: "In the ultimate analysis it [accident neurosis] is a social disease and a function of industrial morale."

Symonds (1962) pointed out that it was valueless to inquire whether the symptoms were organic or functional, because they must always be both. While agreeing with this, I feel that a periodic critical analysis of degrees and probabilities is necessary with each advance in physiological or biochemical knowledge about head injury. The treatment of a disorder predominantly organic must be different from one predominantly psychiatric.

Prima facie, it seems strange that 66% of the head-injured, necessarily a random sample of the population, should be afflicted with neuroticism or excessive cupidity while most of the victims of limb, abdominal, or thoracic injury escape these stigmata. The evidence for neuroticism should be carefully examined.

Evidence for Neuroticism

There are no Abnormal Signs on Physical Examination

This is a notoriously difficult obstacle to precise diagnosis. That a patient should complain of organically determined symptoms of headache, dizziness, lack of energy, poor memory, and difficulty in concentrating and have no physical signs is to some doctors incredible. But the central nervous system is unique in its clinical silence.

A meningioma may attain the size of a cricket ball without causing more than an occasional epileptic fit or transient headache and give rise to no physical signs. A frontal or temporal lobe may be excised without definable abnormality, and thousands of patients have had all the white fibres of both prefrontal regions divided in the operation of leucotomy without detectable physical changes. Patients whose character, mood, and behaviour change after meningitis may have "negative" physical examinations. As Strauss and Savitsky (1934) concluded after a lengthy review of this question: "Failure to understand a clinical phenomenon is no proof of its psychogenicity."

There is an Inverse Relation Between Severity of Injury and Persistence of Post-concussional Sequelae

According to Miller (1961) the more trifling the injury the longer and more vehemently the litigant complains. Of his patients with a post-traumatic amnesia of less than 15 minutes 37% had gross unequivocal psychoneurotic complaints. Only 6% of patients with amnesia of over 72 hours had such complaints. Brock (1960), Russell and Smith (1961), and Symonds (1962) came to opposite conclusions about the significance of post-traumatic amnesia. They believed that though imperfect it was the most reliable and sensitive index of the severity of brain injury.

---

* Read at the Annual Clinical Meeting of the British Medical Association, Londonderry, 1967.

† Department of Neurological Surgery, Royal Victoria Hospital, Belfast 12.

The other comparison made by Miller to show that symptom severity varied inversely with physical damage was between those who had skull fractures and those who had not. Of nine cases with compound fractures none was complicated by neurosis, and "neurotic" symptoms were three times as common in those without as in those with fractures.

These data prove exactly the opposite of what was intended. Percivall Pott (1808) realized that a fracture might protect the patient against the general effects of brain deceleration. He listed vomiting, giddiness, loss of speech and sense, loss of voluntary motion, etc., as general symptoms, and then wrote: "On the other hand the bones of the skull are sometimes cracked, broken, nay even depressed, and the patient suffers none of these symptoms."

Denny-Brown and Russell (1941) found that an animal is rendered unconscious by a much lesser blow if the head is freely movable. The head not free to move is more easily fractured and suffers less of the effects of "cerebral commotion." A great deal of energy is absorbed in fracturing the skull, which is then diverted from the production of shearing stresses in the brain. For this reason biomechanics experts are exploring the possibilities of "tuning" a crash helmet so that it fractures under a certain stress and so protects the contained brain. One expects the patient with a fractured skull to suffer less from concussional effects than his unfractured counterpart who absorbed the same amount of energy on impact.

Unskilled Workers and Less-intelligent Patients Suffer More Prolonged Disability

This is a matter of interest and motivation, and is not confined to the field of trauma. During the last war Commando and Special Service personnel who were off duty for more than 21 days had to transfer to another unit. One could be certain that such selected men after operations for hernia, cartilage derangement, or disc protrusion would be out of bed as soon as permitted and back to their units probably suffering in silence within the statutory three weeks. Some prisoners of war or the more lowly performers of menial tasks in the Services could with difficulty be prised out of hospital in twice the time and be discharged, complaining bitterly, on sick leave.

Symonds and Russell (1943) found that head-injured R.A.F. air crews returned to duty twice as rapidly as ground personnel.

Similarly in civilian practice, the man with the more interesting job and the bigger personal stake in his recovery complains less and returns to his desk sooner.

Personal hazard is also a factor. A civil servant may be able to do his job efficiently in spite of some headache and a sense of abnormal movement, but a scaffold erector or steeplejack will not. Professional men will return to work sooner than manual workers, but it is incorrect to assume that they do not therefore have symptoms. Though 80% of Russell's (1933–4) patients (not entitled to compensation) returned to full work within six months of injury, 40% still had symptoms at the end of 18 months.

It is sometimes said that doctors do not suffer from post-concussional sequelae, but published accounts do not support this belief. Durand Wever (1929) described typical symptoms from an injury for which she was not entitled to claim compensation. Mayer (1929) found that his symptoms continued after his claim was settled, and advised other doctors to believe that their patients' complaints were both real and disabling. Strauss and Savitsky (1934) described a case in which a doctor had symptoms for five months after head injury without loss of consciousness. He continued to work but suffered from headaches, a sense of abnormal movement, lack of concentration, and poor effort tolerance. Compensation was not claimed.

Injuries Sustained during Sporting Activities do Not Have Sequelae

This generalization is partly true. It does not apply to severer ski-ing or rock-climbing accidents nor to "missile" injuries suffered on the hockey field. Hunting and rugby football are usually mentioned as "no-sequelae" sports, though American football, because of the dangerous "protective" devices worn, has abundant records of college boys who never played again after a head injury.

In physical terms this is a matter of speed at impact. The rugby player seldom achieves 20 ft. (6 m.) per second, the huntsman seldom comes off his horse at more than 30 ft. (9 m.) per second. The 30 mile (48 km.) an hour motorist is travelling at 44 ft. (13.4 m.) per second and twice that at 60 miles (96 km.) per hour. Graduation of severity according to speed of impact is well recognized in the Mid-western cities of America, where in hot weather small children stray to the stairs of tenement houses and fall through one or more flights. A fall of one flight, or 15 ft. (4.6 m.) (21 ft. (6.4 m.) per second), seldom results in injury requiring long detention in hospital, two flights (34 ft. (10.4 m.) per second) means a severe head injury, and three or more (44 ft. (13.4 m.) per second) may be fatal.

The question of motivation is again important; the sportsman does not want to give up a pleasurable form of activity, and, if necessary, will suffer the inconvenience of a headache.

Summary of Evidence for Neuroticism

The evidence for the predominance of neurotic symptoms after head injury is not very convincing, particularly if one disregards the litigants who obviously have a powerful motive, conscious and unconscious, for continuing to suffer.

If neurosis is such an important factor one would expect the literature to contain many controlled randomized studies of head-injured patients treated or not treated by psychiatric methods. No such studies exist. Instead are the statements that psychiatric treatment is of no value until claims for compensation are settled—patients not claiming compensation are never mentioned in this connexion. Surprisingly there is an absence of correlation between post-traumatic sequelae and history of previous psychiatric illness, which is mentioned in most reviews.

Though it is often said in our courts of law that recovery will begin at the conclusion of the case and be complete in two years, this is not borne out by 10-year surveys of the German head-injured of the first world war (Goldstein, 1942), or of the American Korean war head-injured (Caveness, 1966).

Of Goldstein's patients 20% became normal workers, 32% worked at one-half to one-third capacity, 30% had a below normal working capacity, and 18% did no work. These were largely missile injuries and not comparable to a civilian group, but the Korean series is equally divided between penetrating and blunt injuries. Of these patients 84% had returned to work after 10 years, but 40% still had symptoms and 27% had not made a satisfactory social and economic adjustment.

Known Organic Factors

That the initial signs of concussion and the symptoms immediately following recovery of consciousness are organic there is no doubt. Loss of consciousness, mass contraction of the limbs, cessation of respiration, rise in blood pressure, loss of corneal reflexes, and dilated pupils are followed by headache, perhaps vomiting, dizziness, confusion, and amnesia. These are all symptoms and signs which could arise from damage to the cranial nerve nuclei between the medulla (X) and the upper brain stem (III), the arousal centre in the reticular formation, the pyramidal tracts, and the vasomotor centre. If damage is sought in the brain of the concussed animal this is the area in which it is mainly found. The nerve cell count in the lateral vestibular nucleus is invariably reduced even after a mild concussional blow. That this is not transitory was shown by Groat and Simmons (1950), who made cell counts in the brain-stem nuclei of guinea-pigs 13 months after a single concussive blow to the movable head.

The mechanism of the medullary injury is uncertain. It may be, as Friede (1961) suggested, a blow to the cervico-medullary junction dealt by the odontoid process as the anterior surface is hyperflexed over it. The brain stem and cord are more probably stretched than struck, as the neck is hyperflexed through about 110 degrees and rapidly decelerated. Breig (1960) demonstrated that the cord is stretched and elongated on neck flexion. As it is fixed by the filum terminale, dentate ligaments, and cranial nerves, especially V, VII, and VIII, this pull will be sharply felt all through the brain stem and forward through the long tracts to where the forebrain is fixed by the optic nerves, olfactory bulbs (sometimes pulled out), and carotid arteries. As a result of this stretching white fibres from the brain stem to the centrum ovale are actually fractured or snapped. Biggart (1936) demonstrated these "fractures" and the resulting end bulbs on the axons by Bielschowsky staining in the brains of patients dying after head injury. But these lesions are present not only in fatal injuries. Nevin (1964) found them all through the white matter of rats subjected to even minor concussive blows. They took about three days to develop (Fig. 1) and were present as constantly as the chromatolysis in the brain stem nuclei described by Windle *et al.* (1944) (Fig. 2). In the same areas he found irregular thickening and fragmentation of the myelin sheaths (Fig. 3).

If concussion causes widespread lesions throughout the white matter it is not surprising that Becker *et al.* (1946) found a deterioration in the maze-running performance of guinea-pigs a month after concussion. Animals already trained lost their skills, while untrained animals were much more difficult to train and retained their new learning badly compared with control animals. It seems more reasonable, therefore, to suppose that injured human subjects concentrate and learn badly, find difficulty in retaining new information, are irritable, anxious, and lacking in insight because they have multiple lesions throughout the white matter, than to label them neurotic because they do not have any of the easily elicited physical signs.

Variations from the Physiological Norm

Though patients after uncomplicated concussion do not have abnormal physical signs, they have been found by special examination to show deviations from normality in the permeability of the blood/C.S.F. barrier, cerebral blood flow, and vestibular responses to threshold stimuli (electronystagmography). Zetterholm (1947) examined 149 head-injured patients six months to two years after head injury for permeability of this blood/C.S.F. barrier to bromine. Of 104 who had normal permeability quotients 63 had no sequelae and only four had severe symptoms. Only eight of 45 with abnormal permeability quotients had no sequelae, and 15 had severe symptoms.

After two years 73 patients were re-examined: 57 were normal, of whom 47 had no sequelae and none was severely

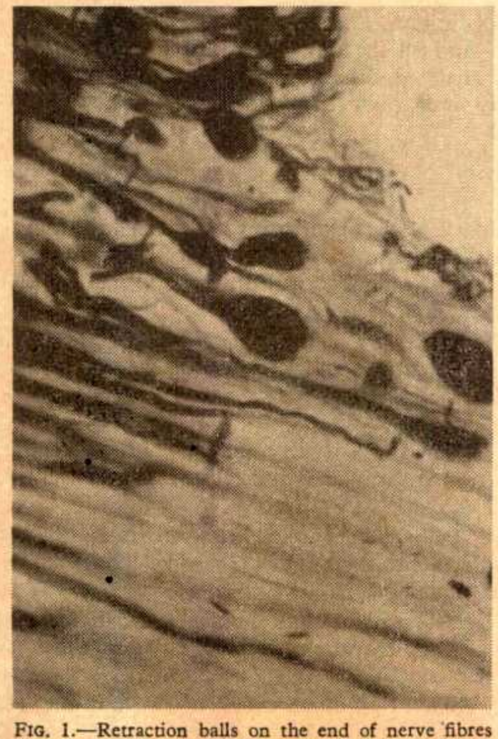


FIG. 1.—Retraction balls on the end of nerve fibres from a rat 10 days after concussional head injury. (Bielschowsky. ×350.)

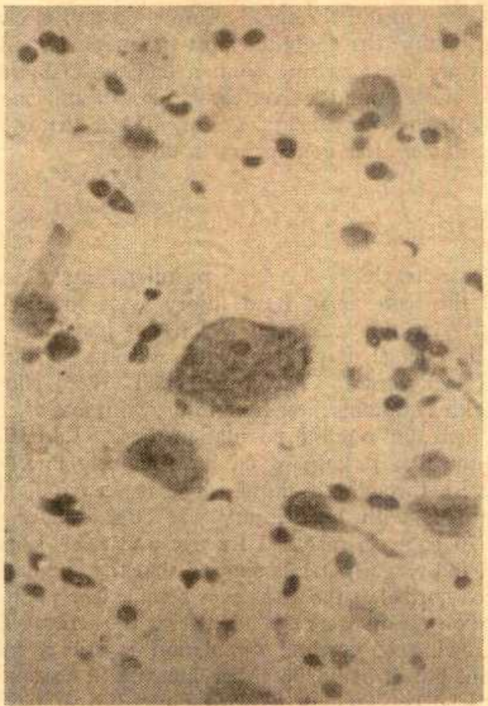


FIG. 2.—Nerve cells in the medulla oblongata showing chromatolysis three days after injury. (Gallocyanin. ×265.)

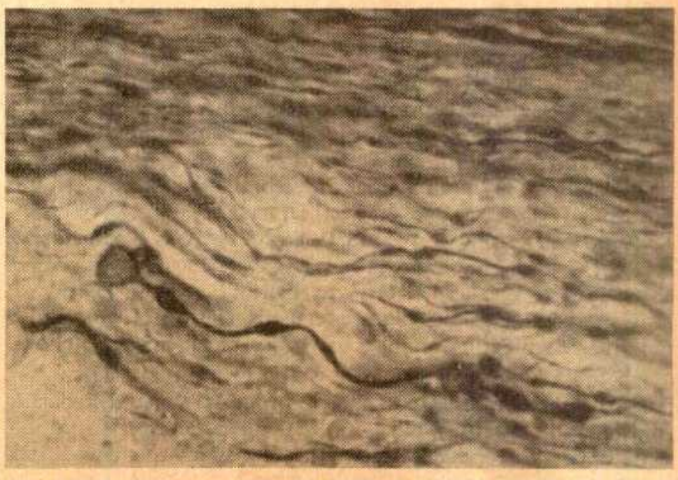


FIG. 3.—Myelin sheaths showing fusiform swelling and vacuole formation seven days after concussion. (Weigert Pal. ×320.)

disabled. Of the 16 with abnormal permeability 12 had sequelae, seven of a severe degree. These figures are statistically significant. The findings have been confirmed by Haxhe (1963), using radioactive bromine. They indicate that one of the effects of brain injury is altered blood/C.S.F. permeability and that its degree correlates with the severity of postoperative sequelae.

Vestibular Function

Though much has been written about labyrinthine damage in head injury Friedman *et al.* (1945) showed that tests of vestibular function did not place the lesion causing post-concussional dizziness in the labyrinth. Since then testing has been greatly refined and includes the electrical recording of nystagmus (electronystagmography). In this way Houdart *et al.* (1966) studied 50 patients with "a subjective syndrome following injuries to the head." In more than half they found a vertical nystagmus appearing in all positions of the head. There were additional minor abnormalities of rhythm and amplitude which they thought were "specific to the traumatic syndrome and apparently authenticating its organic basis." Wilmot (1966), using threshold stimulation and electronystagmography, found the abnormal post-traumatic responses quite different from those arising from a damaged labyrinth; and similar to those found in vertebrobasilar insufficiency. This accords with the experimental finding of chromatolysis in the vestibular nuclei after concussion in animals.

Vascular Factors

Vasomotor instability has been postulated as an aetiological factor in the sequelae of head injury since the earliest days of inquiry. By this was originally meant instability of blood pressure on change of posture with resulting dizziness, faintness, and tachycardia. Taylor and Bell (1966) showed that patients with symptoms after head injury with loss of consciousness had increased cerebral circulation times. Recordings were made of the first passage of an intravenously injected radioactive stream through the head. The mean circulation times of 70 patients with head injury was 20% greater than the mean of 70 controls matched for age and sex. Longitudinal studies of individual patients showed that the circulation times approached normal as the symptoms became less. Patients with compensation claims were excluded from the series. The cause of this slowing of cerebral circulation is still a matter for speculation, but it could be either increase in vasomotor tone at the arterial or capillary level or increased capillary permeability.

Discussion

There is now a great deal of pathological, physiological, and biochemical data to show that patients who absorbed a blow on the head sufficient to cause alteration in consciousness have lesions of varying severity in the medullary pontine nuclei and the white matter, with consequent disorders of vestibular function, capillary permeability, and cerebral blood flow. Minor intellectual disorders are found if sought for by objective psychological testing (Zangwill, 1966). There is also evidence of acute disorders in glucose and pyruvate metabolism (Kurze *et al.*, 1966), water and electrolyte distribution (Van Harreveld, 1966), adenosine triphosphate metabolism (Ishii, 1966), and a rapidly accumulating number of other biochemical reactions.

It is no longer good enough to stand firm on clinical convictions that head-injured patients, if properly managed, socially adjusted, and carefully rehabilitated, will not have "neurotic" symptoms. The evidence from the few series so managed all points in the other direction. We cannot therefore say that the patients have their symptoms because they have been neglected, spoiled, or legally implicated. It is increasingly clear that closed head injury may present any degree of chronic complication from the slightest abnormality to dementia and quadrispasticity (Strich, 1961). Patients who have minor difficulties in concentration and performance which irritate them and make them act unusually are not "neurotic," they are "cerebrally disorganized," and for good organic reasons. How else can we explain the child who comes in from play and asks to be allowed to lie down because he has a headache, the active young man who discovers to his surprise that he is sensitive to the effects of alcohol, or the older man whose family says "he has never been the same since his fall"?

These symptoms are important, firstly, because for all we know they may be preventable, and, secondly, because the number of sufferers increases steadily every year.

They may be preventable—the investigation of the concussed patient stops after neurological examination at skull *x*-ray examination, and treatment is rest in bed until he is well enough to get up. The number of sufferers increases—head injury is now by far the commonest neurological disorder. In Great Britain traffic accidents, industrial injuries, and miscellaneous falls cause over half a million head injuries each year. Of these, 80% are classified as non-dangerous, but about 40% have "concussion" and 15% have continuing symptoms. In round figures there are about 75,000 new patients with post-traumatic symptoms added to the existing number each year. The profession will soon be forced by the magnitude of the problem to take some note of it.

It does not appear as if propaganda or prophylactic measures will reduce the number of traffic accidents. They continue to increase annually in every country along with the climbing traffic density. We shall have to treat the resulting patients, and as a necessary prerequisite we shall have to discover much more than we now know about the physiological and biochemical disorders of acute and chronic post-concussional states. The present surgical endeavour in the treatment of head trauma is almost wholly absorbed in the diagnosis of intracranial bleeding and its treatment. We do everything for the severely damaged 10% and neglect the non-serious 90%. The only head injury sequelae we remotely begin to understand is epilepsy, because it can be observed, assessed, and treated. The less tangible symptoms—headaches, vertigo, irritability, poor concentration, faulty memory, sensitivity to alcohol, loss of libido—and all the other pieces of this so-called syndrome should be analysed, dissected, and investigated until it is known what they are, what they express, and how they can be corrected.

Summary

The history of the relationships between litigation and head trauma and its neurotic sequelae is presented. It is noted that there is a higher rate of so-called neuroticism after head trauma than after trauma to other parts.

The evidence that concussional sequelae are in fact neurotic is examined in detail. It is concluded that, except in litigants, the evidence is poor.

The known organic factors in patients who have symptoms after concussional head injury are reviewed. The influence of lesions seen in the midbrain and white matter of experimentally concussed animals is considered.

A relationship is suggested between these diffuse minor lesions and the emotional and intellectual abnormalities found after head trauma.

Physiological and biochemical changes are described affecting the blood/C.S.F. barrier, cerebral circulation times, and tests of vestibular function.

It is concluded that management of the head-injured patient is based on too many unwarrantable assumptions about the incidence of neuroticism and the absence of important physical

and biochemical abnormalities. It is suggested that research into the large and important group of "non-serious" head injuries has been neglected, to the detriment of their management.

Figs. 1, 2, and 3 are reproduced by kind permission of Dr. N. C. Nevin.

References

Becker, R. F., Groat, R. A., and Windle, W. F. (1946). *Fed. Proc.*, **5**, 7.
Biggart, J. H. (1936). *Pathology of the Nervous System.* Edinburgh.
Breig, A. (1960). *Biomechanics of the Central Nervous System.* Stockholm.
Brock, S. (1960). *Injuries of the Brain and Spinal Cord and Their Coverings*, 4th ed. New York.
Caveness, W. F. (1966). In *Head Injury Conference Proceedings*, edited by W. F. Caveness and A. E. Walker, p. 209. Philadelphia.
Denny-Brown, D., and Russell, W. R. (1941). *Brain*, **64**, 93.
Durand Wever, A. M. (1929). *Münch. med. Wschr.*, **76**, 1879.
Erichsen, J. E. (1866). *On Concussion of the Spine, Nervous Shock, and Other Obscure Injuries of the Nervous System.* New York.
Friede, R. L. (1961). *Arch. Neurol. (Chic.)*, **4**, 449.
Friedman, A. P., Brenner, C., and Denny-Brown, D. (1945). *J. Neurosurg. (Chic.)*, **2**, 36.
Goldstein, K. (1942). *After Effects of Brain Injuries in War*, p. 220. London.
Groat, R. A., and Simmons, J. Q. (1950). *J. Neuropath. exp. Neurol.*, **9**, 150.
Haxhe, J. J. (1963). Blood C.S.F. barrier breakdown. Personal communication.
Hilton, J. (1863). *Lectures on Rest and Pain.* London.
Houdart, R., Cathala, F., Pialoux, P., Raby, D., Fontelle, P., and Vollmer, D. (1966). *Presse méd.*, **74**, 449.
Ishii, S. (1966). In *Head Injury Conference Proceedings*, edited by W. F. Caveness and A. E. Walker, p. 276. Philadelphia.
Kurze, T., Tranquada, R. E., and Benedict, K. (1966). Ibid., p. 254. Philadelphia.
Lishman, W. A. (1966). *Proc. roy. Soc. Med.*, **59**, 261.
Mayer, E. (1929). *Münch. med. Wschr.*, **76**, 2135.
Miller, H. (1961). *Brit. med. J.*, **1**, 919.
—— (1966). *Proc. roy. Soc. Med.*, **59**, 257.
Nevin, N. C. (1964). "Pathology in Cerebral Concussion." Thesis, The Queen's University of Belfast.
Pott, P. (1808). *The Chirurgical Works.* London.
Regler, J. (1879). *Uber die Folgen der Verletzung auf Eisenbahnen.* Berlin.
Russell, W. R. (1933–4). *Trans. med.-chir. Soc. (Edinb.)*, 129.
—— and Smith, A. (1961). *Arch. Neurol. (Chic.)*, **5**, 4.
Strauss, I., and Savitsky, N. (1934). *Arch. Neurol. Psychiat. (Chic.)*, **31**, 893.
Strich, S. J. (1961). *Lancet*, **2**, 443.
Strümpell, A. (1888). *Uber die traumatischen Neurosen.* Berlin.
Symonds, C. (1962). *Lancet*, **1**, 1.
—— and Russell, W. R. (1943). Ibid., **1**, 7.
Taylor, A. R., and Bell, T. K. (1966). Ibid., **2**, 178.
Van Harreveld, A. (1966). *Brain Tissue Electrolytes.* Washington, D.C.
Wilmot, T. J. (1966). *J. Laryng.*, **80**, 1156.
Windle, W. F., Groat, R. A., and Fox, C. A. (1944). *Surg. Gynec. Obstet.*, **79**, 561.
Zangwill, O. L. (1966). *Proc. roy. Soc. Med.*, **59**, 266.
Zetterholm, S. (1947). *Acta psychiat. scand.*, Suppl. No. 45.

Prolapse of the Posterior Leaflet of the Mitral Valve: A Clinical, Familial, and Cineangiographic Study

MARY STANNARD,* M.B., B.S.; J. G. SLOMAN,† M.B., B.SC., M.R.C.P., M.R.C.P.ED., M.R.A.C.P.
W. S. C. HARE,‡ M.D., M.R.A.C.P., F.F.R., F.C.R.A.; A. J. GOBLE,§ M.D., M.R.C.P., F.R.A.C.P.

Brit. med. J., 1967, **3**, 71–74

Mid and late systolic clicks and late systolic murmurs have in the past been regarded as "innocent," and were thought to be due to pericardial adhesions (Wells, 1957; McKusick, 1958; Ongley *et al.*, 1960; Segal and Likoff, 1964). Recently there has been evidence to show that these auscultatory findings are due to an abnormality of the mitral valve and sometimes are associated with a history of anterior chest pain and an abnormal electrocardiogram (Barlow *et al.*, 1963; Barlow, 1965; Tavel *et al.*, 1965; Barlow and Bosman, 1966; Criley *et al.*, 1966; Leon *et al.*, 1966; Linhart and Taylor, 1966). The purpose of this paper is to present our findings in 13 patients with mid or late systolic clicks and late systolic murmurs, with particular reference to the familial nature of this entity and the findings on left ventricular cineangiography and selective coronary arteriography.

Methods and Materials

Of the 13 patients studied six were referred with anterior chest pain, four because a murmur had been detected on routine examination, and three were siblings of patients already known to us. All were assessed clinically, and an electrocardiogram and a phonocardiogram were made. In six cases haemodynamic studies and left ventricular cineangiography were carried out. Selective coronary arteriography was performed in two patients who presented with severe anterior chest pain.

Findings

The clinical features are set out in Table I. There was a definite female preponderance in the series, 11 patients being female and two male. Their ages ranged from 28 to 67, with a mean of 46 years.

Chest pain was a significant symptom in six patients. The pain occurred anteriorly in the chest, was stabbing in quality, and was not related to exertion. In two cases it was severe enough to require analgesics by injection, but most patients had been regarded as suffering from "cardiac neurosis." In no case was there a past history of rheumatic fever or a history of an illness which in retrospect could have been pericarditis. One patient had been involved in a motor-car accident shortly before the murmur was detected, but she could recall no chest injury. Two patients had thyrotoxicosis; one had symptoms of this at the time her murmur was detected and the other developed it subsequently. One patient had been thought to have had a myocardial infarct some years previously, but there was no evidence of this on her electrocardiogram.

The family history was of significance in only one patient whose father and four brothers were said to have coronary artery disease. However, because a familial incidence of this entity had been suggested, we examined the siblings of our

* Research Assistant, Cardiac Department, Royal Melbourne Hospital. Grant in Aid No. G.428, National Heart Foundation of Australia.
† Director, Cardiac Laboratory, Royal Melbourne Hospital.
‡ Professor of Radiology, University of Melbourne.
§ Cardiologist, Royal Melbourne Hospital.

Table I.—*Clinical Features, Electrocardiogram, and Left Ventricular Angiogram in 13 Patients with Mid or Late Systolic Clicks and Late Systolic Murmurs*

Case No.	Sex	Age	Symptoms	Past History	Familial	Auscultation and Phonocardiogram	Electrocardiogram	Angiogram
1	F	42	Nocturnal dyspnoea. Thyrotoxicosis	Car accident	+	Late click. Late systolic murmur	V.E.S. L.V.H. ST–T wave changes II, III, V5, V6	Prolapse posterior cusp mitral valve. Moderate mitral incompetence
2	F	55	Anterior chest pain	—	+	Mid and late clicks. Late systolic murmur	Normal	—
3	F	57	Nil	—	+	Mid-late click. Late systolic murmur	Partial right bundle-branch block	—
4	F	32	15 years' anterior chest pain	—	+ 2 Children normal	Mid and late clicks. Late systolic murmur	L.V.H. Flat T waves with inversion II, III, AVF, V4–V6. V.E.S.	Prolapse posterior cusp mitral valve. Mild mitral incompetence
5	F	40	Nil	—	+ Brother normal	Late click. Soft, late systolic murmur	Normal	—
6	F	36	Severe anterior chest pain	—	3 Children and half-sister normal	Mid-late click. No systolic murmur	Normal	Prolapse posterior cusp mitral valve. No mitral incompetence. Normal coronary arteries
7	F	53	Anterior chest pain. Dyspnoea	—	—	Mid and late clicks. Late systolic murmur	Normal	Prolapse posterior cusp mitral valve. Mitral incompetence. Normal coronary arteries
8	F	44	Anterior chest pain. Dyspnoea	Murmur aged 10 years	—	Mid click. Ejection murmur	V.E.S. Flat ST V4–V6.	Prolapse posterior cusp mitral valve. Mild mitral incompetence
9	M	28	Dyspnoea on exertion	—	—	Mid click. Late systolic murmur	L.V.H.	Prolapse posterior cusp mitral valve. Moderate mitral incompetence
10	F	59	Chest pain. Thyrotoxicosis	—	—	Late click. Early systolic murmur	L.V.H. Tall T waves anterior chest leads	—
11	F	48	Nil	? Infarct	—	Late click. Late systolic murmur	ST depression II and III	—
12	F	67	Angina pectoris	—	—	Late click. Late systolic murmur	ST depression II and III	—
13	M	40	Nil	—	4 Brothers " coronaries "	Multiple clicks	Flat T waves II, III, AVF, V5, V6	—

V.E.S. = Ventricular extrasystoles. L.V.H. = Left ventricular hypertrophy.

patients as the opportunity arose. Three sisters in one family (Cases 1–3) had similar auscultatory findings (Fig. 1): haemodynamic studies were carried out in one of them. In the second family two sisters (Cases 4 and 5) had similar auscultatory findings (Fig. 2), though their brother and the children of one of them were normal. The half-sister and three children of another patient (Case 6) were examined and found to be normal.

The abnormal findings in all cases were limited to auscultation. In no case was there any clinical evidence of ventricular hypertrophy or cardiac failure, and all had normal blood pressure. The first and second sounds were normal, but in all cases clicks were present. In seven cases the click was late-systolic, in two cases mid-systolic, and in four cases multiple. In nine cases a late systolic murmur (Fig. 3) was heard, loudest at the apex, but in two cases isolated clicks were the only abnormal findings. In one case the murmur was very loud and " musical," varying with posture (Fig. 4). The remaining two patients had systolic murmurs.

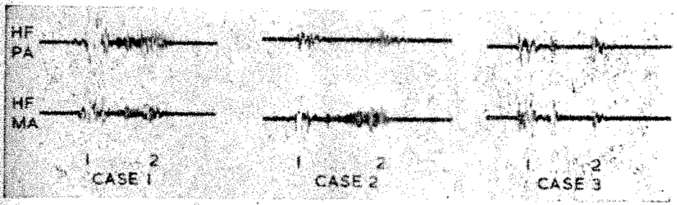


Fig. 1.—Phonocardiograms of three sisters showing first and second heart sounds (1 and 2), the mid-systolic click, and the late systolic murmur. (PA = pulmonary area ; MA = mitral area ; HF = high frequency.)

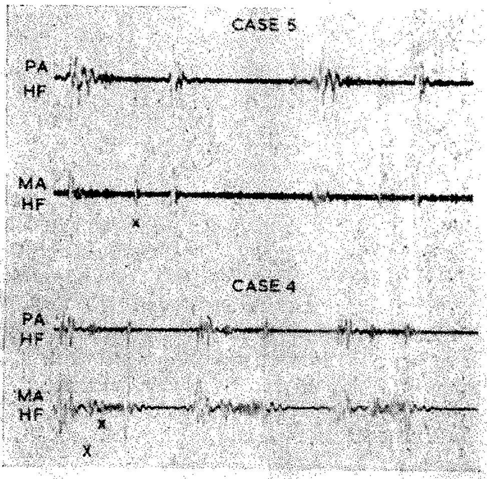


Fig. 2.—Phonocardiograms of two sisters showing the systolic click and late systolic murmur.

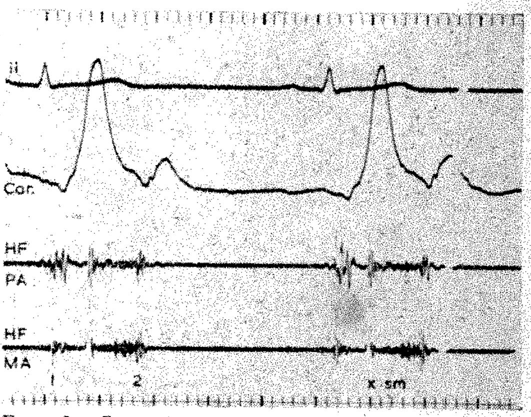


Fig. 3.—Case 9. Phonocardiogram showing the characteristic mid-systolic click (X) and late systolic murmur (SM). (ii = electrocardiogram lead II, Car. = carotid tracing, PA = pulmonary area, MA = mitral area, HF = high frequency.)

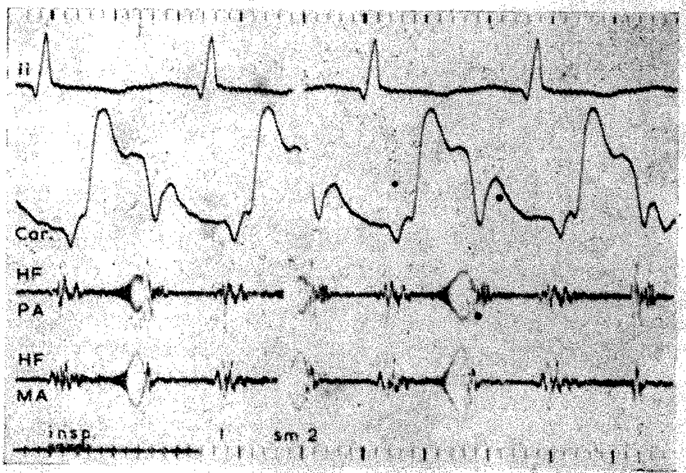


Fig. 4.—Case 4. Phonocardiogram showing loud " musical " late systolic murmur.

The electrocardiograms did not show any constant abnormality. In four patients they were normal. In two of these severe chest pain was the presenting symptom, but no abnormalities appeared during pain or after exercise on a treadmill. In another four left ventricular hypertrophy could be diagnosed (S in V1+R in V5>35 mm.)—in three in association with ST–T wave abnormalities. Four patients had ST or T wave abnormalities alone (see Table I) (in leads II, III, AVF, and the lateral chest leads) and one patient had a partial right bundle-branch block. Ventricular extrasystoles were present in three cases (Figs. 5 and 6). The chest *x*-ray picture in all cases was regarded as being within normal limits, there being no cardiomegaly, left atrial enlargement, or intracardiac calcification. Haemodynamic studies were carried out in six patients (Table II), and in all cases were normal. In particular there was no elevation of the left atrial pressure (pulmonary artery wedge) or of the left ventricular end-diastolic pressure, indicating that the mitral regurgitation was mild.

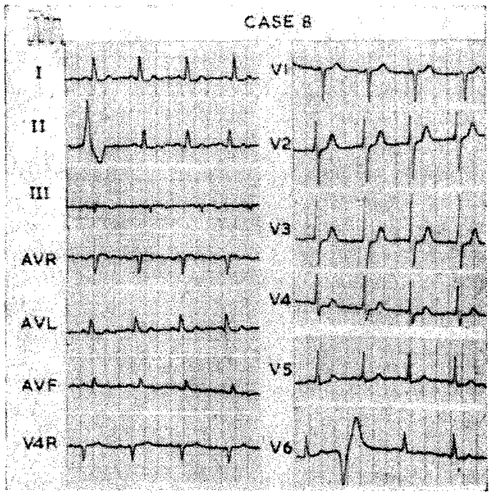


FIG. 5.—Case 8. Electrocardiogram showing ventricular extrasystoles and ST–T wave changes.

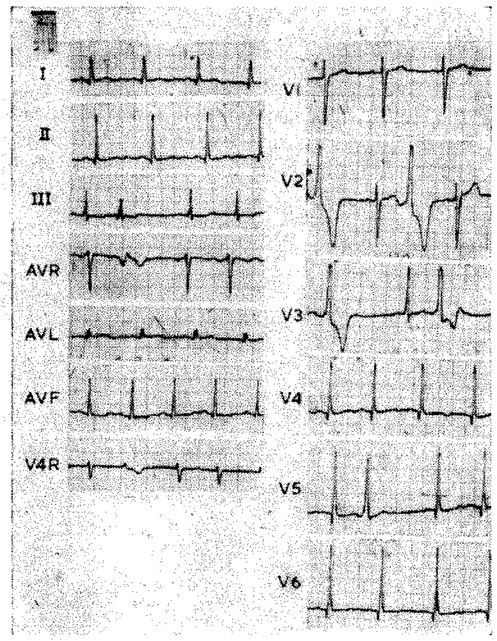


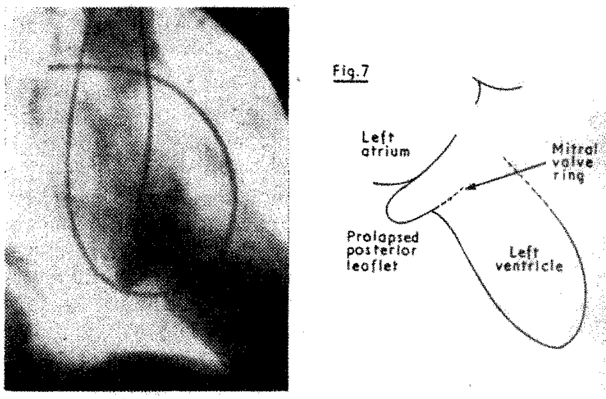
FIG 6.—Case 4. Electrocardiogram showing ventricular extrasystoles and widespread ST–T wave abnormalities

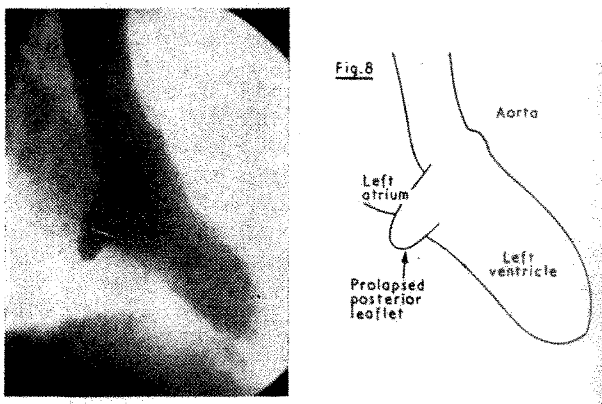
TABLE II.—*Haemodynamic Findings in Six Patients*

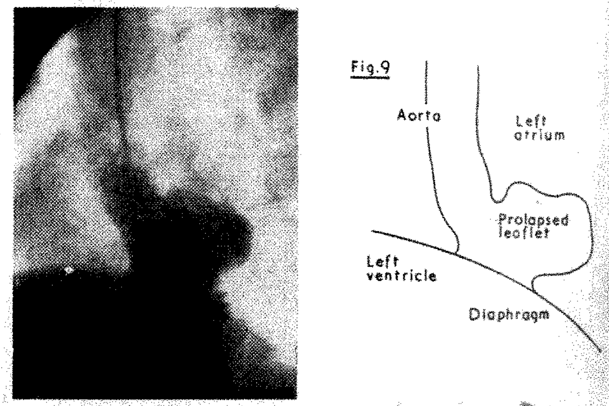
Case No.	Right Atrium	Right Ventricle	Pulmonary Artery	Mean Pulmonary Artery Wedge	Left Ventricle	Aorta	Cardiac Output (l./min.)
	All Pressures in mm. Hg						
1	−3 mean	20/−2	18/3 mean 7	0	110/3	110/60	3·2
4	2 „	17/−2	17/7 „ 13	6	125/−1	115/70	5·8
6	0 „	17/0	18/5 „ 11	5	105/4	105/70	5·6
7	2 „	25/0	25/8 „ 13	3	125/0	125/60	5·3
8	−2 „	20/−3	20/3 „ 8	5	100/−3	100/55	6·2
9	0 „	25/0	23/4 „ 10	3	155/5	125/70	5·7

Left ventricular cineangiography was carried out in six patients. The mitral valve was studied in all six in the right anterior oblique position and in four of these in the left anterior oblique position with the head of the table raised 15 degrees. Prolapse of the posterior leaflet of the mitral valve into the left atrium during ventricular systole was demonstrated in all cases (Figs. 7, 8, and 9). Late mitral regurgitation was present in the five patients with a late systolic murmur, but was absent in the patient with an isolated click.

In addition, selective coronary arteriography was performed in the two patients with severe chest pain, and in both cases the coronary arteries showed no abnormality. The coronary arteries showed no evidence of atheroma and all major branches could be seen clearly, including the branches along the diaphrag-







FIGS. 7 and 8.—Left ventricular angiograms (and line drawings) in right anterior oblique position showing prolapse of the posterior le of the mitral valve into the left atrium and mitral regurgitat FIG. 9.—Left ventricular angiogram (and line drawing) in the left ante oblique position, with the head of the table elevated 15 degrees, show prolapse of the posterior leaflet of the mitral valve into the left atri matic aspect of the heart which supply the papillary muscles (James, 1965). There was no evidence of phasic narrowing of the circumflex artery during ventricular systole.

Discussion

We consider that the finding of a mid or late systolic click and a late systolic murmur in the mitral area is suggestive, if not diagnostic, of prolapse of the posterior leaflet of the mitral valve. Few patients have been investigated, but all reports to date have confirmed the presence of this abnormality in those patients with the characteristic auscultatory findings. Barlow and Bosman (1966) investigated only those patients with an abnormal electrocardiogram, but we have shown, as have other authors, that this is not necessary for diagnosis.

The cause of the chest pain and the abnormal electrocardiogram, where present, remains obscure. Barlow and Bosman (1966) have suggested that the prolapsing posterior leaflet causes compression of the circumflex branch of the left coronary artery, and that ischaemia of the posterior myocardium results. Selective coronary arteriography was performed in two of our patients because of the presence of severe chest pain, but in neither case was there any evidence to support this hypothesis.

The familial incidence of this entity has been noted by other authors, and we have confirmed this in two families. Extensive family studies were not carried out, and we therefore do not know whether the lesion is usually familial.

There was no other obvious aetiological factor. Mitral incompetence has been described after chest injury (McLaughlin *et al.*, 1964), but the only patient with a past history of chest injury had two siblings similarly affected. Rheumatic fever or pericarditis could not be diagnosed, even retrospectively, in any case. Phillips *et al.* (1963) have described a late systolic murmur after papillary muscle infarction, and it was thought that the chest pain might have been indicative of papillary muscle ischaemia, leading to a functional abnormality of the chordae tendineae. However, we have demonstrated that the valve abnormality can exist in the absence of either chest pain or coronary artery disease. Barlow and Bosman (1966) have also described this lesion in association with Marfan's syndrome, but none of our patients had stigmata of this condition.

Leon *et al.* (1966) have shown that both the click and the murmur arise from the mitral valve, and Criley *et al.* (1966) have recorded that the click corresponds with the maximal ballooning of the posterior leaflet. The click therefore presumably arises either from stretching of the posterior leaflet itself or from its attached chordae tendineae. The late systolic murmur is due to mitral regurgitation occurring late in systole, and was absent in the patient in whom prolapse of the posterior leaflet without regurgitation was demonstrated.

In all the patients studied to date no material has been available for anatomical investigation. However, Barlow (personal communication, 1966) has described marked enlargement of the posterior leaflet of the mitral valve at necropsy in a patient who had a late systolic murmur and a "non-ejection" click. In addition there have been reports (Osmundson *et al.*, 1961 ; Hudson, 1965) of the finding of a "hooded" or "parachute" deformity of the posterior leaflet of the mitral valve at post-mortem examination, though in these cases there was no record of the auscultatory findings. Normally the posterior leaflet of the mitral valve occupies only one-third of the total valve area (Chiechi *et al.*, 1956), and therefore it would seem that in these cases there is an actual increase in the size of the posterior leaflet of the mitral valve. There is also support for the theory that the prolapse of the posterior leaflet of the mitral valve is due to an abnormality of the attached chordae tendinae. Four normal hearts were dissected in order to study the anatomy of the chordae tendineae attached to the posterior leaflet of the mitral valve. When the chordae tendineae of the "third order" (Chiechi *et al.*, 1956) were severed it was seen that prolapse of the posterior leaflet into the left atrium could occur, whereas when a major chorda tendinea was severed the valve became completely incompetent. We therefore believe that the anatomical abnormality in these patients will prove to be enlargement of the posterior leaflet of the mitral valve together with an abnormality of the chordae tendineae or papillary muscles.

It has been suggested by Linhart and Taylor (1966) that prophylaxis for bacterial endocarditis should be administered to these patients. However, the majority of our patients had had most or all of their teeth extracted without developing bacterial endocarditis, and therefore prophylaxis may be unnecessary.

It has also been suggested that the mitral regurgitation in this condition may ultimately reach a sufficient degree to warrant surgery (Linhart and Taylor, 1966). This is of course possible, but in our patients subjected to haemodynamic studies there was no evidence of cardiac decompensation, even in those past middle age. In one of our patients the prolapse was associated with a systolic click without a late systolic murmur or mitral regurgitation. This patient will be followed closely to see if the late systolic murmur and mitral regurgitation eventually develop.

Summary

Thirteen patients with mid or late systolic clicks and late systolic murmurs were studied. Haemodynamic studies and left ventricular angiography were performed in six of these, and confirmed the presence of prolapse of the posterior leaflet of the mitral valve and mitral regurgitation. Coronary artery disease as the cause of chest pain and an abnormal electrocardiogram was not confirmed on selective coronary arteriography. The familial nature of this entity was confirmed.

We wish to thank the physicians of the Royal Melbourne Hospital who referred patients for study. The line drawings were done by Miss J. Miles.

REFERENCES

Barlow, J. B. (1965). *J. chron. Dis.*, **18**, 665.
—— and Bosman, C. K. (1966). *Amer. Heart J.*, **71**, 166.
—— Pocock, W. A., Marchand, P., and Denny, M. (1963). Ibid., **66**, 443.
Chiechi, M. A., Lees, W. M., and Thompson, R. (1956). *J. thorac. Surg.*, **32**, 378.
Criley, J. M., Lewis, K. B., Humphries, J. O'N., and Ross, R. S. (1966). *Brit. Heart J.*, **28**, 488.
Hudson, R. E. B. (1965). *Cardiovascular Pathology*. London.
James, T. N. (1965). *Circulation*, **32**, 1020.
Leon, D. F., Leonard, J. J., Kroetz, F. W., Page, W. L., Shaver, J. A., and Lancaster, J. F. (1966). *Amer. Heart J.*, **72**, 325.
Linhart, J. W., and Taylor, W. J. (1966). *Amer. J. Cardiol.*, **18**, 164.
McKusick, V. A. (1958). *Cardiovascular Sound in Health and Disease*. Baltimore.
McLaughlin, J. S., Cowley, R. A., Smith, G., and Matheson, N. A. (1964). *J. thorac. cardiovasc. Surg.*, **48**, 261.
Ongley, P. A., Sprague, H. B., Rappaport, M. B., and Nadas, A. S. (1960). *Heart Sounds and Murmurs*. New York.
Osmundson, P. J., Callahan, J. A., and Edwards, J. E. (1961). *Circulation*, **23**, 42.
Phillips, J. H., Burch, G. E., and De Pasquale, N. P. (1963). *Ann. intern. Med.*, **59**, 508.
Segal, B. L., and Likoff, W. (1964). *Amer. Heart J.*, **67**, 757.
Tavel, M. E., Campbell, R. W., and Zimmer, J. F. (1965). *Amer. J. Cardiol.*, **15**, 719.
Wells, B. (1957). *Brit. Heart J.*, **19**, 129.

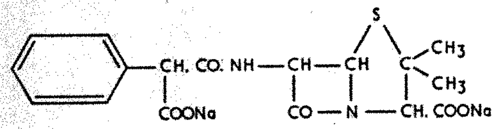
Carbenicillin[*]: A New Semisynthetic Penicillin Active against *Pseudomonas pyocyanea*

E. T. KNUDSEN,[†] M.B., B.S., F.C.PATH.; G. N. ROLINSON,[†] D.SC.; R. SUTHERLAND,[†] B.SC.

Brit. med. J., 1967, 3, 75–78

Carbenicillin (disodium α-carboxybenzylpenicillin; BRL 2064) is a new semisynthetic penicillin with a wide spectrum of activity against Gram-positive and Gram-negative bacteria. In particular, carbenicillin shows a certain level of activity against *Pseudomonas pyocyanea* (*Pseudomonas aeruginosa*), and the compound is also active against many strains of *Proteus vulgaris, Proteus rettgeri,* and *Proteus morganii,* which are typically resistant to ampicillin.

The structure of carbenicillin is as follows:



The compound, which should be stored in the refrigerator, is readily soluble in water, giving a clear neutral solution, which shows no significant loss of activity after 24 hours at room temperature and is stable in the refrigerator for at least seven days. In acid solution carbenicillin is relatively unstable, the half-life at *p*H 2 being approximately two hours at room temperature and approximately 30 minutes at 37° C.

Antibacterial Activity of Carbenicillin

The antibacterial spectrum of carbenicillin is shown in Table I. Minimum inhibitory concentrations were determined by serial dilution of the drug in agar, and one drop of an overnight broth culture of each organism was used as inoculum.

TABLE I.—*Antibacterial Spectrum of Carbenicillin*

	Minimum Inhibitory Concentration (µg./ml.)*
Escherichia coli	5·0
Klebsiella aerogenes	250
Salmonella typhi	12·5
Shigella flexneri	5·0
,, *sonnei*	5·0
Pseudomonas pyocyanea	50
Proteus mirabilis	2·5
,, *morganii*	5·0
,, *rettgeri*	2·5
,, *vulgaris*	5·0
Haemophilus influenzae	0·5
Staphylococcus aureus Oxford	0·5
,, *aureus*†	50
β-Haemolytic streptococcus	0·25
Streptococcus faecalis	25
,, *pneumoniae*	0·5
Bacillus subtilis	1·25
Sarcina lutea	0·5
Clostridium tetani	0·25
,, *welchii*	0·25

* Serial dilution in agar; inoculum, one drop of an overnight culture.
† Penicillinase-producing strain.

Carbenicillin is active against *Escherichia coli, Salmonella* species, *Shigella* species, *Proteus mirabilis*, and *Haemophilus influenzae,* and in this respect the spectrum of activity is similar to that of ampicillin, although carbenicillin is in general rather less active than ampicillin. Most strains of *Klebsiella aerogenes* are resistant to carbenicillin and the level of activity against enterococci (*Streptococcus faecalis*) is relatively low. Carbenicillin is active against pyogenic streptococci, pneumococci, and penicillin-sensitive strains of staphylococci, although the compound is considerably less active in this respect than penicillin G or ampicillin. Carbenicillin is not stable to staphylococcal penicillinase and is not active against penicillin-resistant strains of staphylococci. The activity of carbenicillin against several strains of *Pr. vulgaris*, *Pr. rettgeri*, and *Pr. morganii* is shown in Table II. These species of proteus are characteristically resistant to ampicillin, and in the experiment shown in Table II all the strains required an ampicillin concentration of at least 50 µg./ml. to prevent growth. In contrast, many of these strains were relatively sensitive to carbenicillin and in some cases were inhibited by concentrations as low as 1.25 µg./ml. Strains of *Pr. mirabilis,* however, which are resistant to ampicillin are also resistant to carbenicillin. The reason for the activity which carbenicillin shows against certain ampicillin-resistant proteus appears to be due to greater stability of the compound towards the penicillinases produced by these organisms. On the other hand, penicillinase-producing strains of *Pr. mirabilis*, like those of *Kl. aerogenes*, inactivate both carbenicillin and ampicillin.

TABLE II.—*Activity of Carbenicillin Against Ampicillin-resistant Strains of Proteus*

		Minimum Inhibitory Concentration (µg./ml.)*	
		Carbenicillin	Ampicillin
Proteus morganii	A	1·25	50
	F	1·25	50
	G	1·25	50
rettgeri	A	1·25	50
	I	2·5	250
	B	12·5	250
vulgaris	I	2·5	250
	A	5·0	125
	E	5·0	250
	G	50	> 500
	H	250	> 500
,, *mirabilis*	8	> 500	> 500
	889	> 500	> 500

* Determined by serial dilution in agar. The inoculum was one drop of an overnight broth culture, and M.I.C. values were read after 18 hours at 37° C.

The most significant feature of the antibacterial spectrum of carbenicillin is the activity against *Ps. pyocyanea*. In terms of the minimum inhibitory concentration the activity against this pathogen is relatively low, since for most strains a concentration in the order of 50 µg./ml. is required to prevent growth. However, from the clinical point of view activity is essentially meaningful in relation to the concentration of drug which can be reached at the site of infection. Carbenicillin itself is remarkably free from toxic effects (Acred *et al.*, 1967) and can be administered in sufficient dosage to obtain concentrations in the serum which are inhibitory to typical strains of *Ps. pyocyanea*, and the drug is also excreted in high concentration in the urine.

One characteristic of the activity of carbenicillin against *Ps. pyocyanea* is that in serial dilution tests to determine the minimum inhibitory concentration the drug does not show a sharp end-point when the inoculum is very heavy. This is illustrated in Fig. 1. Serial dilutions of carbenicillin in nutrient agar were prepared in Petri dishes and an area of the agar surface of each plate was inoculated with an undiluted overnight broth culture of a strain of *Ps. pyocyanea* applied with a cotton-wool swab. In this way the inoculum on each plate was at least 10 million organisms. A similar series of plates was also inoculated in the same way, using the same culture of *Ps. pyocyanea* but diluted 1/100 to give an inoculum of approximately 100,000 organisms. The strain of *Ps. pyocyanea* used in this experiment was a recent clinical isolate and was typical with regard to its sensitivity to carbenicillin. With the use of the undiluted culture as inoculum growth was very markedly diminished at a concentration of 25 μg./ml. carbenicillin, but a number of colonies were present even at a concentration of 50 μg./ml. and growth could only be said to have been prevented on the plate containing 125 μg./ml. However, when the inoculum was diluted 1/100 inhibition of growth was very pronounced at a concentration of 12.5 μg./ml., and at a concentration of 25 μg./ml. only three or four colonies were seen.

---

[*] Pyopen is the registered trade mark of Beecham Research Laboratories for carbenicillin.
[†] Beecham Research Laboratories, Brentford, Middlesex.

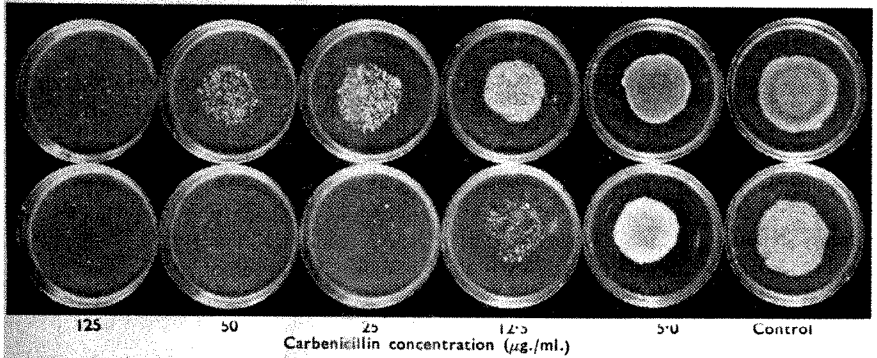


Fig. 1.—Activity of carbenicillin against a typical strain of *Ps. pyocyanea*. Serial dilutions of carbenicillin in nutrient agar were prepared in Petri dishes and an area of the agar surface of each plate was inoculated, using a cotton-wool swab. An undiluted overnight broth culture of *Ps. pyocyanea* was used to inoculate the upper row of plates and a 1/100 dilution of the same culture was used to inoculate the lower row.

Thus, in experiments of the type shown in Fig. 1, with the use of typical strains of *Ps. pyocyanea* and a very heavy inoculum level, some scanty growth may be seen with concentrations of carbenicillin as high as 125 μg./ml., and consequently if the criterion of the "minimum inhibitory concentration" is one of complete inhibition of all trace of growth the M.I.C. with a heavy inoculum may well be as high as 250 μg./ml. or more. However, the amount of growth at such concentrations is extremely meagre indeed, and with an inoculum only slightly smaller a sharp end-point is seen with complete inhibition of growth at a concentration of carbenicillin of 25–50 μg./ml.

Minimum inhibitory concentrations of carbenicillin for 111 clinical isolates of *Ps. pyocyanea* are shown in Table III. These inhibitory concentrations were determined by preparing serial dilutions of carbenicillin in agar as described above, and one drop of a 1/100 dilution of an overnight broth culture of each isolate was used as inoculum. It will be seen from Table III that the majority of the strains were inhibited by a concentration of 25–50 μg./ml. carbenicillin. In comparison, the inhibitory concentrations of ampicillin and benzylpenicillin against most strains of *Ps. pyocyanea* are of the order of 1,000–5,000 μg./ml. or greater.

Table III.—*Activity of Carbenicillin Against Pseudomonas pyocyanea*

No. of Strains	Minimum Inhibitory Concentration (μg./ml.)* and No. of Strains					
	250	125	50	25	12·5	5·0
111	5	8	61	31	6	

* Determined by serial dilution in agar. The inoculum was one drop of a 1/100 dilution of an overnight broth culture, and M.I.C. values were read after 18 hours at 37° C.

The effect of the inoculum size on the determination of the minimum inhibitory concentration is not due to destruction of the drug as in the case of penicillin G and penicillin-resistant staphylococci. Carbenicillin is itself stable to the penicillinase produced by typical strains of *Ps. pyocyanea*. Furthermore, the effect of inoculum size does not appear to be due to growth of resistant mutants present in a large inoculum. When tests are carried out using as inoculum the growth which occurs in the presence of high concentrations of carbenicillin the result obtained is the same as that seen with the original culture—that is, marked suppression of growth at concentrations of 25 μg./ml., but with scanty growth nevertheless persisting up to a concentration as high as 125 μg./ml.

As might be expected, this effect of inoculum size on the minimum inhibitory concentration of carbenicillin is also seen with tests carried out in liquid medium. With a heavy inoculum—for example, one drop of undiluted broth culture—growth appears normal with formation of pigment and pellicle up to a concentration of approximately 12.5 μg./ml. carbenicillin, but at 25 μg./ml. there is generally absence of pellicle and pigment and a markedly diminished amount of growth, although complete inhibition of growth may be obtained only with concentrations as high as 250 μg./ml. With a slightly smaller inoculum a sharp end-point is obtained, and with most strains of pseudomonas the minimum inhibitory concentration under these conditions is usually about 50 μg./ml.

Carbenicillin is bactericidal, and typical results with a strain of *Ps. pyocyanea* are shown in Fig. 2. Over the first seven hours a concentration of 50 μg./ml. usually results in a kill of at least 99% of the original inoculum, but thereafter some resumption of growth takes place which may even increase to a visible amount after 24 hours. When this growth is used as inoculum in a repeat test the same kill is again obtained over the first seven hours, followed by a certain amount of growth. The reason for this bactericidal effect followed by growth is not known, but it would not appear to be due to the selection of resistant mutants present in the original inoculum, nor is it due to inactivation of carbenicillin during the experiment.

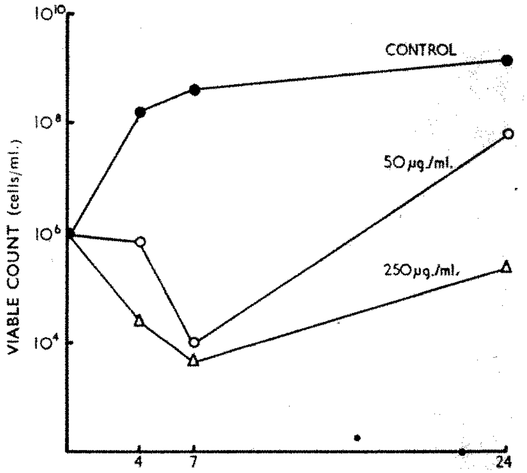


Fig. 2.—Bactericidal activity of carbenicillin against *Pseudomonas pyocyanea*.

Development of Resistance

Experiments involving repeated subculture of staphylococci and various Gram-negative bacilli, including *Ps. pyocyanea*, in the presence of carbenicillin, indicate that emergence of resistance takes place in a stepwise fashion which is characteristic of penicillins.

Effect of Serum on Activity

Carbenicillin is not highly bound to serum proteins. Sensitivity tests carried out in human serum show that the activity of carbenicillin is not significantly diminished in the presence of serum. Determinations of the extent of binding by ultrafiltration indicate that in human serum approximately 53% of the drug is unbound.

Disc Sensitivity Testing with Carbenicillin

With 6-mm. paper discs containing 100 μg. carbenicillin all strains of *Ps. pyocyanea* tested in this laboratory have given zones of inhibition of 12–20 mm. with a heavy inoculum and zones of 18–30 mm. with a dilute inoculum. With a heavy inoculum a number of colonies are usually visible within the zone of inhibition, although when these colonies are picked off and retested they show the same sensitivity as the original culture and again give rise to a number of colonies within the clear zone of inhibition.

In the case of Gram-negative bacilli other than pseudomonas—for example, *E. coli* and *Proteus* species—a 25-μg. disc would be suitable for sensitivity testing. With use of a heavy inoculum inhibition zones of 20 mm. or more are usually obtained with strains that are inhibited by 5 μg./ml. carbenicillin.

Absorption and Excretion in Man

Assay of Carbenicillin in Serum and Urine

The concentration of carbenicillin in serum and in urine was determined by the cup-plate biological assay method. Details of the technique were as previously described (Knudsen and Rolinson, 1960) except that *Ps. pyocyanea* NCTC 10490 (Ellsworth strain, 1973) was used as test organism. *Sarcina lutea* and *Staphylococcus aureus* are unsuitable as assay organisms because carbenicillin contains a small amount of benzylpenicillin and this may appear in the serum and in the urine together with the carbenicillin. Since *S. lutea* and *Staph. aureus* are many times more sensitive to benzylpenicillin than to carbenicillin, the presence of traces of benzylpenicillin may invalidate the assay. *Ps. pyocyanea* NCTC 10490, on the other hand, is sensitive to carbenicillin but relatively resistant to benzylpenicillin. The culture is unusually sensitive to carbenicillin, showing a minimum inhibitory concentration of approximately 1.25 μg./ml., and using this strain it is possible to assay concentrations of carbenicillin as low as 2.5 μg./ml., while benzylpenicillin at concentrations of up to 500 μg./ml. fails to show any zone of inhibition. Standard solutions of carbenicillin from 1 to 100 μg./ml. were prepared in human serum, and, where necessary, serum specimens were suitably diluted in human serum to give a level within this range of concentration. For the assay of urine samples the standard solutions of carbenicillin were prepared in M/20 phosphate buffer *p*H 7, and urine samples were also diluted as required, using the same buffer.

Oral Administration

Carbenicillin in gelatin capsules was given at a dose of 500 mg. to healthy fasting volunteers. Serum samples were taken at ½, 1, 2, 4, and 6 hours after administration of the dose, and urine was collected over the period 0 to 6 hours. No carbenicillin (that is, less than 1 μg./ml.) was detected in the serum, and the quantity present in the urine amounted to less than 1% of the dose administered. It would appear, therefore, that carbenicillin is not absorbed to any appreciable extent when administered orally.

Intramuscular Administration

Carbenicillin was administered by intramuscular injection to groups of healthy adult volunteers as single doses of 250 mg., 500 mg., and 1,000 mg. The 250-mg. dose was given in a volume of 1 ml. of water for injection, and the 500-mg. and 1,000-mg. doses were dissolved in 2 ml. of water. Blood specimens were collected ½, 1, 2, 4, and 6 hours after administration, and the urine was collected during the six-hour period after dosing. Results of these studies are summarized in Table IV.

TABLE IV.—*Mean Serum Concentrations of Carbenicillin After Intramuscular Injection in Adult Volunteers*

No. of Subjects	Dose (mg.)	Serum Concentration (μg./ml.)						% of Dose Excreted in Urine over 0–6 hrs.
		½-hr.	1 hr.	2 hrs.	3 hrs.	4 hrs.	6 hrs.	
10	250	5·9	7·9	5·7	2·6	< 2·0	< 2·0	71
9	500	13·7	17·7	13·2	—	2·0	< 2·0	82
16	1,000	21·6	25·3	22·1	—	10·9	3·7	84

Mean serum peak levels of 7.9 μg./ml. carbenicillin were obtained one hour after administration of the 250-mg. dose, and these declined to <2 μg./ml. after four hours. Increasing the dose to 500 mg. resulted in serum concentrations twice as high as those obtained with the 250-mg. dose, but these declined to barely detectable concentrations after four hours. Impressive results were obtained with the 1,000-mg. dose, the mean serum concentrations being greater than 20 μg./ml. for the first two hours after injection, falling to 10.9 μg./ml. at four hours.

The amounts of carbenicillin excreted in the urine during the first six hours after injection were 71% of the dose with the 250-mg. dose, 82% of the 500-mg. dose, and 84% of the 1,000-mg. dose, producing average carbenicillin concentrations in the urine of 1,000 to 2,000 μg./ml. with the 500-mg. dose and 2,000 to 4,000 μg./ml. with the 1,000-mg. dose.

The effect of probenecid was investigated in a crossover study in which 10 subjects were given 1,000 mg. carbenicillin by the intramuscular route. One week later the same subjects took oral probenecid (1 g.) 10 hours and one hour before receiving 1,000 mg. intramuscular carbenicillin. The administration of probenecid resulted in a marked increase in the carbenicillin serum concentrations (Table V and Fig. 3) and in a significant reduction in the rate of elimination of carbenicillin from the serum.

Chromatographic examination of the urine after intramuscular administration of carbenicillin showed no evidence of the formation of biologically active metabolites.

Although carbenicillin is primarily of interest for its activity against *Ps. pyocyanea,* the compound is active against a wide range of bacteria, including *E. coli* and various ampicillin-resistant proteus species, and it seems probable that intramuscular doses of 500 to 1,000 mg. carbenicillin might be successfully used to attain serum, tissue, and urine concentrations adequate for the treatment of infections caused by these organisms. On the other hand, the activity of carbenicillin against *Ps. pyocyanea* is such that inhibitory concentrations of carbenicillin with respect to this particular pathogen are not likely to be achieved in serum and tissue by intramuscular

TABLE V.—*Effect of Probenecid on Serum Levels and Urinary Excretion of Carbenicillin in Healthy Adult Volunteers. (Carbenicillin Dose 1 g. by Intramuscular Injection)*

	No. of Subjects	Mean Serum Concentration (μg./ml.)					% of Dose Excreted in Urine over 0–6 hrs.
		½-hr.	1 hr.	2 hrs.	4 hrs.	6 hrs.	
With probenecid*	10	25·7	39·9	48·0	27·4	19·4	48
Without probenecid	10	26·8	29·4	22·2	10·8	3·3	84

* 1 g. 1 hour and 10 hours before administration of carbenicillin.

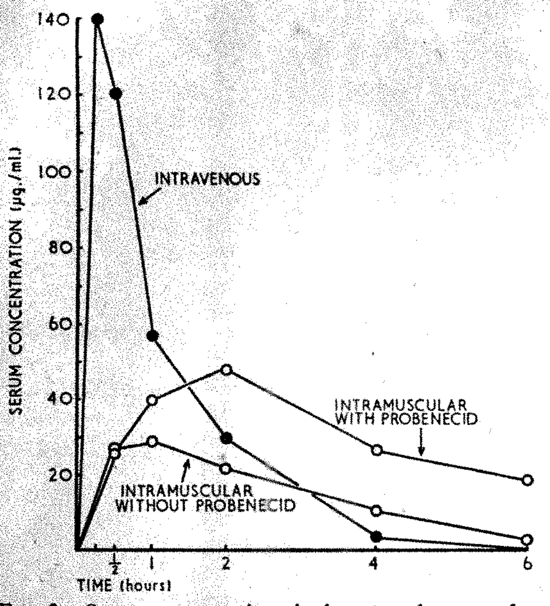


FIG. 3.—Serum concentrations in human volunteers after intramuscular and intravenous administration of 1 g. of carbenicillin.

dosing. Nevertheless, the urine concentrations attained after intramuscular administration of carbenicillin are greatly in excess of the minimum inhibitory concentrations of the drug against *Ps. pyocyanea*, and the results of clinical trials indicate that 1,000 mg. of carbenicillin given four times daily by the intramuscular route may be adequate for the treatment of acute urinary tract infections due to this organism.

Intravenous Administration

Two subjects were given 1,000 mg. of carbenicillin by slow intravenous injection. The penicillin was dissolved in 10 ml. of sterile water for injection and administered over a period of three minutes. Serum concentrations of greater than 100 µg./ml. carbenicillin were obtained during the first half-hour after administration of the compound, although at four hours only trace amounts of carbenicillin were detected (Table VI and Fig. 3).

From the bacteriological studies, concentrations of carbenicillin in the order of 100 µg./ml. would be expected to inhibit the growth of most strains of *Ps. pyocyanea*, but in view of the rapid elimination of the drug from the body frequent administration would probably be necessary. In practice the results of clinical studies have shown that, for the treatment of septicaemia, tissue infections, and chronic urinary tract infections due to *Ps. pyocyanea*, carbenicillin should be given at a dose of 1 g. hourly by the intravenous route, preferably together with probenecid, in order to maintain inhibitory concentrations in the body.

TABLE VI.—*Serum Concentration of Carbenicillin After Intravenous Administration of 1 g.*

Subject	Serum Concentration (µg./ml.)					
	¼-hr.	½-hr.	1 hr.	2 hrs.	4 hrs.	6 hrs.
A	140	127	60	28	3·7	<3·0
B	140	114	55	32	4·4	<3·0

Summary

Carbenicillin is a new semisynthetic penicillin active against *Pseudomonas pyocyanea*. The compound shows a broad spectrum of activity against Gram-positive and Gram-negative bacteria and is active against strains of *Proteus vulgaris, Pr. rettgeri*, and *Pr. morganii*, which are typically resistant to ampicillin. With a very heavy inoculum of *Ps. pyocyanea* marked inhibition of growth occurs with carbenicillin at 25 to 50 µg./ml., but some very scanty growth may persist even at concentrations of 125 to 250 µg./ml. With a slightly smaller inoculum complete inhibition of growth occurs at 25 to 50 µg./ml. Carbenicillin is bactericidal and is not highly bound to serum protein. Carbenicillin is not absorbed when given by mouth, but high concentrations of the drug are obtained in serum after intramuscular or intravenous administration, and these levels are increased and are more prolonged with concomitant use of probenecid. Carbenicillin is excreted in high concentration in the urine.

We thank Dr. J. H. C. Nayler for preparing the carbenicillin used in these studies, Mr. D. Lawson for the photograph in Fig. 1, and Mrs. Eleanor Fairclough for technical assistance.

REFERENCES

Acred, P., Brown, D. M., Knudsen, E. T., Rolinson, G. N., and Sutherland, R. (1967). *Nature (Lond.)*. In press.
Knudsen, E. T., and Rolinson, G. N. (1960). *Brit. med. J.*, 2, 700.

Prophylaxis and Therapy for *Pseudomonas aeruginosa* Infection with Carbenicillin and with Gentamicin

R. J. JONES,* M.SC., PH.D.; E. J. L. LOWBURY,* M.A., D.M., F.C.PATH.

Brit. med. J., 1967, 3, 79–82

The polymixins have for many years been the antibiotics of choice for the treatment of infection with *Pseudomonas aeruginosa*; but although they are active against all strains in vitro their clinical value has been limited. In the treatment of burns, local applications were found to have prophylactic value (Jackson, Lowbury, and Topley, 1951; Cason and Lowbury, 1960), but systemic administration has been less effective in the control of invasive infection (Tumbusch *et al.*, 1961; Kefalides *et al.*, 1964; Jones, Jackson, and Lowbury, 1966).

Two new antibiotics with promising activity against *Ps. aeruginosa* have recently been developed. Gentamicin (Weinstein *et al.*, 1963) is a broad-spectrum antibiotic which is reported to have good activity in vitro and therapeutic value in patients infected with *Ps. aeruginosa* (Bulger, Sidell, and Kirby, 1963; Klein, Eickhoff, and Finland, 1964; Barber and Waterworth, 1966). Carbenicillin (B.R.L. 2064) is a semi-synthetic penicillin with moderate activity in vitro against *Ps. aeruginosa.*

In this paper we report studies which showed that parenteral administration of carbenicillin and of gentamicin protected burned mice against invasive infection with strains of *Ps. aeruginosa*. The use of carbenicillin in the treatment of patients whose burns were infected with *Ps. aeruginosa* was studied in a small controlled trial.

Materials and Methods

Assessments of Prophylaxis and Therapy

Protection of burned mice against virulent strains of *Ps. aeruginosa* was assessed by methods described elsewhere (Jones and Lowbury, 1965; Jones *et al.*, 1966). Mice were anaesthetized with ether and given full-skin-thickness burns of approximately 5% of the body surface. Three hours after burning, the surface of the burned area was inoculated with approximately 700 million viable cells of *Ps. aeruginosa.*

Treatment with antibiotics was started, firstly, immediately after burning and before inoculation with *Ps. aeruginosa,* to assess their prophylactic value, and, secondly, 24 hours, 48 hours, and 72 hours after inoculation with *Ps. aeruginosa,* to assess the therapeutic value of the antibiotics. A group of six burned infected mice was included in each experiment as a control.

All mice were examined and weighed daily for a period of 14 days. Bacterial cultures on blood agar and cetrimide agar (Brown and Lowbury, 1965) were obtained on alternate days from burns of mice receiving the highest dosage of antibiotics. Necropsy examinations, which included cultures of heart blood, were made on all mice that died.

Strains of Ps. aeruginosa

Two strains, B4 and P14, which had previously been found virulent for the mouse and which differed in serotype, were used in the experiments. The saline suspensions inoculated on burns were prepared from overnight cultures on nutrient agar. Strains rendered resistant to the antibiotics by habituation in vitro (see below) were also tested.

Antibiotic Treatment

The antibiotics were administered, in separate experiments, by intraperitoneal and intramuscular routes. Two injections were given each day (at 10 a.m. and 5 p.m.) for five days, and one injection (full dosage) on days 6 and 7. Dosage was adjusted in relation to the surface area of the animal, estimated from its weight (Bushby, 1964; Butler and Richie, 1960); on this basis approximately 660 and 1,000 mg. of carbenicillin per kg. per day and 12 and 18 mg. of gentamicin per kg. per day were selected for treatment of mice. Carbenicillin was also tested at lower dosages (approximately 330 and 160 mg./kg./day). Colistin sulphomethate was tested at 40 and 400 mg./kg./day; in earlier experiments (Jones *et al.*, 1966) approximately 80 mg./kg./day of colistin sulphomethate had been used.

Levels of antibiotics in the serum of burned and of unburned mice were obtained from assays on pooled serum of groups of three mice taken at intervals of half-hour, three hours, and six hours after intraperitoneal administration of the antibiotics. The assay was by a tube dilution method with a sensitive strain of *Staphylococcus aureus* (Oxford) for gentamicin and of *Ps. aeruginosa* (Elsworth) and (in earlier tests) of *Staph. aureus* (Oxford) for carbenicillin; a strain of *Ps. aeruginosa* (B4) was also used for assay of colistin sulphomethate. The inoculum was 0.02 ml. of a 1/1,000 dilution of a broth culture of the test organism.

A group of mice was also treated prophylactically with methicillin (5,000 mg./kg./day).

Mixed Infection with Penicillinase-producing Organisms

Mixed infections with *Ps. aeruginosa* and *Staph. aureus* are common in burned patients. To determine whether the presence of penicillinase-producing bacteria interferes with the protective value of carbenicillin against *Ps. aeruginosa,* prophylaxis with the antibiotic was assessed in groups of mice infected by the application to burns of *Ps. aeruginosa* (B4 and P14) and a similar inoculum of a penicillinase-producing strain of *Staph. aureus* (1899).

Antibiotic Sensitivity Tests

Strains of *Ps. aeruginosa* were tested for sensitivity to carbenicillin, gentamicin, and colistin sulphomethate by a tube dilution method; the inoculum was 0.02 ml. of 10^{-3} dilutions of overnight broth cultures in nutrient broth containing doubling dilutions of the antibiotic.

Tests for Inactivation of Carbenicillin by Penicillinase

Penicillinase-producing strains of *Staph. aureus* (B/4324 and B/4327) were inoculated in nutrient broth containing carbenicillin (1,000 µg. per ml.); after incubation for two hours at 37° C. the culture was filtered through a Hemmings filter and tested for residual activity by diffusion from Heatley cylinders on blood agar plates seeded with sensitive strains of *Staph. aureus* (Oxford strain) and *Ps. aeruginosa* (strain B4) (Lowbury, Topley, and Hood, 1952).

---

* The M.R.C. Industrial Injuries and Burns Research Unit, Birmingham Accident Hospital.

Tests for Production of Penicillinase by Ps. aeruginosa

Strains of *Ps. aeruginosa*, including those which had acquired resistance to carbenicillin in vitro, were tested for diffusible penicillinase by estimation of residual penicillin after incubation for two hours of fresh cultures in infusion broth containing 100 µg. per ml. of carbenicillin and 100 units per ml. of penicillin G; filtrates were tested on blood-agar plates seeded with *Staph. aureus* (Oxford strain).

Habituation of Ps. aeruginosa to the Antibiotics

Strains of *Ps. aeruginosa* (B4 and P14) were tested for the emergence of resistant variants by serial subculture in tubes of broth containing ranges of doubling dilutions of carbenicillin and gentamicin; daily subcultures were made to new test ranges from the tubes containing the highest concentration of antibiotics which did not inhibit growth. Tests for stability of resistance acquired in these strains were made by subculture in the absence of the antibiotics.

Results

Sensitivity of Strains.—Table I shows the distribution of minimal inhibitory concentrations (M.I.C.) of carbenicillin, gentamicin, and colistin sulphomethate for 80 miscellaneous strains of *Ps. aeruginosa*, mostly from burns, and 26 typed strains, including 14 distinct serotypes. With one exception, the M.I.C.s of carbenicillin were in the range 32–128 µg./ml.; the M.I.C. of gentamicin was in the range 1 to 4 µg./ml., and that of colistin sulphomethate was from 1 to 8 µg./ml. Two strains used in the studies on mice (B4 and P14) were inhibited by carbenicillin at M.I.C.s of 64 and 128 µg./ml. and by gentamicin at 0.5 and 4 µg./ml.; both strains were inhibited by colistin sulphomethate at an M.I.C. of 4 µg./ml. The M.I.C.s of methicillin for two strains of *Ps. aeruginosa* were 1,000 and 4,000 µg. per ml.

TABLE I.—*Sensitivity of 106 Strains of Ps. aeruginosa to Three Antibiotics*

Antibiotic	Strains	No. of Strains Inhibited by M.I.C. (µg./ml.)								Total Strains
		128	64	32	16	8	4	2	1	
Carbenicillin	Miscellaneous	11	47	21	0	0	0	0	1*	80
	Type strains	5	21	0	0	0	0	0	0	26
Gentamicin	Miscellaneous	0	0	0	0	0	17	48	15	80
	Type strains	0	0	0	0	0	13	12	1	26
Colistin sulphomethate	Miscellaneous	0	0	0	0	7	34	33	6	80
	Type strains	0	6	0	0	1	11	12	2	26

* Elsworth strain.

Inactivation of Carbenicillin by Penicillinase.—Penicillinase-producing strains of *Staph. aureus* were found to destroy the activity of carbenicillin against both *Staph. aureus* and *Ps. aeruginosa.*

Prophylaxis against Ps. aeruginosa.—The results summarized in Table II show that mice infected with *Ps. aeruginosa* (B4 and P14) by application of the organism to fresh burns were protected against invasion and fatal septicaemia when courses of prophylactic treatment with carbenicillin were given. Intraperitoneal and intramuscular injections were equally effective. Similar treatment with gentamicin prevented invasion and death when the infecting strain was B4, but it had a smaller effect against P14, which was less sensitive to gentamicin. Colistin sulphomethate, on the other hand, showed little or no prophylactic effect at any of the three dosage levels tested, including those reported earlier (Jones *et al.*, 1966), and methicillin was also ineffective. The burns of the infected mice in all series appeared red, with some areas of moisture. Heavy growths of *Ps. aeruginosa* were isolated from swabs taken from the burns of infected mice, whether treated with antibiotics or not. At necropsy the infected mice showed pathological changes described elsewhere (Jones *et al.*, 1966), including usually the presence of *Ps. aeruginosa* in blood from the heart.

TABLE II.—*Prophylaxis by Antibiotics Against Ps. aeruginosa Infection in Burned Mice*

Treatment Group	Infecting Strain of *Ps. aeruginosa*	Dosage of Antibiotic (mg./kg./day)	Route of Administration	No. of Mice			Mean Survival Time of mice which died (Days)	*Ps. aeruginosa* in Blood Culture at Necropsy
				Died	Survived	% Deaths		
Controls:								
Burned uninfected ..	—	—	—	3	63	4·5	3·0	—
Burned infected	B4	—	—	87	33	72·5	5·2	86
" "	P14	—	—	41	19	68	5·4	41
Carbenicillin	B4	1,000	IP	0	11	0*	—	—
	B4	660	IP	2	8	20*	12·5	1
	B4	330	IP	5	4	55	6·0	5
	B4	165	IP	6	4	60	5·0	6
	B4	1,000	IM	0	12	0*	—	—
	P14	1,000	IP	1	10	9·0†	(14·5)	1
	P14	660	IP	0	12	0†	—	—
Gentamicin	B4	12	IP	1	11	8·0‡	(4·0)	1
	B4	12	IM	0	12	0‡	—	—
	P14	18	IP	4	8	33·3§	8·5	4
	P14	12	IP	7	5	58	3·8	6
Colistin sulphomethate	B4	40	IP	8	4	67	5·0	8
	B4	400	IP	5	1	83	2·4	4
	B4	40	IM	6	6	50	5·7	6
	P14	40	IP	7	5	58	3·8	6
Methicillin	B4	5,000	IP	11	1	92	4·5	11

Significance tests.—The results of experiments marked with the same footnote symbol are grouped together; they were compared with the results in untreated mice infected with the same strain of *Ps. aeruginosa*. * $\chi^2 = 48{\cdot}4$, $P < 0{\cdot}001$ (strain B4). † $\chi^2 = 24{\cdot}5$, $P < 0{\cdot}001$ (strain P14). ‡ $\chi^2 = 42{\cdot}3$, $P < 0{\cdot}001$ (strain B4). § $\chi^2 = 3{\cdot}8$, $P = 0{\cdot}05$ (strain P14).

Blood Levels of the Antibiotics.—The concentration of antibiotics in the pooled serum from groups of burned and unburned mice bled at half an hour, three hours, and six hours after administration of a single dose are shown in Table III; inhibitory levels of carbenicillin and of gentamicin were found in the first sample. In mice which had recently received 5% burns the serum level of gentamicin in relation to dosage was high compared with that of carbenicillin. In tests with unburned mice, serum levels half an hour after injection of gentamicin were much lower. No difference between burned and unburned mice was found in serum levels of carbenicillin. The serum from mice treated with colistin sulphomethate did not contain detectable levels of the antibiotic.

TABLE III.—*Assays of Antibiotics in Serum of Mice After Intraperitoneal Administration*

Antibiotic	Mice	Dosage (mg./kg./dose)	Concentration of Antibiotics in Serum (µg./ml.)		
			½ Hour after Dose	3 Hours after Dose	6 Hours after Dose
Carbenicillin	Burned	500	128	16	<2
		330	256	32	—
	Unburned	500	128	8	>2
Gentamicin	Burned	9	128	8	—
		6	64	2	<0·5
	Unburned	6	4	<2	<1
		9	8	<2	—
Colistin sulphomethate	Burned	20	<2·6	<2·6	<2·6
	Unburned	20	<1·3	<1·3	<1·3

TABLE IV.—*Therapeutic Effects of Carbenicillin and Gentamicin in Burned Mice Infected with Ps. aeruginosa*

Treatment Group*	Infecting Strain of *Ps. aeruginosa*	Time when Treatment was Started (Hours after Inoculation with *Ps. aeruginosa*)	No. of Mice which		% Deaths
			Died	Survived	
Carbenicillin	B4	24	1	5	17
	B4	48	6	6	50
	B4	72	4	2	67
Centamicin	B4	24	0	6	0
	B4	48	4	8	33
	B4	72	4	2	67

*Dosage.—Carbenicillin: 1,000 mg./kg./day, IP, for 7 days. Gentamicin: 12 mg./kg./day, IP, for 7 days.

Use of Carbenicillin and Gentamicin on Mice with Burns Already Infected.—When courses of treatment with carbenicillin or gentamicin were started 24 hours after inoculation of burns with *Ps. aeruginosa* (strain B4) the survival rate was as high or almost as high as it was in the series given prophylaxis (Table IV). When longer delays occurred before treatment was started a larger proportion of mice died with infection.

Prophylaxis by Carbenicillin against Ps. aeruginosa in the Presence of Penicillinase-producing Staphylococci.—In mice protected with carbenicillin (1,000 mg./kg./day) there were three deaths out of 12 with invasive *Ps. aeruginosa* infection when a penicillinase-producing *Staph. aureus* was also inoculated on the burn (Table V); in those inoculated with *Ps. aeruginosa* alone and similarly protected there were two deaths out of 33. *Ps. aeruginosa,* but not *Staph. aureus,* was found in the blood culture of the mice which died.

TABLE V.—*Prophylaxis by Carbenicillin in Burned Mice Infected with Ps. aeruginosa and a Penicillinase-producing Staph. aureus*

Treatment Group	Infecting Strains of		No. of Mice which			*Ps. aeruginosa* in Blood Culture at Necropsy
	Ps. aeruginosa	*Staph. aureus*	Died	Survived	% Deaths	
No antibiotic	B4	1899	3	3	50	3
	P14	1899	5	1	83	4
Carbenicillin	B4	1899	1	5	17	1
	P14	1899	2	4	33	2

Habituation of Ps. aeruginosa to Carbenicillin and Gentamicin in vitro.—Strains of *Ps. aeruginosa* showed moderate increases of resistance on repeated subcultures in subinhibitory concentrations of the antibiotics. For strain B4, increases in M.I.C. from 64 to 1,024 μg./ml. of carbenicillin and from 0.5 to 4 μg./ml. of gentamicin were obtained; increases in resistance of strain P14 were from 128 to 2,048 μg./ml. carbenicillin and from 4 to 64 μg./ml. of gentamicin. The strain rendered resistant to carbenicillin grew as small colony variants which produced oxidase and grew on cetrimide agar, but showed poor fluorescence; unlike the sensitive parent strain, they produced a diffusible penicillinase which inactivated benzylpenicillin. There was no reversion to sensitivity on repeated subculture in the absence of carbenicillin. The strains rendered resistant to gentamicin were also of small colony type, but they produced moderate amounts of fluorescein; reversion to sensitivity on subculture did not occur.

Tests with burned mice (Table VI) showed that variants resistant to carbenicillin were avirulent, while those which were resistant to gentamicin appeared to have diminished virulence. Unlike the sensitive parent strains, they were not found on the burns of mice later than on the day of inoculation.

TABLE VI.—*Mortality of Burned Mice Infected with Strains of Ps. aeruginosa Rendered Resistant in vitro to Carbenicillin and to* Gentamicin

Infecting Strain of *Ps. aeruginosa*	Sensitivity Pattern	No. of Mice which			*Ps. aeruginosa* in Blood Culture at Necropsy
		Died	Survived	% Deaths	
B4	Sensitive to carbenicillin and gentamicin ..	87	33	72·5	86
	Resistant to carbenicillin	0	6	0	—
P14	Sensitive to carbenicillin and gentamicin ..	41	19	64	41
	Resistant to carbenicillin	0	6	0	—
	Resistant to gentamicin	3	3	50	2

Administration of Carbenicillin to Patients with Burns

To assess the value of carbenicillin in the treatment of burns infected with *Ps. aeruginosa* a controlled therapeutic trial was started. On the first appearance of *Ps. aeruginosa* in cultures from one or more burns, patients were allocated alternately to treatment and control groups. Those in the treatment group were given a seven-day course of carbenicillin (in adults 1 g. six-hourly by intramuscular injection, with probenecid 0.5 g. six-hourly). Local treatment of the burns was with a cream containing 0.5% silver nitrate and 0.1% chlorhexidine, or with penicillin cream, or with neomycin chlorhexidine tulle gras; in previous experience none of these methods had been effective in removing *Ps. aeruginosa* from burns. The burns were swabbed at changes of dressings (usually every two or three days) and examined for *Ps. aeruginosa* and other bacteria as described elsewhere (Lowbury, 1960; Brown and Lowbury, 1965).

Because of recent success in prophylaxis against *Ps. aeruginosa* in this unit, especially with silver nitrate compresses and cream (Cason *et al.,* 1966), the number of patients available for study in this trial has been very small.

An interim analysis showed that 10 out of 23 burns in nine patients treated with carbenicillin lost *Ps. aeruginosa* during or immediately after the course of treatment. Out of 23 burns in the seven patients of the control series, only one showed the loss of *Ps. aeruginosa* in a corresponding period of time. There was a significant difference in the proportion of burns from which *Ps. aeruginosa* was eliminated in the two groups of the trial ($\chi^2 = 6.3$, $P < 0.02$).

In addition to these patients two others were treated with carbenicillin because the heavy colonization of their burns with *Ps. aeruginosa* was thought to be causing severe clinical infection (not septicaemic). One patient was a man aged 62 with burns of the legs (approximately 12% of the body surface, mostly partial skin loss); he was admitted from another hospital 14 days after injury with cellulitis of both legs, and was severely ill, with confusion, rapid irregular pulse, signs of bronchitis, intestinal distension, and loose green stools; blood examination showed a haemoglobin level of 9.9 g./100 ml., a leucocytosis (W.B.C. 18,000, polymorphonuclear neutrophils 87%, lymphocytes 9%, monocytes 4%), E.S.R. 60 mm./hour (Wintrobe), and a blood urea of 135 mg./100 ml. A heavy growth of *Ps. aeruginosa* was isolated from the burns in pure culture. Blood cultures were sterile, but the severity of the patient's illness was considered to be associated with infection by *Ps. aeruginosa.*

During a course of treatment with carbenicillin (continued for three weeks) the patient's condition improved rapidly, and *Ps. aeruginosa* disappeared from six out of eight of the burns. Assays of carbenicillin in the serum while the patient had renal insufficiency showed 16 μg./ml. at one hour, 32 μg./ml. at three hours, and 64 μg./ml. at five hours after the injection of a dose of the antibiotic. At a later stage, when the kidney function had recovered, serum levels of carbenicillin were lower (16 μg./ml. at three hours and at six hours after administration of the drug).

Another patient with burns heavily colonized with *Ps. aeruginosa* and having normal kidney function was given carbenicillin for seven days with probenecid (2 g./day). Assays of the drug in the patient's serum showed levels of 48 μg./ml. at one hour, 32 μg./ml. at three hours, and 32 μg./ml. at five hours after a dose of carbenicillin. Two of the three burns were cleared of *Ps. aeruginosa* and one showed a reduction in their numbers during the course of treatment.

Sensitivity of Ps. aeruginosa to Carbenicillin during the Trial

In two of the eleven patients treated with carbenicillin *Ps. aeruginosa* isolated after the course of treatment was more resistant (M.I.C. 265 μg./ml.) than the strain initially present (M.I.C. 64 μg./ml.). Tests on the "resistant" strains from one of these patients showed no penicillinase production. The phage type of the more resistant variant was the same as that of the strain present before treatment.

Discussion

Infection of burns with *Ps. aeruginosa* is commonly acquired in hospital. Usually the organism remains localized, colonizing slough and exudate, with no ill effect except some interference with skin grafts and consequent delays in healing (Jackson *et al.*, 1951). Occasionally it causes invasive infection with cellulitis, invasion of the walls of small blood vessels, and in some cases septicaemia (Fraenkel, 1906; Jackson *et al.*, 1951; Rabin *et al.*, 1961; Teplitz *et al.*, 1964a, 1964b; Sevitt, 1964).

This complication is often fatal, and antibiotic treatment is likely to fail even when it removes the organism from the lesions, because of irreparable damage which has occurred by the time invasion is recognized (Jones *et al.*, 1966). For this reason it is important that high-risk cases should receive effective prophylaxis. Silver nitrate compresses (Moyer *et al.*, 1965; Cason, Jackson, Lowbury, and Ricketts, 1966) and isolators (Cason *et al.*, 1966) are useful barriers against contamination, but they are not invariably successful. A second line of defence for such cases is systemic prophylaxis by antisera or by antibiotics.

The two antibiotics studied in this paper, like the specific antisera recently described by Jones *et al.* (1966), protected mice against invasion by *Ps. aeruginosa.* All strains of *Ps. aeruginosa* which were tested were at least moderately sensitive to carbenicillin and highly sensitive to gentamicin; variants which became resistant to carbenicillin on habituation in vitro had lost virulence for mice, and an apparent reduction in virulence was found also in gentamicin-resistant variants obtained in this way.

Gentamicin is more active than carbenicillin in vitro against *Ps. aeruginosa,* and smaller doses are recommended for treatment. Carbenicillin on the other hand, though only moderately active in vitro, was more successful than might have been expected in its prophylactic action against *Ps. aeruginosa* in mice.

In burned patients treated with carbenicillin and probenecid the highest blood levels were rarely higher than the minimal inhibitory concentration for the infective strains; nevertheless, a significantly larger proportion of burns were cleared of *Ps. aeruginosa* in patients treated with carbenicillin than in the untreated controls. This clearance was associated with persistence of or replacement by other organisms in the burns.

Study on a larger series of patients is needed for an assessment of this unexpectedly favourable result; meanwhile it is possible that the local application of silver nitrate and chlorhexidine, though ineffective by itself, may have contributed to the effect of systemic treatment with carbenicillin against *Ps. aeruginosa.*

None of the patients studied in the trial had septicaemia; a considerably higher dosage would undoubtedly be required for successful treatment in such cases.

Gentamicin was less effective than carbenicillin in prophylaxis against the less sensitive of the two strains tested, though the dosage was sufficient to give inhibitory serum levels in the mice; gentamicin (unlike carbenicillin) was found in much higher concentration in the serum of mice which had recently been burned than in unburned mice. The combined use of carbenicillin and gentamicin, like that of gentamicin and ampicillin (Bulger and Kirby, 1963), might be expected to have a synergistic action and deserves study. Both agents may be useful in the protection of patients treated with cytotoxic drugs and other high-risk cases.

The failure of colistin sulphomethate to protect mice was associated with an absence of detectable colistin in the serum of mice receiving treatment with the antibiotic. Kitamoto, Fukaya, and Honma (1962) have also reported an absence of colistin in the serum of treated mice, though the antibiotic was detected in the kidneys at necropsy. In burned patients, however, appreciable blood levels and evidence of some therapeutic value from very large dosage of colistin sulphomethate have been reported (Jones *et al.*, 1966).

Summary

A series of 106 strains of *Pseudomonas aeruginosa* were sensitive in tube dilution tests to gentamicin (M.I.C. 1 to 4 μg./ml.) and moderately sensitive to a new semisynthetic penicillin, carbenicillin (M.I.C. 32 to 128 μg./ml.); one strain was found to be more sensitive to carbenicillin. Carbenicillin was inactivated by the penicillinase of *Staph. aureus.*

Groups of mice were infected by inoculation of small burns with two strains of *Ps. aeruginosa*; about 70% of the mice infected with these strains died with septicaemia. Courses of treatment with carbenicillin gave serum levels in burned or unburned mice up to 128 μg./ml., and the mice were completely protected against both strains. Gentamicin gave peak blood levels in recently burned mice of 64–128 μg./ml. but lower levels (4–8 μg./ml.) in unburned mice; gentamicin protected the animals against the more sensitive strain of *Ps. aeruginosa* only (M.I.C. 0.5–1 μg./ml.). Similar results were obtained with treatment by carbenicillin or by gentamicin, starting at the time of infection or 24 hours later. In most experiments colistin sulphomethate gave no evidence of protection.

A small controlled trial in progress on patients with burns has shown that *Ps. aeruginosa* was removed from a significantly larger proportion (10/24) of burns in patients treated with carbenicillin and probenecid than in untreated controls (1/23). The highest blood levels of carbenicillin (48–64 μg./ml.) were in the same range as its minimal inhibitory concentration against the infecting strains.

A strain of *Ps. aeruginosa* which acquired resistance to carbenicillin in vitro was converted to a small colony form and showed a loss of virulence for burned mice. In a similar experiment with gentamicin the resistant variants were also small colony forms, but retained some virulence for mice.

We wish to thank Beecham Research Laboratories for supplies of BRL 2064 and information about the antibiotic, Roussel Laboratories for supplies of gentamicin, our technical colleagues for their co-operation, and the surgeons and nursing staff of the Burns Unit for permission to use clinical data. We also thank Dr. M. T. Parker for phage-typing strains of *Ps. aeruginosa.*

REFERENCES

Barber, M., and Waterworth, P. M. (1966). *Brit. med. J.*, **1**, 203.
Brown, V. I., and Lowbury, E. J. L. (1965). *J. clin. Path.*, **18**, 752.
Bulger, R. J., and Kirby, W. M. M. (1963). *Amer. J. med. Sci.*, **246**, 717.
—— Sidell, S., and Kirby, W. M. M. (1963). *Ann intern. Med.*, **59**, 593.
Bushby, S. R. M. (1964). In R. J. Schnitzer and F. Hawking's *Experimental Chemotherapy*, **1**, 50. New York.
Butler, A. M., and Richie, R. H. (1960). *New Engl. J. Med.*, **262**, 903.
Cason, J. S., Jackson, D. M., Lowbury, E. J. L., and Ricketts, C. R. R. (1966). *Brit. med. J.*, **2**, 1288.
—— and Lowbury, E. J. L. (1960). *Lancet*, **2**, 501.
Feller, I. (1965). *Second International Congress for Research in Burns, Edinburgh*, p. 56.
Fraenkel, E. (1906). *Virchows Arch. path. Anat.*, **183**, 405.
Jackson, D. M., Lowbury, E. J. L., and Topley, E. (1951). *Lancet*, **2**, 137.
Jones, R. J., and Lowbury, E. J. L. (1965). *Lancet*, **2**, 623.
—— Jackson, D. M., and Lowbury, E. J. L. (1966). *Brit. J. plast. Surg.*, **19**, 43.
Kefalides, N. A., Arana, J. A., Bazan, A., Velarde, N., and Rosenthal, S. M. (1964). *Ann. Surg.*, **159**, 496.
Kitamoto, O., Fukaya, K., and Honma, H. (1962). *J. Antibiotics (Tokyo)*, Series B, **15**, 7. (Cited in R. J. Schnitzer and F. Hawking's *Experimental Chemotherapy*, 1964, **3**, 217. New York.)
Klein, J. O., Eickhoff, T. C., and Finland, M. (1964). *Amer. J. med. Sci.*, **248**, 528.
Lowbury, E. J. L. (1960). *Brit. med. J.*, **1**, 994.
—— Topley, E., and Hood, A. M. (1952). *Lancet*, **1**, 1036.
Moyer, C. A., Brentano, L., Gravens, D. L., Margraf, H. W., and Monafo, W. W. (1965). *Arch. Surg.*, **90**, 812.
Rabin, E. R., Graber, C. D., Vogel, E. H., Finkelstein, R. A., and Tumbusch, W. A. (1961). *New Engl. J. Med.*, **265**, 1225.
Sevitt, S. (1964). *Acta chir. plast.*, **6**, 173.
Teplitz, C., Davis, D., Mason, A. D., and Moncrief, J. A. (1964a). *J. surg. Research*, **4**, 200.
—— —— Walker, H. L., Raulston, G. L., Mason, A. D., and Moncrief, J. A. (1964b). Ibid., **4**, 217.
Tumbusch, W. J., Vogel, E. H., Butkiewicz, J. V., Graber, C. D., Larson, D. L., and Mitchell, E. T. (1961). *J. Trauma*, **1**, 22.
Weinstein, M. J., Luedemann, G. M., Oden, E. M., and Wagman, G. H. (1963). *Antimicrobial Agents and Chemotherapy*, p. 1.

Observations on Urinary White Cell Excretion Before and After Surgery

R. M. LINDSAY,* M.B.; B. LUNAN,† M.B.; J. McGEACHIE,‡ M.D., M.C.PATH.
A. L. LINTON,§ M.B., M.R.C.P.ED., M.R.C.P.GLASG.

Brit. med. J., 1967, 3, 83–85

Quantitative determination of the cells excreted in the urine has until recently been regarded as a cumbersome and time-consuming procedure (*Lancet*, 1961). Houghton and Pears (1957) attempted to simplify the technique, and McGeachie and Kennedy (1963) described a method of semi-quantitative cell counting which was suitable for routine use yet was much more accurate than the ordinary wet-film technique. In the course of a recent study of renal function after surgery (Lindsay *et al.*, 1965) it was observed that there was a considerable difference between urinary white cell excretion rates before and after surgery in many patients, so further investigation of this was undertaken.

Patients and Methods

A group of 138 patients (81 males and 57 females) undergoing surgery in a general surgical ward were studied. The surgical procedures ranged from ligation of varicose veins to total colectomy, and any patient having direct interference with the genitourinary tract (including catheterization) was excluded. All had general anaesthesia. Preoperatively each patient was questioned about urinary tract symptoms, and any definite history of urinary tract infection or catheterization was recorded. Semi-quantitative cell counts, as described by McGeachie and Kennedy (1963), were performed on clean midstream specimens of urine, the examination being carried out within two hours of collection. In all cases the urinary cells were stained by the method of Prescott and Brodie (1964) to differentiate between white cells and tubular cells. Each patient was seen again 24 to 48 hours after operation; urinary symptoms were recorded and the cell count was repeated. Urine volumes were recorded, and patients who excreted less than 600 ml. of urine between 24 and 48 hours after operation were excluded.

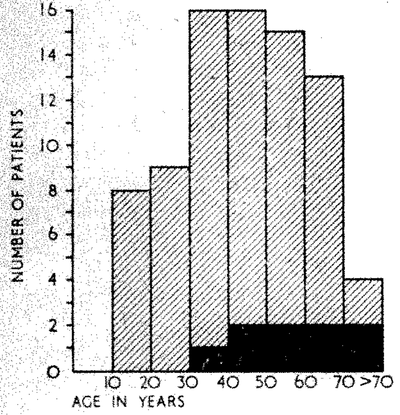


FIG. 1

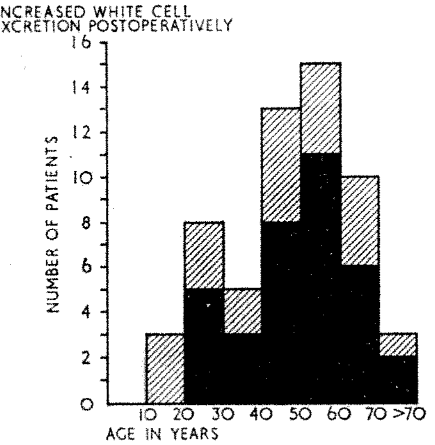


FIG. 2

FIG. 1.—Age distribution of 81 males—general surgical group. FIG. 2.—Age distribution of 57 females—general surgical group.

In 62 consecutive patients in the group urine was sent for bacteriological examination before and after operation. Delays in transmission of specimens to the laboratory were minimized, and bacterial counting was done by the method described by McGeachie and Kennedy (1963).

In a further group of 14 patients (4 males and 10 females) fully quantitative cell counts were done before and after operation. These were carried out on accurate three-hour urine collections kept acid to litmus and refrigerated during the collection. The cells were counted by the method of Houghton and Pears (1957) after staining by Prescott and Brodie's method (1964). Bacterial counts were performed concurrently on all of these specimens.

A further group of 46 patients (23 males and 23 females) aged 9 to 80 years undergoing minor surgery on the ear, nose, or throat were studied in addition to the 152 general surgical patients.

Results

The staining technique of Prescott allows the counting of white blood cells, red blood cells, tubular cells, and squamous epithelial cells. A considerable difference was found between rates of excretion preoperatively and postoperatively only for white cells; no further reference will be made to the other types of cell counted.

In the general surgical group, of the 81 males only 5 (6%) had a urinary white cell count above the normal range preoperatively, and 9 (11%) had an abnormal cell count postoperatively, including all the five originally abnormal. Of the 57 females of this group 6 (10.5%) showed an abnormal cell count preoperatively, but 35 (61%) were abnormal postoperatively.

As shown in the Table, seven of the nine males with an increased white cell excretion postoperatively gave a history of urinary tract infection or of catheterization. The relation of history of urinary infection or catheterization in the females is also shown in the Table. The age distribution of all patients with an abnormal postoperative white cell count is given in Figs. 1 and 2.

Bacterial counts were carried out in 39 consecutive male patients. No bacterial count of more than 100,000 organisms

Correlation Between Past History and an Increased Urinary White Cell Excretion Postoperatively in 81 Males

Past History	Males			Females		
	No.	Cell Count		No.	Cell Count	
		Negative	Positive		Negative	Positive
+	8	1	7	8	2	6
−	73	71	2	49	20	29

---

* Senior House Officer in Medicine, Royal Infirmary, Glasgow C.4.
† Senior House Officer in Surgery, Royal Infirmary, Glasgow C.4.
‡ Senior Lecturer in Bacteriology, Royal Infirmary, Glasgow C.4.
§ Consultant Physician in Renal Diseases, Western Infirmary, Glasgow W.1.

per ml. was obtained preoperatively and only one postoperatively. This was associated with an abnormal cell count. In the 38 male patients who were negative bacteriologically two abnormal cell counts were obtained postoperatively, associated with negative cultures. Both patients had been given antibiotics since the day of operation.

Of the 23 consecutive female patients in whom bacterial counts were done four had above 100,000 organisms per ml. preoperatively and five postoperatively (the latter five includes the previous four), all of the positive postoperative counts being associated with abnormal urinary white cell excretion. A further five patients had increased white cell excretion postoperatively, but negative culture; three of these five had been receiving antibiotics since operation.

In the 14 patients in whom fully quantitative cell counts were done the upper limit for normal white cell excretion rate was chosen as 400,000 cells per hour; this is higher than most authors suggest (Addis, 1926; Rofe, 1955; Houghton and Pears, 1957; Hutt *et al*., 1961). Of the 10 female patients so examined only one had an abnormal cell excretion rate preoperatively, and this was associated with a bacterial count in excess of 100,000 organisms per ml. (Fig. 3). Postoperatively there were five cases with abnormal white cell excretion, four of which were associated with positive bacterial counts. Of the four male patients in whom fully quantitative cell counts were done none showed increased white cell excretion either before or after operation (Fig. 4).

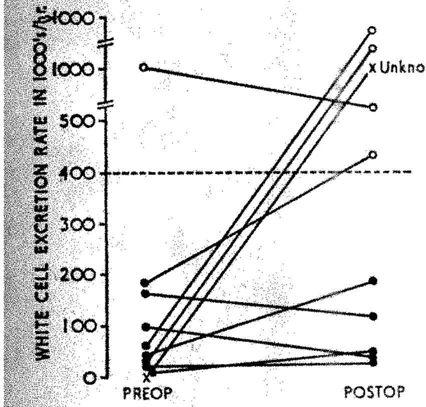


FIG. 3

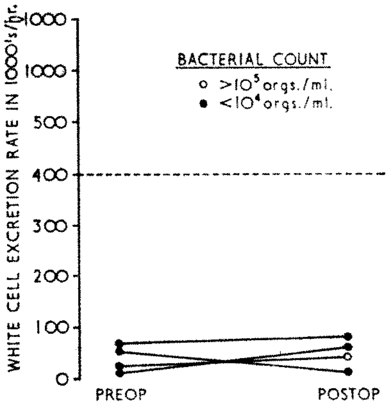


FIG. 4

FIG. 3.—White cell excretion rates and bacterial counts in 10 females undergoing general surgery. FIG. 4.—White cell excretion rates and bacterial counts in four males undergoing general surgery.

In the additional group of 46 patients who were studied while undergoing minor surgery of the ear, nose, or throat, none of the 23 males had positive cell counts or bacterial counts at any time. Of the 23 females four showed an abnormal rise in urinary white cell excretion after surgery, and three of them gave a past history of urinary tract infection.

In the whole group of 198 patients only four females complained of urinary symptoms postoperatively, and in each case this was associated with increased white cell excretion. There was no evidence that type of surgery or duration of anaesthesia had any influence on the numbers of patients showing increased white cell excretion or significant bacteriuria.

Discussion

This study has shown that in many patients undergoing surgery unrelated to the genitourinary system there is a marked rise in urinary white cell excretion postoperatively. Furthermore, this phenomenon was noted in 61% of the females studied, but in only 11% of the males. The rise in the females is highly significant ($P<0.001$). The increased white cell excretion rate was confirmed in a small number of cases by fully quantitative cell counts, and bacterial counting suggested that in most cases it was accompanied by significant bacteriuria (>100,000 organisms per ml.). There did not appear to be any relation between type of surgery or duration of anaesthesia and the increased white cell excretion. Almost all of the male patients who showed increased white cell excretion postoperatively had a history of previous urinary tract infection or of catheterization; this relation was less definite in the females.

With unexpected findings of this nature the accuracy of the techniques used must always be questioned. The increased white cell excretion was detected by the semi-quantitative technique of McGeachie and Kennedy (1963), which does not take into account the volume of urine passed. It is obviously possible that oliguria might give false-positive results, but all oliguric patients were excluded from the study. Almost all of the patients studied passed more than 1 litre of urine between 24 and 48 hours after operation, and at this urine volume the upper limit of normal for the McGeachie and Kennedy method corresponds to a urinary excretion of 350,000 white cells per hour; the authors themselves established that the method gives few false-positive results. Fully quantitative cell counts confirmed the findings, 400,000 white cells excreted per hour being taken as the upper limit of normal, as is generally accepted (Hutt *et al*., 1961; Kennedy *et al*., 1964). The use of the differential staining techniques described by Prescott and Brodie (1964) ensured that the cells counted were white cells and not the otherwise indistinguishable small renal tubular cells.

Prescott (1966) suggested that the normal urinary white cell excretion rate for males is much lower than for females, and it might be that this would explain the sex difference noted in the present study. However, almost none of the males showed any rise at all in white cell excretion rates, while the vast majority of females who are recorded as showing positive cell counts were very clearly above the upper limit of normal even for females. The fact that we have observed this marked sex difference would militate against another possible explanation of postoperative rise in white cell excretion, the use of analgesics, which may increase urinary cell excretion. In addition, Prescott (1965) showed that the increased cell count after analgesic ingestion was due to a rise in renal tubular cell excretion, not leucocytes. Finally, bacterial counting strongly suggests that the cases in this series which showed a rise in white cell excretion very often had significant bacteriuria also.

Houghton and Pears (1957) studied variations in the rate of leucocyte excretion in the urine of normal subjects; they found no differences with age or sex, and only slight differences with posture and time of collection. On the other hand, Prescott (1966) showed a marked sex difference, considerable variation from patient to patient, and even from time to time in the same patient. It must be remembered, however, that these differences were all within the normal range. Other documented reasons for increases in urinary leucocyte excretion to above the normal range are urinary tract infections, during fever in pneumonia (Goldring, 1931), in pregnancy (Elden and Cooney, 1935), and after vigorous exercise (Roberts, 1935). None of these situations was applicable to the present study.

The cause of the abnormalities recorded in this paper remains uncertain. The marked sex difference, the fact that males showing a rise in white cell excretion postoperatively almost all had a previous history of urinary tract infection, and the association of pyuria and significant bacteriuria all suggest that the phenomenon is related in some way to urinary tract infection. It might be suggested that pooling of urine in the bladder postoperatively contributed to the significant bacteriuria or even to the pyuria, but the collections were not made on the first postoperative day, and it is unlikely that this would explain the marked sex difference. It is highly unlikely that over 60% of apparently normal women had latent urinary tract infection, but perhaps the changes we have observed are in some way related to the unknown cause underlying the increased susceptibility of the female to urinary tract infection.

Summary

Semi-quantitative urinary white cell counts were performed in 198 patients before and after surgery. A significant rise in white cell excretion rates was found in 61% of the females but in only 11% of the males. The results were confirmed in a further group of patients by means of fully quantitative cell counts, and bacterial counting showed that this pyuria was often associated with significant bacteriuria. The possible significance of these findings is discussed.

References

Addis, T. (1926). *J. clin. Invest.*, **2**, 409.
Elden, C. A., and Cooney, J. W. (1935). Ibid., **14**, 889.
Goldring, W. (1931). Ibid., **10**, 355.
Houghton, B. J., and Pears, M. A. (1957). *Brit. med. J.*, **1**, 622.
Hutt, M. S. R., Chalmers, J. A., MacDonald, J. S., and de Wardener, H. E. (1961). *Lancet*, **1**, 351.
Kennedy, W. P. U., Ormonde, N. W. H., and Murdoch, J. McC. (1964). *Brit. J. Urol.*, **36**, 354.
Lancet, 1961, **2**, 1077.
Lindsay, R. M., Linton, A. L., and Longland, C. J. (1965). *Lancet*, **1**, 978.
McGeachie, J., and Kennedy, A. C. (1963). *J. clin. Path.*, **16**, 32.
Prescott, L. F. (1965). *Lancet*, **2**, 91.
—— (1966). *Clin. Sci.*, **31**, 425.
—— and Brodie, D. E. (1964). *Lancet*, **2**, 940.
Roberts, A. M. (1935). *J. clin. Invest.*, **14**, 31.
Rofe, P. (1955). *J. clin. Path.*, **8**, 25.

Use of Diazepam in Treatment of Severe Convulsive Status Epilepticus

MAURICE J. PARSONAGE,* M.B., B.SC., F.R.C.P., D.C.H. ; JOHN W. NORRIS,† M.B., M.R.C.P.

Brit. med. J., 1967, **3**, 85–88

During the past three years diazepam (Valium) has been used extensively, both in Europe and in the U.S.A., chiefly as a tranquillizing agent but also as an anticonvulsant (Gross and Kaltenbäck, 1963 ; Goldstein, 1963 ; Trolle, 1965). Until recently there have been comparatively few published accounts of its use in the treatment of status epilepticus. One of the earliest was that of Naquet *et al.* (1965), and others were by Gastaut *et al.* (1965), Iborra (1965), Piqué and Henking (1965), Revol *et al.* (1965), Bamberger and Matthes (1966), and Lombroso (1966).

In common with chlordiazepoxide (Librium) and nitrazepam (Mogadon), diazepam is a member of the benzodiazepine group of drugs. It has tranquillizing, muscle relaxant, and anticonvulsant actions. In experimental animals its depressant action has been found to act mainly on structures in the limbic system, including the hippocampus, amygdala, and reticular formation (Randall *et al.*, 1961 ; Morillo, 1962 ; Hernández-Peón *et al.*, 1964 ; Schallek *et al.*, 1964 ; Schallek and Kuehn, 1965). It has also been shown that seizures arising in the amygdala in rats can be prevented by the prior administration of this drug (Eidelberg *et al.*, 1965). The literature relative to this subject has been extensively reviewed by Boyer (1966).

We report here the use of diazepam in the treatment of nine severe cases of convulsive status epilepticus.

Material and Methods

There were four males and five females, whose ages ranged from 11 to 53 years (Table I). In practically all cases the epilepsy was of long standing and probably associated with gross brain damage. In at least six of the nine patients there was a probable source of seizure discharge in one or other frontal lobe, and in several instances there had been previous episodes of convulsive status epilepticus.

After admission to hospital all patients were at first given diazepam in 10-mg. doses (1 ampoule), either intravenously or intramuscularly as required. When it became apparent that the drug had only a transient action it was given as an intravenous infusion, initially in a dosage of 100 mg. in 1 litre of physiological saline. Latterly, intravenous infusions of 100 mg. of the drug in 500 ml. of saline were given.

All patients had the usual nursing care, with particular attention to respiratory function and to fluid and electrolyte balance. Whenever it was thought necessary tracheostomy and controlled respiration were employed. Tests for liver function were carried out in Cases 5–9. In most of the patients E.E.G. studies had previously been carried out with resulting location

TABLE I

Case No.	Sex and Age	Origin of Seizure Discharge	Duration of Epilepsy and Associated Findings	Aetiology	Precipitating Factors
1	F 17	R. frontal	Since infancy	Unknown	Meningo-encephalopathy of unknown cause
2	M 35	Primary subcortical	Since birth. Mental retardation	Unknown	None
3	M 38	Primary subcortical	Since birth. Mental retardation	Unknown	None
4	F 19	? R. frontal	Since age 8. Personality change	? Measles encephalopathy at age 8	Change in anticonvulsant regimen
5	F 15	R. frontal	Since birth. Mental retardation	Unknown	None
6	F 18	L. cerebral hemisphere	Since cerebral illness in infancy	? Meningitis	Reduction of anticonvulsants during drug detoxication
7	M 12	L. frontal	Since birth. Mental retardation	Unknown	Pneumonia and withdrawal of anticonvulsants
8	M 11	L. frontal	Since age 5. Mental retardation	Febrile illness at age 5. (? Encephalitis)	None
9	F 53	R. frontotemporal	3 years	Degenerative arterial disease	Inadvertent sudden withdrawal of anticonvulsants (?)

---

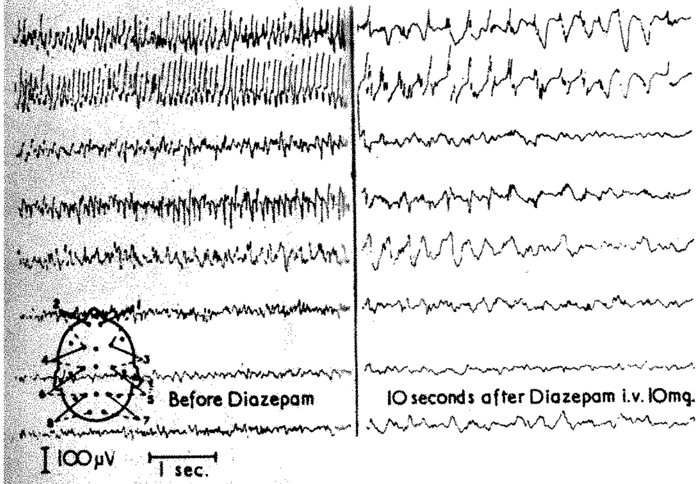
* Consultant Neurologist, General Infirmary at Leeds, Leeds 1.

† Registrar, Neurological Department, General Infirmary at Leeds, Leeds 1.

of sources of seizure discharge, but further recordings were performed as often as possible during treatment of the status epilepticus.

Results

The results are summarized in Table II. Immediate control of seizures was obtained in seven of the nine patients. In most of these the effect of diazepam was very rapid, being evident within 10–20 seconds of the beginning of the injection (see Illustration). In Cases 1 and 6 the control was not enduring, and it was deemed advisable to resort to the use of other methods of treatment (intravenous paraldehyde, etc.).



Showing the rapid interruption of seizure discharge in the E.E.G. after the intravenous administration of diazepam (Case 9).

In Case 2 treatment with diazepam was abandoned at an early stage because of initial uncertainty concerning the effects of giving the drug in high dosage. For the same reason a similar policy was adopted in Case 3, and the seizures were eventually suppressed only with great difficulty with the aid of curarization and controlled respiration, together with the combined administration of phenobarbitone and phenytoin in high dosage. This patient was subsequently found to be severely demented.

In Cases 4 and 8 complete control of seizures was obtained after giving 10 mg. of diazepam intramuscularly. Thereafter it was given as an intravenous infusion over a period of three days while the patients were in the intensive care unit. When the seizures recurred the following day they were easily controlled with paraldehyde.

Case 7 was remarkable for the fact that control of seizures was not obtained even after the administration of 190 mg. of diazepam. The patient, a backward boy aged 12, remained in a comatose state and eventually died at the end of five weeks, presumably as a result of severe brain damage. His seizures had continued almost uninterrupted for nearly three weeks, despite curarization and controlled respiration and finally the institution of hypothermia.

In Case 9, after the intravenous administration of only 17.5 mg. of diazepam, the blood pressure fell to 70/50 from a level on admission of 105/70. In the belief that this might be due to diazepam, the drug was discontinued and intravenous paraldehyde given. However, as the seizures remained uncontrolled and the blood pressure had become stabilized at a level of 90/50, a further 131.5 mg. of diazepam was given as an intravenous infusion in conjunction with controlled respiration. Though control of seizures was soon obtained in this way, without any further fall in blood pressure, the patient remained in a comatose state and died two days later. At necropsy an infarction of the left cerebral hemisphere was found, adjudged to be some four to five days old. It was confined to the cortical territory of the middle cerebral artery, two branches of which were found to be occluded by fibrin clot. A similar clot was attached to the intima on the dorsal wall of the abdominal aorta. In the inferomedial portion of the right temporal lobe there was gliosis of the white matter adjacent to the amygdaloid nucleus and satellitosis of cortical neurones in the deeper laminae. In this area many small arteries showed collagenous change, and similar changes were found in the corresponding area in the left temporal lobe but without any associated gliosis. There was no evidence of hypoxic damage or incisural sclerosis in either temporal lobe.

It seems likely that the degenerative vascular changes seen in the right temporal lobe in this fatal case were related to the epilepsy, particularly since they were associated in life with a local slow wave and sharp wave abnormality in the E.E.G., indicating local neuronal hyperexcitability. In view of the estimated age of the left cerebral infarction it appeared very probable that it had occurred before diazepam therapy was begun, though its relation to the onset of the status epilepticus remains problematical. Furthermore, it also seems very likely that the blood pressure had already begun to fall before treatment was started, since this patient is known to have had a blood pressure of at least 150/90 in the past.

TABLE II.—*Summary of Results*

Case No.	Previous Treatment	Treatment with Diazepam				Supplementary Treatment	Total Duration of Status (days)	Final Result
		Day Treatment Begun	Maximum Dose in 24 hours	Total Amount Given	Effect			
1	Paraldehyde on 1st day	2nd	30 mg.	30 mg. over 24 hours	Temporary control	Paraldehyde	6	Ultimate control. Residual mild left hemiparesis
2	Paraldehyde (i.m.) and phenytoin (i.v.) for 3 days	3rd	30 ,,	30 mg. over 24 hours	Temporary control	Controlled respiration. Thiopentone (i.v.)	3	No change
3	Paraldehyde 10 ml. (i.m.) on 1st day	1st	40 ,,	70 mg. over 2 days	Unsatisfactory control	Controlled respiration. Curarization. Phenobarbitone and phenytoin	8	Severe dementia
4	None	1st	150 ,,	335 mg over 7 days	Temporary control i.m. but complete when given i.v.	None	7	No change
5	None	1st	160 ,,	170 mg. over 3 days	Satisfactory control	Paraldehyde	17	Persistent elevation of serum alkaline phosphatase level
6	None	1st	200 ,,	900 mg. (approx.) over 7 days	Temporary control	Controlled respiration. Intracarotid amylobarbitone	4–5	No change
7	Paraldehyde (i.m.) on 1st day	2nd	140 ,,	190 mg. over 3 days	None	Controlled respiration. Paraldehyde. Hypothermia	20	Severe brain damage. Died
8	None	1st	150 ,, (approx.)	350 mg. over 7 days	Complete control	None	2–3	No change
9	None	1st	149 mg.	169 mg. over 2 days	Satisfactory control	Controlled respiration. Paraldehyde	3	Hypotension. Cerebral infarction. Died

Side-effects

A hypnotic effect was evident to some degree in most cases when the dosage of diazepam exceeded 10 mg. intravenously. In higher dosage semicoma usually supervened, but this was always transient. There were, however, no abnormal mental changes as described by Femi-Pearse (1966).

A tendency to the development of tolerance became evident when continuous intravenous infusions of diazepam were employed in dosages ranging from 300 to 500 mg. spread over a period of two to three days. This was particularly striking in Case 6, in which the drug appeared to lose its effect on the seizures, and this could not be restored when intermittent intravenous injections were given subsequently.

There were no cases in which respiratory suppression occurred as a result of the administration of diazepam. No abnormalities of the peripheral blood picture or of renal function were encountered.

Evidence of abnormal liver function was found in three patients (Cases 5, 8, and 9). In the first of these there had been an illness six months previously characterized by fever, lymphadenopathy, and hepatosplenomegaly which was thought to be due to a toxic reaction to methoin therapy. After the administration of just over 100 mg. of diazepam there was found to be a rise in the serum aspartate aminotransferase level to 62 units, while that of the serum alkaline phosphatase had risen to 19.6 K.A. units. The serum alanine aminotransferase level remained normal. The serum aspartate aminotransferase level returned to normal within a week, whereas the alkaline phosphatase level has remained raised (30–40 K.A. units). In Case 8 a rise of the serum aspartate aminotransferase level to 64 units was found after two days' treatment with approximately 250 mg. of diazepam, but this had returned to normal at the end of a week. In Case 9 the serum aspartate aminotransferase level had risen to 68 units on the second day of treatment, but the patient did not survive long enough for any further estimations to be made.

In no case was there any evidence of tissue necrosis at the site of injection.

Discussion

In all our patients except one (Case 7) the immediate suppressant effect of diazepam on convulsive seizures was clearly evident. This was seen, however, only when the drug was given intravenously, and we were not able to confirm the observation of Naquet *et al.* (1965) that status epilepticus was terminated within minutes of the intramuscular injection of diazepam. It is noteworthy that Piqué and Henking (1965) used the intravenous route in all their cases, whereas Iborra (1965) and Gastaut *et al.* (1965) used both the intravenous and the intramuscular routes. However, since the two routes were often used in the same patient it is difficult to conclude which was the more effective.

In our first three patients diazepam was given in relatively small doses intermittently lest dangerous side-effects should occur, and also after other treatment had proved to be ineffective; even so, the effect of diazepam was appreciable, and satisfactory control of seizures might have been achieved if larger doses had been given. In the remaining six patients treatment with diazepam was begun earlier and much larger doses were given by continuous infusion. In four of these good control of seizures was obtained, though in Case 6 it was only temporary and other measures had to be used.

Case 7 was remarkable for the fact that neither the administration of diazepam nor any of the other measures used had any obvious effect on the seizures. This patient was a mentally retarded boy aged 12 who had had previous episodes of status epilepticus and who lapsed into a severely demented state before death finally occurred, despite eventual interruption of his continuous epileptic state.

Though respiratory depression has always been regarded as a possible side-effect of diazepam, there have apparently been very few reports of this ever having occurred to a dangerous degree. Indeed, Femi-Pearse (1966) has reported the use of as much as 720 mg. daily in the treatment of tetanus without ill-effect. Gastaut *et al.* (1965) quote the case of a 9-month-old baby whose hemiclonic status was stopped by giving 6 mg. of diazepam intramuscularly but whose breathing then became shallow. There appeared, however, to be a slow spontaneous return later to normal respiration. In none of our cases was there any indication of respiratory depression that could be attributed to diazepam administration, though we felt it was advisable always to be prepared for such a complication.

The findings in Case 9 have been described in detail in view of the possibility that the administration of diazepam may have played some part in causing the hypotension and cerebral infarction. We have, however, given reasons why we think this unlikely. It would appear, therefore, that in none of our cases was there any evidence of depression of vital centres, despite the infusion of comparatively large amounts of diazepam.

With doses of more than 10 mg. a hypnotic effect was observed in most of our cases, and this had to be taken into account when assessing conscious levels. The development of tolerance was also a notable feature; this usually became evident within 24 hours of beginning an intravenous infusion, and appeared to be related to the total dosage given. Furthermore, when tolerance had occurred in this way it apparently could not be obviated by afterwards giving the drug intermittently. Side-effects such as mental disturbances and diuresis (Femi-Pearse, 1966) or ataxia and diplopia (Payne and Ishmael, 1963; Trolle, 1965) were not observed in our cases.

It is doubtful if the abnormal results of the liver function test in three of our cases could be attributed to treatment with diazepam. In the first of these (Case 5) such abnormalities could not certainly be dissociated either from previous anticonvulsant therapy or from the presumed toxic reaction to methoin in which there had been involvement of the reticuloendothelial system. Unfortunately, liver function tests had not been carried out at the time of this illness. In the other two patients (Cases 8 and 9) the raised serum aspartate aminotransferase levels could have been due to secondary effects of the status epilepticus, such as severe muscular contraction and widespread tissue hypoxia.

On the basis of the results of treatment in our small series of cases of severe convulsive status epilepticus we feel that diazepam has a useful and important part to play in the control of such states. It appears to be an effective agent, rapid in its action and apparently free from serious side-effects. It provides a useful alternative method to treatment with barbiturates and paraldehyde. Indeed, there is much to be said for regarding it as the treatment of choice in the management of all types of status epilepticus at the present time.

Summary and Conclusions

The results of the treatment with parenteral diazepam (Valium) in a series of nine cases of severe convulsive status epilepticus are reported.

In seven out of the nine patients immediate rapid control of seizures was obtained. In two of these control was only temporary, but in one of them this may have been due to inadequate dosage. Treatment by intravenous infusion was found to be the most effective method.

No serious side-effects occurred which could with certainty be attributed to treatment with diazepam.

Two patients died. In one case this was apparently due to vascular occlusion causing extensive cerebral infarction. In the second all measures used failed to control the seizures and death occurred as a result of severe brain damage.

It is concluded that intravenous diazepam therapy has a useful and important part to play in the treatment of severe convulsive status epilepticus.

We would like to acknowledge our indebtedness to Roche Products Limited for financial assistance and to Dr. John Garrod for his interest and helpful advice. We are grateful to Dr. Denis Harriman for the necropsy findings in Case 9 and to Dr. Kenneth Exley for help with the manuscript. We should also like to thank Mrs. Grace Murray for help in preparing the illustrations and Miss Hilary Stevens for typing the manuscript.

REFERENCES

Bamberger, Ph., and Matthes, A. (1966). *Z. Kinderheilk.*, **95**, 155.
Boyer, P. A., jun. (1966). *Dis. nerv. Syst.*, **27**, 35.
Eidelberg, E., Neer, H. M., and Miller, M. K. (1965). *Neurology (Minneap.)*, **15**, 223.
Femi-Pearse, D. (1966). *Brit. med. J.*, **2**, 862.
Gastaut, H., Naquet, R., Poiré, R., and Tassinari, C. A. (1965). *Epilepsia (Amst.)*, **6**, 167.
Goldstein, N. (1963). *Dia méd. urug.*, **29**, 4492.
Gross, H., and Kaltenbäck, E. (1963). *Helv. med. Acta*, **30**, 660.
Hernández-Peón, R., Rojas-Ramirez, J. A., O'Flaherty, J. J., and Muzzuchelli-O'Flaherty, A. L. (1964). *Int. J. Neuropharmacol.*, **3**, 405.
Iborra, J. E. (1965). *Proceedings of 8th International Conference on Neurology, Vienna*, vol. IV/1, 375.
Lombroso, C. T. (1966). *Neurology (Minneap.)*, **16**, 629.
Morillo, A. (1962). *Int. J. Neuropharmacol.*, **1**, 353.
Naquet, R., Soulayrol, R., Dolce, G., Tassinari, C. A., Broughton, R., and Loeb, H. (1965). *Electroenceph. clin. Neurophysiol.*, **18**, 427.
Payne, R. W., and Ishmael, W. K. (1963). *West. Med.*, **4**, 40.
Piqué, E. R., and Henking, R. (1965). *Psychiat. et Neurol. (Basel)*, **150**, 214.
Randall, L. O., *et al.* (1961). *Curr. ther. Res.*, **3**, 405.
Revol, M., Courjon, J., Gerin, P., and Fischer, G. (1965). *Rev. neurol.*, **113**, 266.
Schallek, W., and Kuehn, A. (1965). *Med. Pharmacol. exp. (Basel)*, **12**, 204.
—— Zabransky, F., and Kuehn, A. (1964). *Arch. int. Pharmacodyn.*, **149**, 467.
Trolle, E. (1965). *Acta neurol. scand.*, **41**, Suppl. No. 13, 535.

Intermittent Haemodialysis: Insertion and Care of the Silastic-Teflon Cannula

G. J. A. CLUNIE,* M.B., F.R.C.S., F.R.C.S.ED.; A. M. MARTIN,† M.B., M.R.C.P.ED.
B. NOLAN,‡ M.B., F.R.C.S., F.R.C.S.ED.

Brit. med. J., 1967, **3**, 88–90

The exteriorized Silastic-Teflon arteriovenous cannula introduced by Quinton, Dillard, Cole, and Scribner (1962) has simplified vessel access in patients requiring intermittent haemodialysis. Cannula complications still cause considerable discomfort and inconvenience to the patient, however, and account for much of the medical and surgical attention required. In the renal unit of the Royal Infirmary, Edinburgh, where this system of cannulation has been in regular use since October 1964, a number of modifications in the technique of insertion and aftercare of the cannulae have been made, and these are described in this report.

Insertion

All procedures were carried out in a surgical theatre. The nondominant arm was used wherever possible, the vessels cannulated being the radial artery close to the wrist and a forearm vein of adequate size. Leg cannulae were used primarily in three men whose work involved repetitive arm movements, and secondarily in one woman after loss of arm sites. The posterior tibial artery immediately proximal to the medial malleolus and the long saphenous vein at a slightly higher level provided satisfactory leg vessels (Fig. 1). Many patients requiring intermittent dialysis showed extensive atherosclerosis, and patency of and adequacy of flow through the ulnar or dorsalis pedis arteries were checked before ligation of the vessels used for cannulation.

The technique used was similar to that described by Hegstrom, Quinton, Dillard, Cole, and Scribner (1961) and by Quinton *et al.* (1962). Both local and regional block anaesthesia proved satisfactory, but general anaesthesia was used in children or where multiple procedures were performed. Care was taken to avoid placing the subcutaneous loop over bone, since this caused early erosion of the overlying skin. Longitudinal incisions were used over the artery to allow adequate exposure, but the wounds were closed in at least two layers to bury the cannulae as deeply as possible. Transverse incisions were used for vein cannulation (Clark and Parsons, 1966), the security of closure and avoidance of later erosion through the wound compensating for lack of access in the more superficially placed vein. A single vertical incision proved satisfactory where artery and vein lay close together and at approximately the same level, and was particularly useful in the leg.

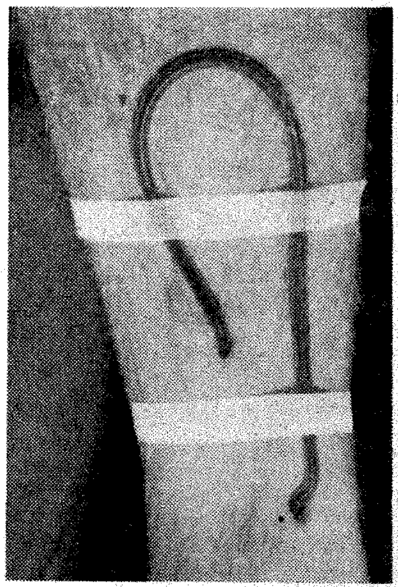


FIG. 1.—Case 1. Leg cannulae 18 months after insertion.

The Teflon tip used was the largest compatible with the original vessel diameter, and vein tips were always at least one

---

* Lecturer, Department of Surgical Science, University of Edinburgh, Edinburgh 8.
† Registrar, Renal Unit, Royal Infirmary, Edinburgh 3.
‡ Consultant Surgeon, Royal Infirmary, Edinburgh 3.

size larger than arterial, in order to avoid pressure gradients in the shunt. Crimp and joint rings at the Silastic-Teflon junction were used initially (Fig. 2A), but as the internal rings tended to ulcerate they were replaced by extending the distal vessel ligature around the cannula. A single break shunt (Fig. 2B) with a long venous Silastic segment (Sevitt, Comty, Rottka, and Shaldon, 1964) was used, and the original Teflon-to-Teflon external bayonet junction was replaced by the insertion of a large vessel tip between the Silastic ends. The making and breaking of this junction was later made easier by discarding the external rings. No accidental leaks have occurred with this simplified system. External metal stabilizers caused skin reactions and were therefore replaced by Micropore Tape (Minnesota Mining and Manufacturing Company).

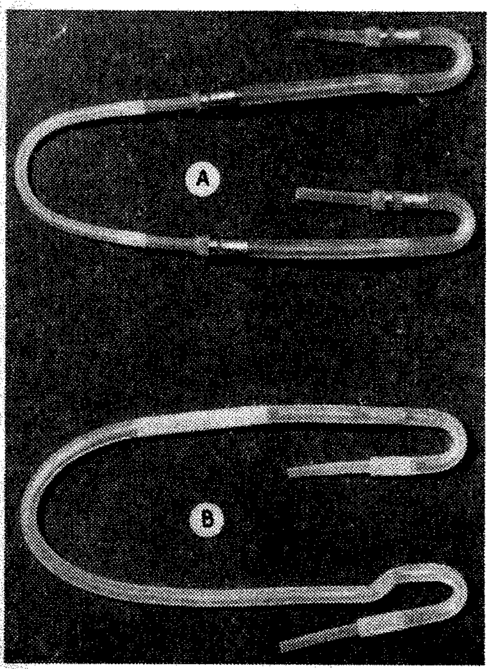


FIG. 2.—A, Original form of shunt with crimp and joint rings, short Silastic segments, and an external Teflon loop. B, Simplified form of shunt without rings, a long venous Silastic segment, and a single external Teflon break.

Movement of the cannulated limbs was reduced postoperatively by elevation in a sling for two days in the case of the upper limb, and by confinement to bed for 10 days in that of the lower limb. Splints were not used. Skin sutures were removed at two weeks. Wound healing was appreciably faster and more satisfactory when the patient's general condition was good, or had been improved by blood transfusion and peritoneal dialysis (Pendras and Smith, 1966). Use of the shunt was avoided within seven days of insertion so far as was possible, but earlier dialysis did not compromise the life of the cannulae.

Aftercare

The daily dressing and toilet described by Quinton *et al.* (1962) was not used, and, unless there was leakage between dialysis, the dressings were left undisturbed until the time of the next treatment. All patients showed skin reactions to cleansing agents used at the time of treatment, and a simple mechanical toilet with swabs soaked in normal saline was found to be more satisfactory. Bacteriological swabs were taken before and after each dialysis from the cannula exit wounds and the exposed ends of the external Teflon break. Light dressings and bandages were used to allow free use of the limb, the proximal end of the loop being loosely covered to allow frequent inspection by the patient for clotting.

Results

The cumulative experience in 11 patients over 12.1 patient-years between 1 October 1964 and 30 September 1966 is shown in the Table. Patients under treatment for less than three months and those who were treated for short periods before renal transplantation were not included in the series. Cannulae functioning on 30 September 1966 were thought to have failed on that day in order to estimate mean cannula survival times. The mean arterial cannula life was 7.6 months and the venous 7.3 months.

Experience in **11** *Cases*

Case No.	Age	Sex	Cannula Failures		Treatment Duration	Clotting	Infection	Erosion
			Artery	Vein				
*1	25	M	0	1	23 months	4	1	0
*2	20	M	0	1	18 ,,	2	1	0
*3	34	M	1	2	18 ,,	10	3	0
*4	20	F	2	2	18 ,,	7	5	0
5	33	M	1	2	15 ,,	12	0	0
*6	26	F	1	1	14 ,,	0	3	3
*7	34	F	2	1	13 ,,	8	4	2
8	19	F	0	0	8 ,,	1	0	0
*9	39	F	0	0	6 ,,	0	0	0
*10	37	M	1	0	6 ,,	4	2	1
*11	27	M	0	0	6 ,,	0	1	0

* Shunts functioning on 30 September 1966.

The two main limiting factors were clotting and infection. Forty-eight episodes of clotting occurred in 8 of the 11 patients, leading to loss of cannulae on 10 occasions. One of these cannulae also showed evidence of infection. In the majority of patients episodes of clotting were due either to an external cause such as kinking or compression of the shunt or to exposure to cold, as in a man with leg cannulae who stood in a river for four hours while fishing. Episodes of spontaneous clotting occurred fairly often in a smaller group of patients, and appeared to be due either to hypovolaemia secondary to serum protein deficiency or to a phlebitis of obscure origin. Declotting was easily carried out with the methods described by Hegstrom *et al.* (1961) and by Pendras and Smith (1966) if the patient reported within three hours of the episode, particularly if there

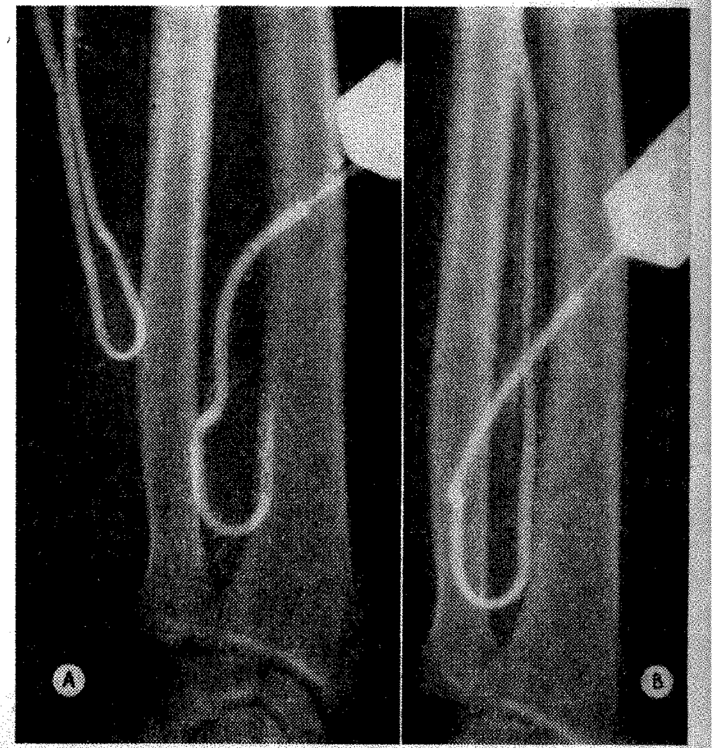


FIG. 3.—A, Arteriogram performed after routine declotting procedures. This cannula has been clotted for 24 hours. B, Further arteriogram after streptokinase infusion: the small clot at the vessel tip was easily dislodged by suction, and flow restored.

was an obvious mechanical cause. If flow was still unsatisfactory after attempted declotting, clots were occasionally dislodged or vessel spasm was overcome by the slow infusion of a solution of 20,000 international units of heparin in 500 ml. of saline. Angiograms were performed by the injection of 3 to 4 ml. of 60% Urografin via the open end of the cannula (Fig. 3) in resistant cases. An attempt was then made to dissolve visualized clot by the injection of 250,000 units of streptokinase (Kabikinase) in 2 ml. of sterile water into the cannula, which was clamped for 30 minutes. Flow was restored by this procedure on four of the seven occasions on which it was used. Where declotting was not successful, one limb or occasionally both limbs of the shunt were replaced. Anticoagulants were used systemically after recurrent episodes of clotting, and were particularly valuable where there was evidence of phlebitis.

Twenty episodes of infection occurred in 8 of the 11 patients, being secondary to skin erosion over the venous loop on seven occasions. Nine of these infections led to loss of cannulae. The causative organism was *Staphylococcus aureus*, except in two cases where a β-haemolytic streptococcus was isolated. Septicaemia secondary to cannula infection occurred in two patients, and was successfully treated by antibiotics without loss of the cannulae. Nasal, throat, and perineal swabs were taken before insertion of cannulae and at intervals thereafter. Attempts were made to eradicate nasal and skin carriage of staphylococcus, but persistent carriers were treated with lincomycin (Lincocin), cloxacillin (Orbenin), or methicillin (Celbenin) from the time of insertion of cannulae for periods of two to four weeks. If infection became established and persisted in spite of antibiotic therapy, the cannulae were removed and another limb was cannulated next day under antibiotic cover. In four patients with infected arterial cannula wounds persistent bleeding occurred, and was found to be due to false aneurysm formation. Bleeding was controlled by proximal ligation of the vessel and removal of the cannula. A more detailed analysis of these infections, with particular reference to phage typing and the source of the organisms, will be presented elsewhere.

Summary

Two years' experience with the Silastic-Teflon arteriovenous cannula system in the management of patients with chronic renal failure by intermittent haemodialysis is reported. The mean arterial cannula survival time was 7.6 months and the venous survival time 7.3 months. Careful attention to a number of apparently minor points during insertion improved cannula survival. The two limiting factors in cannula life were clotting and infection. Declotting was usually achieved if the patient attended within three hours. If flow was unsatisfactory after using standard declotting procedures angiography was performed and streptokinase infused into the cannula. Flow was restored in four out of seven cannulae by this method. The causative organism was *Staphylococcus aureus* in almost all the cases of infection. Antibiotics were used both prophylactically and therapeutically, but cannula removal and replacement in another limb was necessary in 9 out of 20 cases of infection.

We wish to thank Dr. J. S. Robson and Professor M. F. A. Woodruff for permission to report on cases under their care, and for their advice and encouragement; Dr. R. W. Tonkin for the bacteriological investigations; Dr. D. J. Sinclair and Dr. T. A. S. Buist for the angiographic studies; and Mr. A. Patterson for the photographs.

References

Clark, P. B., and Parsons, F. M. (1966). *Brit. med. J.*, **1**, 1200.
Hegstrom, R. M., Quinton, W. E., Dillard, D. H., Cole, J. J., and Scribner, B. H. (1961). *Trans. Amer. Soc. artif. intern. Organs*, **7**, 47.
Pendras, J. P., and Smith, M. P. (1966). Ibid., **12**, 222.
Quinton, W. E., Dillard, D. H., Cole, J. J., and Scribner, B. H. (1962). Ibid., **8**, 236.
Sevitt, L., Comty, C., Rottka, H., and Shaldon, S. (1964). *Proceedings of the European Dialysis and Transplant Association*, **1**, 271.

Prevention of Urinary Infection by Means of Closed Drainage into a Sterile Plastic Bag

W. A. GILLESPIE,* M.D., F.C.PATH., F.R.C.P.I., M.R.C.P.; G. G. LENNON,† M.B., CH.M., F.R.C.O.G., M.M.S.A.
K. B. LINTON,‡ PH.D., B.SC.; G. AUDREY PHIPPEN,§ S.R.N.

Brit. med. J., 1967, **3**, 90–92

If urinary infection is to be avoided when indwelling catheters are used, bacteria must be prevented from entering the bladder or destroyed soon after they enter. Infection through the catheter may be prevented by drainage into a closed sterile container. Passage of bacteria between catheter and urethral wall (an important route of infection in females) may be diminished by immobilizing the indwelling catheter. Application of these measures, together with disinfection of the urethra and bladder when catheters were inserted, reduced the postoperative urinary infection rate in gynaecological patients from 97 to 13% (Gillespie, Lennon, Linton, and Slade, 1962, 1964).

Drainage bottles containing formalin, which were used in these studies, were troublesome to prepare. We report here the results obtained with the use of closed sterile plastic bags instead of bottles.

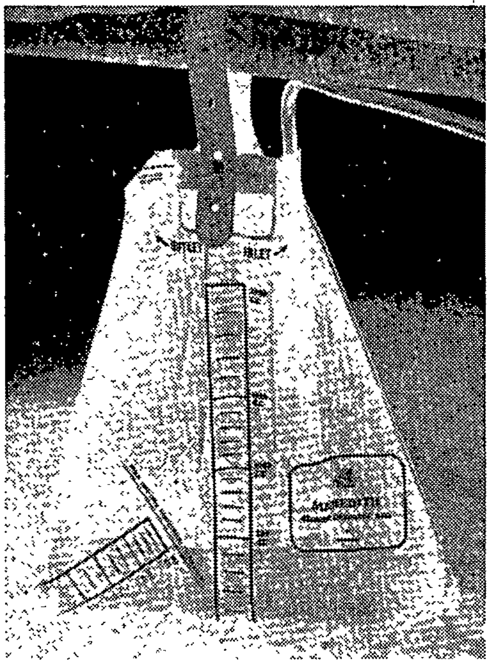
Materials and Methods

Meredith‖ urine drainage bags were used after 1 January 1965 (see Photograph). The drainage tube, which is sealed into the bag, ends in a valve, a flat collapsible plastic tube. Any increase of pressure in the bag closes the valve and prevents reflux of urine into the tube.

The patients, all of whom had uninfected urine initially, underwent gynaecological operations similar to those in the previous investigation and were treated in the same ward. Their bladders were drained by indwelling Foley catheters for four days after operation; during the next few days most patients were catheterized intermittently, between one and six times in all, to remove residual urine. Except for the substitution of plastic bags for bottles, the postoperative treatment was the same as before (Gillespie *et al.*, 1964); Foley catheters were immobilized by fitting plastic sponge collars which were smeared twice daily with chlorhexidine (Hibitane) obstetric cream. Chlorhexidine was also used to disinfect the urethra and bladder every time a catheter was inserted.

---

* Professor of Clinical Bacteriology, University of Bristol.
† Professor of Obstetrics and Gynaecology, University of Bristol.
‡ Lecturer in Medical Bacteriology, University of Bristol.
§ Ward Sister, United Bristol Hospitals.
‖ Supplied by Eschmann Bros. and Walsh Ltd., Shoreham-by-Sea, Sussex.



Meredith plastic drainage bag with non-return valve.

Results

The results of the present and previous trials are summarized in Table I. The first results with plastic bags were disappointing; more than half the patients became infected. The fault, however, was probably not in the valve or bag. Culture of urine samples taken simultaneously from the tube above the valve and from the bag showed that bacteria were rarely present in the bag before they appeared in the tube. It seemed likely that bacteria entered the catheter when the drainage tube was disconnected to change the bag when it became full. The point of disconnexion, where the tube joined the catheter, was under the bedclothes, near the patient, and therefore liable to heavy contamination. Moreover, plastic tubes lack elasticity and are difficult to connect and disconnect neatly. Accordingly, several precautions were taken to prevent entry of bacteria when changing bags. The plastic drainage tube was cut short a few inches above the bag and connected to the catheter by a sterile rubber tube. When the bag became full it was detached from the lower end of the rubber tube, a less heavily contaminated site and farther from the patient. The infection rate fell to 17% (Table I).

Though the modifications which caused this improvement probably would not be practicable in a busy ward, the results showed the danger of infection by bacteria entering when full bags were detached from the catheter. The next stage in the trial, therefore, was to use one bag for each patient, as a reservoir, and never change it. The drainage tube was connected to the catheter before the patient left the theatre. When the bag became full it was emptied through an opening distal to the valve, made by cutting off a corner opposite the point of entry of the drainage tube (see Photograph). The bag was tilted and the urine poured into a pail containing phenolic disinfectant. The corner of the bag was then sealed with waterproof tape until the next emptying. Seventy-four patients were treated by reservoir drainage; 17 (23%) became infected (Table I).

Study of the responsible bacteria suggested that most infections occurring during the period of full precautions were caused by self-infection, whereas previously, with open drainage and no special precautions, cross-infection was very common. During the initial period there were many mixed infections by *Klebsiella, Proteus vulgaris, Pr. rettgeri, Pr. mirabilis,* and *Escherichia coli* (Table I).

Many strains of *Klebsiella* and *Proteus* were resistant to several antibiotics and probably indicated cross-infection (Gillespie, Linton, Miller, and Slade, 1960). When the infection rate fell after the introduction of precautions, most of the resistant bacteria disappeared. Most of the infections that still occurred were caused by *E. coli* and *Pr. mirabilis,* which probably came from the patients themselves. Support for this belief was obtained by testing *Pr. mirabilis* isolates by Dienes's method (Dienes, 1946; Kippax, 1957). Of 12 isolates which were examined, 10 were distinct from each other. Hence most infections during the period of full precautions were probably due to a fault in the management of the catheter and not in the method of drainage. The recent preponderance of *Pr. mirabilis* may be due to the fact that it is less sensitive than *E. coli* to chlorhexidine (Table II).

Discussion

Several methods may be used to prevent infection during indwelling catheterization. All should incorporate some form

TABLE II.—*Minimum Inhibitory Concentrations of Chlorhexidine for the Strains of E. coli and Pr. mirabilis from Urine Infected During the Use of Plastic Reservoir Drainage Bags*

M.I.C. of Chlorhexidine	*E. coli*	*Pr. mirabilis*
1/2,000	0	2
1/4,000	0	4
1/8,000	0	4
1/16,000	0	2
1/32,000	0	0
1/64,000	0	1
1/128,000	0	0
1/256,000	0	0
1/512,000	3	0
Total	3	13

TABLE I.—*Incidence and Causative Bacteria of Postoperative Urinary Infection in Gynaecological Patients, in Relation to Method of Treatment*

Method of Drainage	Other Special Precautions	Infection Rate	Bacteria				
			E. coli	*Klebsiella*	*Proteus* spp.	*Str. faecalis*	Other
					Previous Series		
Open drainage	None	33*/34 (97%)	15	13	21	13	3
Closed drainage into bottles containing formalin	None	35*/47 (74%)	18	3	10	7	3
	Immobilized indwelling catheter. Urethra and bladder disinfected during subsequent intermittent catheterization	26/194 (13%)	6	0	14	6	0
					Present Series		
Plastic bag with non-return valve: Used once	Immobilized indwelling catheter. Urethra and bladder disinfected during subsequent intermittent catheterization	8/15 (53%)	2	0	2	4	0
Used once with extra precautions		5/30 (17%)	2	0	1	2	0
Used as reservoir		17/74 (23%)	3	0	13	1	0

* Some infections were mixed.

of closed sterile drainage. Disposable sterile plastic bags are convenient, but many that have appeared on the market are unsatisfactory, since though they are sterile initially they become contaminated during use (Roberts, Linton, Pollard, Mitchell, and Gillespie, 1965). The bag should remain closed during use and should be designed to prevent reflux of urine into the drainage tube. This is important, since small numbers of bacteria may pass from the urethra to the bladder and thence to the bag, where they may multiply and, if reflux is allowed, re-enter the bladder in large numbers. The longer the period of drainage the greater the chance of infection arising in this way. It would be dangerous to place a disinfectant in a non-rigid receptacle, since compression might force it back into the bladder. Kunin and McCormack (1966) described the use of a reservoir drainage bag without a valve. However, it is difficult to compare their results with ours, because few of their patients were gynaecological. Moreover, most of their patients received antimicrobial drugs, whereas none of ours did. Several drainage bags with valves have appeared on the market. We have found the valve of the Meredith bag to be the most efficient of those we have seen. In laboratory tests in which the bag was filled with contaminated urine it was impossible to force bacteria back through the valve by compressing the bag. However, when a partly filled bag was laid gently on the floor, and not compressed, a slow reverse flow could sometimes be detected. In practice, such slow leakage would be opposed by the flow of urine, which also would oppose the movement of motile bacteria.

Perhaps the greatest risk of infection during closed drainage is by bacteria that gain access to the catheter when the receptacle is detached because it is full. It follows that if reflux can be avoided it should be safer (and more economical) to use the bag as a reservoir and empty it periodically without detaching it from the drainage tube and catheter. The infections that occurred in our patients during drainage into reservoir bags were attributable, for the most part, to invasion of the bladder by bacteria, especially *Pr. mirabilis,* which passed along the outside of the catheter, probably because they were rather insensitive to the chlorhexidine that was used to exclude bacteria from this route.

Patients and nurses preferred the plastic bags to the glass drainage bottles, which ambulant patients found cumbersome. It remains to be seen how efficient the bags will be during longer periods of drainage and after prostatectomy, when it is sometimes necessary to irrigate the bladder.

Summary

Sterile disposable plastic bags with non-return valves were used for closed drainage of urine after gynaecological operations. It was found best to use the bag as a reservoir, joining it to the catheter before the patient left the theatre and not detaching it until the indwelling catheter was removed four days later. The bag was emptied periodically through an opening distal to the valve. Of 74 patients who were treated in this way, 17 (23%) became infected. This was a slightly greater rate of infection than that observed during a previous period when bottles containing formaldehyde were used as receptacles. The infections probably were not attributable to faults in the drainage bag or valve, but to bacteria which passed from the urethra into the bladder outside the catheter, despite the precautions taken to exclude them.

We thank Eschmann Bros. and Walsh Ltd. for a supply of Meredith drainage bags.

REFERENCES

Dienes, L. (1946). *Proc. Soc. exp. Biol. (N.Y.)*, **63**, 265.

Gillespie, W. A., Lennon, G. G., Linton, K. B., and Slade, N. (1962). *Brit. med. J.*, **2**, 13.

—— —— —— —— (1964). Ibid., **2**, 423.

—— Linton, K. B., Miller, A., and Slade, N. (1960). *J. clin. Path.*, **13**, 187.

Kippax, P. W. (1957). Ibid., **10**, 211.

Kunin, C. M., and McCormack, R. C. (1966). *New Engl. J. Med.*, **274**, 1155.

Roberts, J. B. M., Linton, K. B., Pollard, B. R., Mitchell, J. P., and Gillespie, W. A. (1965). *Brit. J. Urol.*, **37**, 63.

Medical Memoranda

Methaqualone Addiction and Delirium Tremens

Brit. med. J., 1967, **3**, 92–93

Four cases of addiction to the non-barbiturate hypnotic methaqualone have been reported (Madden, 1966). The probability that these patients were physically dependent on methaqualone has been disputed (Martin, 1966) because of failure to show an abstinence syndrome. We now document another case, which was associated on withdrawal with the clinical syndrome of delirium tremens characteristic of the barbiturate–alcohol type of dependence.

CASE REPORT

A 47-year-old married man had suffered from rheumatoid arthritis since 1947. In turn he took increasing quantities of barbiturates (developing macrocytic anaemia), of an analgesic mixture containing phenacetin (developing nephrocalcinosis and renal tubular acidosis), of thalidomide (developing peripheral neuropathy), and later chloral hydrate.

For four years before admission he had been taking increasing doses of methaqualone, and for at least some months before admission had taken neither alcohol nor any other drug. In the weeks prior to being admitted (January 1966) he was taking 60 150-mg. tablets of methaqualone daily.

He was found unconscious one evening (two days before admission) and his stocks of methaqualone were destroyed. Next evening he was restless and confused, and complained of seeing strangers in dark corners of the room.

On admission he was in delirium with obvious tremor. He was anxious and restless, and had visual hallucinations of which he was afraid. His temperature was 100° F. (37.8° C.), with brisk reflexes, and blood pressure 130/70. The liver was palpable 2 cm. below the costal margin. A combination of promazine 600 mg. daily, phenobarbitone 1 g. daily, and paraldehyde 10 ml. intramuscularly as required for states of agitation was only partially successful in controlling his restlessness and led to intoxication (with slurred speech, ataxia, and nystagmus). However, the administration of thioridazine (Melleril) in doses up to 800 mg. daily, starting on the fourth day, resulted in dramatic improvement and rapid recovery.

DISCUSSION

Delirium tremens has not only been produced experimentally by withdrawal of addicting doses of barbiturates (Isbell *et al.*, 1950) and alcohol (Isbell *et al.*, 1955), but has now been recorded also with chloral hydrate, paraldehyde, glutethimide

(Doriden), methyprylone (Noludar), ethchlorvynol (Arvynol), and meprobamate (Miltown, Equanil) (*Brit. med. J.*, 1964; Wood and Flippin, 1965). The clinical features described in these studies correspond very closely with those found in our patient.

Methaqualone has been shown to be a potent hypnotic (Parsons and Thomson, 1961; Duchastel, 1962). It is marketed in the United Kingdom as Melsedin, and in combination with diphenhydramine as Mandrax. It is sold in the U.S.A. as Quaalude. Melsedin was described as a non-barbiturate hypnotic that "produces natural sleep" and to which neither tolerance nor addiction had been attributed. The makers have told us that they now know of four cases of addiction, in addition to the one reported here, three of the patients concerned having a history of addiction also to barbiturates or alcohol (J. W. Buckler, personal communication, 1966).

Mandrax is claimed to have an action that is "quite different from that of the barbiturates and almost all other hypnotics." No addiction had been reported to the makers, who pointed out (February 1966) that their product had been generally available for only four months (A. L. Macnair, personal communication, 1966).

Though recent neurophysiological methods of investigation of the action of drugs on sleep (Oswald and Thacore, 1963; Oswald and Priest, 1965) may eventually clarify the relevance of withdrawal syndromes, at present the clinical picture of delirium tremens is one means of categorizing the pharmacological action of psychotropic drugs. Apart from the remarkable experiments of Isbell and his colleagues it seems that at present we must rely on those patients who abuse their drugs to assist us in this classification.

We are grateful to Professor J. A. Strong for permission to report this case, and to the manufacturers for the information mentioned above.

ROBIN B. LOCKHART EWART, M.B., CH.B., B.SC.,
Department of Medicine, Western General Hospital, Edinburgh 4.

ROBIN G. PRIEST, M.B., B.S., M.R.C.P.ED., D.P.M.,
Department of Psychiatry, University of Edinburgh.

REFERENCES

Brit. med. J., 1964, 2, 1412.
Duchastel, Y. (1962). *Canad. med. Ass. J.*, 86, 586.
Isbell, H., Altschul, S., Kornetsky, C. H., Eisenman, A. J., Flanary, H. G., and Fraser, H. F. (1950). *Arch. Neurol. Psychiat. (Chic.)*, 64, 1.
—— Fraser, H. F., Wikler, A., Belleville, R. E., and Eisenman, A. J. (1955). *Quart. J. Stud. Alcohol*, 16, 1.
Madden, J. S. (1966). *Brit. med. J.*, 1, 676.
Martin, G. J. (1966). Ibid., 2, 114.
Oswald, I., and Priest, R. G. (1965). Ibid., 2, 1093.
—— and Thacore, V. R. (1963). Ibid., 2, 427.
Parsons, T. W., and Thomson, T. J. (1961). Ibid., 1, 171.
Wood, H. P., and Flippin, H. F. (1965). *Amer. J. Psychiat.*, 121, 1127.

Thrombocytopenic Purpura in Patient with Autoimmune Haemolytic Anaemia, Successfully Treated with Mercaptopurine

Brit. med. J., 1967, 3, 93–94

Before the introduction of corticosteroids in 1949 splenectomy and blood transfusions were the only well-established treatments for autoimmune haemolytic anaemia (Dacie, 1954; Schwartz and Dameshek, 1962). Corticosteroids rapidly became the treatment of choice, splenectomy being reserved for refractory cases. Dameshek and Schwartz (1960) reported the use of purine antagonists in the management of autoimmune haemolytic anaemia, and this has now been accepted as an additional treatment. It has been suggested that primary thrombocytopenic purpura and acquired haemolytic anaemia might have a common aetiology (Evans *et al.*, 1951), since thrombocytopenia may be a feature of autoimmune haemolytic anaemia, and in a proportion of cases platelet antibodies can be demonstrated.

In the following case a relapse of thrombocytopenic purpura occurred in a patient with autoimmune haemolytic anaemia who had previously been treated by corticosteroids and splenectomy. High doses of corticotrophin temporarily controlled the thrombocytopenia, which later was successfully treated with mercaptopurine.

CASE REPORT

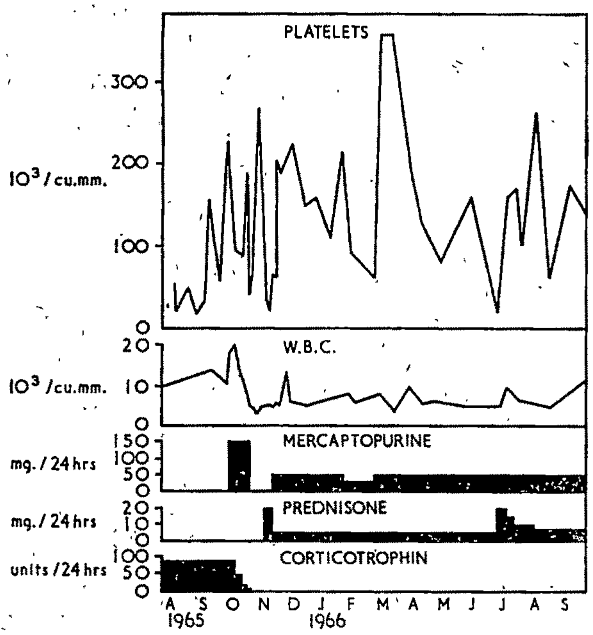
A 17-year-old youth was admitted to hospital in January 1962 with a three-months history of increasing weakness and lassitude. Immediately before admission he developed high fever, became jaundiced, and started passing dark urine. There was no relevant past or family history, and no history of blood transfusion or exposure to drugs or poisons.

Physical examination showed a febrile, pale, jaundiced youth with slight hepatosplenomegaly. Investigations showed haemoglobin 3.5 g./100 ml.; reticulocytes 31%; W.B.C. 22,800/cu. mm., normal differential; platelets 48,000/cu. mm.; serum bilirubin 5.2 mg./100 ml. (1.5 mg. direct). A direct Coombs test was positive. Autoimmune haemolytic anaemia was diagnosed and treatment with prednisone was started, and within four weeks the peripheral blood picture had returned to normal. On a maintenance dose of prednisone 10 mg./day he remained well, with a normal haemoglobin and platelet count, until early in 1964, when he developed a diffuse petechial rash. Platelets numbered 24,000/cu. mm., and after increased doses of prednisone (20 mg./day) had failed to control the thrombocytopenia splenectomy was performed in March 1964. The platelet count did not rise greatly after operation, and prednisone 10 mg./day was restarted with considerable improvement. On this dose of prednisone for the next year the platelet count remained between 100,000 and 200,000/cu. mm.

In July 1965 he was readmitted to hospital with a recurrence of purpura and a platelet count of 20,000/cu. mm. A corticotrophin infusion produced a satisfactory rise in platelet count to 200,000/cu. mm., and this was maintained as long as the dosage of corticotrophin was not dropped below 80 i.u./day. During a two-months course of corticotrophin administration the patient gained 35 lb. (15.9 kg.) and developed many features of Cushing's syndrome.

In October he was admitted to hospital for a trial of mercaptopurine. On examination he presented the appearance of Cushing's syndrome, with moonface, buffalo hump, high colour, and abdominal striae. Blood pressure was 160/120. The initial peripheral blood picture was: Hb 14.9 g./100 ml.; W.B.C. 11,800/cu. mm., normal differential; platelet count 230,000/cu. mm.; E.S.R. 3 mm. in first hour; blood was also examined for lupus erythematosus cells with negative results. A direct Coombs test was positive in a dilution of 1/16, but serological study failed to reveal platelet or leucocyte agglutinins or incomplete platelet antibodies, and the red cell antibody showed no specificity. Apart from a serum potassium of 2.7 mEq/l. on admission, later corrected by oral potassium supplements, other electrolytes were all normal. The urine contained a trace of sugar. Blood-volume studies showed a normal red cell mass and plasma volume, and $T\frac{1}{2}$ ^{51}Cr red cell survival was 27.5 days.

At the time of admission on 4 October he was receiving corticotrophin 40 i.u. b.d. On the following day treatment with mercaptopurine 150 mg. o.d. was started, and during the next three weeks the corticotrophin was gradually reduced, finally being stopped on 24 October. Meanwhile the patient noticed transient symptoms of dizziness and lassitude. At the same time the urine became free of sugar, the blood pressure settled to normal, and he lost 14 lb. (6.4 kg.) in weight. During a 23-days course of treatment with mercaptopurine the platelet count ranged between 40,000 and 180,000/cu. mm., and the white cell count fell steadily from 21,000 soon after admission to 3,200 (see Chart).



Effect of treatment on platelet and white cell count.

The patient was discharged without purpura on 8 November, with a platelet count of 270,000/cu. mm. He was not receiving treatment. Five days later, having developed diffuse purpura, he was readmitted to hospital with a platelet count of 33,000/cu. mm. Prednisone 20 mg./day was started immediately, but when, on 19 November, a platelet count was only 62,000/cu. mm. mercaptopurine was reintroduced at a dosage of 50 mg./day and the prednisone cut to 5 mg./day. Three days later a platelet count was 204,000/cu. mm., and during the next two and a half months on this drug regimen it remained between 100,000 and 200,000/cu. mm.

On 1 February 1966 the dosage of mercaptopurine was halved to 25 mg./day, and this was followed on 1 March by a recurrence of purpura (platelets 58,000/cu. mm.). Mercaptopurine was increased to 50 mg./day, and a week later there was no new purpura and the platelets were 360,000/cu. mm. On this regimen of treatment the patient remained well until 3 July, when he developed purpura. When seen at the hospital two days later a platelet count was 18,000/cu. mm., W.B.C. 5,600/cu. mm., and Hb 16 g./100 ml. No cause for the relapse of purpura was established, and the dosage of prednisone was increased to 20 mg./day. Eight days later there was no sign of purpura, a platelet count was 186,000/cu. mm. and W.B.C. 10,800/cu. mm. Since then the dosage of prednisone has been gradually reduced, and at the time of writing the patient was very well, had no leucopenia, and was able to work as a clerk. On several occasions during the last few months when the prednisone was omitted for a few days he has complained of feeling unwell, but this always cleared as soon as the prednisone was restarted.

DISCUSSION

The occurrence of autoimmune haemolytic anaemia and thrombocytopenia has been recognized for many years (Evans and Duane, 1949). The frequency of their association is not known, but in a series of 83 cases of autoimmune haemolytic anaemia (warm antibody) reported by Dausset and Colombani (1959) 13.2% had a concurrent thrombocytopenia.

In addition to corticosteroids antimetabolite drugs have recently been reputed to be beneficial in the treatment of haemolytic anaemia and thrombocytopenia. Richmond *et al.* (1963) reported a case in which a fulminating haemolytic anaemia and thrombocytopenia developed some time after splenectomy for idiopathic thrombocytopenia. Large doses of corticosteroids were ineffective and thymic irradiation produced only transitory improvement. The thrombocytopenia and anaemia were finally controlled by Imuran (azathioprine) and actinomycin C. Matthews (1965) reported the successful use of Imuran in the treatment of a patient with idiopathic autoimmune haemolytic anaemia and idiopathic thrombocytopenia associated with diffuse hypergammaglobulinaemia, amyloidosis, hypoalbuminaemia, and plasmacytosis. Bouroncle and Doan (1966) reported seven cases of refractory idiopathic thrombocytopenic purpura treated with Imuran. In four of their cases several months' treatment with prednisone and Imuran led to a remission of thrombocytopenia, which was sustained when the drugs were stopped. In two of their cases a definite improvement in platelet count accompanied continuous treatment with the same drugs.

In this case thrombocytopenia developed two years after the appearance of an autoimmune haemolytic anaemia, which was then in remission. Prednisone successfully controlled the thrombocytopenia after splenectomy had failed. A further two years later thrombocytopenia relapsed. Large doses of corticotrophin produced a temporary remission, but in view of the rapid development of signs of corticosteroid overdosage alternative treatment was essential. A trial of mercaptopurine proved successful, and the patient remained well on a maintenance dosage of mercaptopurine and prednisone. This case supports the finding of Bouroncle and Doan (1966) that corticosteroids seem to have an additive effect with antimetabolites in obtaining remission of thrombocytopenia.

My thanks are due to Professor T. A. J. Prankerd and Dr. R. N. Tattersall for permission to publish this case; and to Dr. A. J. Bowdler, who performed the plasma volume and red cell survival studies.

M. H. N. TATTERSALL, M.A., M.B., B.CHIR.

REFERENCES

Bouroncle, B. A., and Doan, C. A. (1966). *New Engl. J. Med.*, 275, 630.
Dacie, J. V. (1954). *The Haemolytic Anaemias.* London.
Dameshek, W., and Schwartz, R. (1960). *Trans. Ass. Amer. Phycns*, 73, 113.
Dausset, J., and Colombani, J. (1959). *Blood*, 14, 1280.
Evans, R. S., and Duane, R. T. (1949). Ibid., 4, 1196.
—— Takahashi, K., Duane, R. T., Payne, R., and Liu, C.-K. (1951). *Arch. intern. Med.*, 87, 48.
Matthews, R. J. (1965). *Amer. J. Med.*, 39, 972.
Richmond, J., Woodruff, M. F. A., Cumming, R. A., and Donald, K. W. (1963). *Lancet*, 2, 125.
Schwartz, R., and Dameshek, W. (1962). *Blood*, 19, 483.

Current Practice

TODAY'S DRUGS

With the help of expert contributors we publish below notes on a selection of drugs in current use.

Radioiodine Therapy of Thyrotoxicosis

Isotopes of iodine are used principally in the investigation of thyroid function, and the chief therapeutic application of radioiodine (^{131}I) is in the treatment of thyrotoxicosis.

Radiobiological Effects

The body does not distinguish the radioisotopes of iodine from stable iodine (^{127}I), and consequently radioiodine enters the circulating iodide pool. This pool normally consists of stable iodide derived from the diet and from the breakdown of the thyroid hormones. Radioiodine is taken up from the iodide pool by the thyroid and is incorporated into the structure of the thyroid hormones. These are released into the circulation and are transported to the tissues. After the breakdown of the hormones the radioiodine, like the stable iodine, may be taken up by the thyroid again and recycled.

The radiation dose from an isotope depends partly on the physical half-life; for ^{131}I this is eight days. Within the body, however, biological factors are also important. The proportion of the dose taken up by the thyroid, the rate of elimination of the radioiodine from the body, and the mass of the thyroid all influence the dose of radiation absorbed from a given quantity of radioiodine. These variables can be estimated and together they determine the effective biological half-life of the radioiodine.

The effects of radioiodine are immediate death of a proportion of the thyroid cells and impairment of secretion and, subsequently, failure of the surviving cells to divide. Furthermore, the ability of the cell to divide is related to the dose of radioiodine. These effects have been shown in laboratory animals[1 2] and can be deduced from observations in man.[3 4]

Dosage

Radioiodine is usually dispensed in a carrier solution of sodium iodide and is tasteless. The dose is taken by mouth.

There is no uniform method for calculating the ^{131}I dose. Most centres aim to give a fixed radiation dose to the thyroid and this is estimated from the 24- or 48-hour uptake of a tracer dose of ^{131}I and the mass of the thyroid. The latter is usually assessed by palpation but is often inaccurate. The mean estimate of a group of observers will be more accurate than a single observation, and experience in estimating preoperative thyroid weights will help to improve an individual doctor's estimates.[5] Alternatively it is possible to calculate the mass of the thyroid from a thyroid scintiscan.[6] Some therapists still prescribe arbitrary doses based on their clinical assessment of the patient without reference to the thyroid size.

Clinical Effect

The response to radioiodine is not immediate. At least six weeks elapse before any definite improvement is observed, and clinical progress thereafter is variable. The experience of most centres is that about 20 to 30% of patients are still thyrotoxic at the end of a year.[7]

If the patient becomes euthyroid there is the problem of post-^{131}I hypothyroidism occurring later. At first it was thought that hypothyroidism would appear in the first 12 months and that the chance of hypothyroidism developing after then was remote. Long-term follow-up studies of patients treated with radioiodine, however, have revealed an unexpected picture. The incidence of hypothyroidism rises steadily and in 10 years reaches 40 to 50% of all patients treated.[4 8-11] Furthermore, even after this interval there is no evidence of a plateau in the incidence of hypothyroidism.

The presentation of hypothyroidism is frequently insidious and patients who fail to attend a clinic for follow-up are more likely to be hypothyroid; in fact, they probably default owing to the inertia so characteristic of their defective thyroid function. Thus, an incomplete follow-up of patients may grossly underestimate the true incidence of hypothyroidism.

The delay in the control of thyrotoxicosis and the rising incidence of hypothyroidism after radioiodine have led to a reappraisal of the methods of treatment. Many suggestions for improvements in current techniques have been made. Some have little factual evidence to support them. It has been stated that an uneven distribution of ^{131}I in the thyroid is partly responsible for the subsequent hypothyroidism,[12] and prior antithyroid medication has been claimed to produce a more uniform distribution. In a few centres fractionation of the dose is favoured; repeated small doses are given over a few weeks. More recently transient suppression of function in one lobe by external irradiation before radioiodine therapy has been proposed.[13] It is argued that the irradiated lobe will thus survive the ^{131}I-irradiation because uptake of the isotope will be temporarily suppressed. This technique poses additional problems of dosage, and the same criticism can be made of more involved methods of calculating the ^{131}I dose.[14]

Many authorities advocate repeated doses of radioiodine with rapid control of the thyrotoxicosis and acceptance of a high incidence of hypothyroidism. Where regular follow-up is not practicable large doses of radioiodine have been proposed followed by the immediate institution of full replacement doses of thyroxine, thus anticipating the almost inevitable hypothyroidism. With this approach one loses all opportunity of studying the problem further, but in some areas social and economic factors prevail and make this the best compromise. If the patients are not to suffer steps must be taken to ensure that the thyroxine will be taken regularly. There is no published evidence of the reliability of patients in this clinical situation, but experience in other circumstances is not reassuring.

More recently clinical evidence has been published showing that lower ^{131}I doses produce less hypothyroidism.[5] Experimental evidence already existed showing that the radiation dose to the thyroid was the major factor in determining the number of thyroid cells which survived.[1 3] A clinical trial of different doses of radioiodine with over 500 patients has shown a markedly lower incidence of hypothyroidism in a five-year period when smaller doses of ^{131}I were used.[5] Three years after treatment the proportion of euthyroid patients was the same as in the group treated with the higher dose. This study employed a single dose of radioiodine, and persisting thyrotoxic symptoms were promptly controlled with antithyroid drugs. This medication was eventually discontinued when the patient had been maintained on a low dose for some time and further treatment appeared unnecessary. The use of antithyroid drugs after lower doses of radioiodine offers a satisfactory programme of treatment for thyrotoxicosis. The delay in the control of symptoms is overcome and the use of lower doses of radioiodine greatly reduces the incidence of hypothyroidism.

Selection of Patients

Radioiodine therapy has usually been restricted to patients over 40 years of age. This decision arose from uncertainty about the side-effects of ^{131}I therapy, and particularly the effects upon the gonads. Apart from this restriction ^{131}I therapy is suitable for all patients. The advantages of radioiodine therapy are the ease of administration, which can be arranged on an outpatient basis, and the rarity of recurrence of thyrotoxicosis. Compared with thyroid surgery there is no risk to the recurrent laryngeal nerves, tetany never supervenes, and the general hazards of majory surgery are avoided. This aspect is especially important in older patients. Careful follow-up of patients after thyroid surgery reveals an incidence of hypothyroidism varying from 5% to 25%, and there is a definite risk of recurrence. Antithyroid medication alone will control the patient's symptoms, but the relapse after a prolonged course of tablets is 60–80% in patients over 40 years of age.

Side-effects

Theoretically radiation from ^{131}I might induce leukaemia or thyroid cancer, but the available evidence does not support either possibility in adults. The incidence of leukaemia is the same in those patients who have had radioiodine therapy as in a population of the same age and sex distribution.[15, 16] Likewise, neoplasms do not appear to be induced in adults, although in children ^{131}I therapy has resulted in thyroid cancers.[17] When antithyroid drugs are used after radioiodine therapy the dosage should be reduced to control the symptoms without producing hypothyroidism. There is experimental evidence in rats that high doses of antithyroid drugs after ^{131}I therapy can produce neoplastic changes in the thyroid.[18] Presumably the excessive stimulation by thyroid-stimulating hormone, which occurs in hypothyroidism, is partially responsible for these changes in the irradiated thyroid cells. Thyrotoxic crises after radioiodine have been described but are rare. Early transient hypothyroidism is an uncommon feature—in contrast to the late-onset hypothyroidism which is permanent. It has been suggested that an autoimmune reaction in the thyroid might be initiated by the irradiation. Although there is a slight rise in the antibody titres it is not sustained and there is no evidence that this mechanism is related to the post-^{131}I hypothyroidism.[19] Effects on other iodide-concentrating tissues have not been described, but the relatively low uptakes are unlikely to result in any significant radiation.

Conclusion

Radioiodine therapy offers a convenient and effective form of treatment for thyrotoxicosis. Experience has shown the two main disadvantages to be delay in the control of thyrotoxicosis and a rising incidence of hypothyroidism. Other side-effects are very rare. Experimental studies have led to a better understanding of the effects of radioiodine on the thyroid cell. These observations, coupled with long-term reviews of patients treated with radioiodine, have offered both an explanation and a possible solution to the problem of hypothyroidism after ^{131}I therapy. Lower doses of radioiodine will reduce the incidence of hypothyroidism. At the same time the proportion of euthyroid patients after a few years is not diminished and recurrence of thyrotoxicosis has not proved to be a problem. Lower doses of radioiodine delay control of hyperthyroidism, but the use of antithyroid drugs to suppress symptoms until the radioiodine has been effective is a rational approach and one which avoids repeated doses of radioiodine. Further clinical trials will reveal the optimum dose of radioiodine, which may well be lower than those already studied.

REFERENCES

[1] Al-Hindawi, A. Y., and Wilson, G. M., *Clin. Sci.*, 1965, **28**, 555.
[2] Philp, J. R., *Postgrad. med. J.*, 1966, **42**, 437.
[3] Greig, W. R., *Scot. med. J.*, 1966, **11**, 307.
[4] Green, M., and Wilson, G. M., *Brit. med. J.*, 1964, **1**, 1005.
[5] Smith, R. N., and Wilson, G. M., ibid., 1967, **1**, 129.
[6] Myhill, J., Reeve, T. S., and Figgis, P. M., *Amer. J. Roentgenol.*, 1965, **94**, 828.
[7] Crooks, J., *Current Topics in Thyroid Research*, ed. C. Cassano and M. Andreoli, 1966, p. 1208. London.
[8] Beling, U., and Einhorn, J., *Acta radiol. (Stockh.)*, 1961, **56**, 275.
[9] Dunn, J. T., and Chapman, E. M., *New Engl. J. Med.*, 1964, **271**, 1037.
[10] McGirr, E. M., Thomson, J. A., and Murray, I. P. C., *Scot. med. J.*, 1964, **9**, 505.
[11] Nofal, M. N., Beierwaltes, W. H., and Patno, M. E., *J. Amer. med. Ass.*, 1966, **197**, 605.
[12] Fraser, R., Abbatt, J. D., and Stewart, F. S., *Brit. J. Radiol.*, 1954, **27**, 23.
[13] Trotter, W. R., *Current Topics in Thyroid Research*, ed. C. Cassano and M. Andreoli, 1966, p. 1159. London.
[14] Myhill, J. A., Hales, I. B., and Reeve, T. S., ibid., 1966, p. 1143.
[15] Pochin, E. E., *Brit. med. J.*, 1960, **2**, 1545.
[16] —— *Proc. roy. Soc. Med.*, 1964, **57**, 564.
[17] Kogut, M. D., *et al.*, *New Engl. J. Med.*, 1965, **272**, 217.
[18] Doniach, I., *Brit. med. Bull.*, 1958, **14**, 181.
[19] Einhorn, J., Fagraeus, A., and Jonsson, J., in *Current Topics in Thyroid Research*, ed. C. Cassano, and M. Andreoli, 1966, p. 1137. London.

ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Familial Tendency in Cancer

Q.—*What is the evidence, if any, that a tendency to cancer is familial?*

A.—Cancer is not a single disease but a group of many different diseases with some features in common.

There is a strong familial tendency in the susceptibility to a few, mainly rare, types of cancer—e.g., cancer of the colon and rectum associated with familial polyposis, cancer of the central and peripheral nervous system associated with von Recklinghausen's neurofibromatosis multiplex, and a number of other rare hereditary syndromes, and cancer of the skin associated with xeroderma pigmentosum. In the case of most of the commoner types of human cancer, however, a familial tendency, if it exists at all, is very weak. In this connexion particular attention has been directed towards cancer of the breast.[1]

It is perhaps interesting to consider the question also from a theoretical point of view. Studies on laboratory animals strongly suggest that genetic factors affect both the spontaneous incidence of cancers of particular types and the ease with which they can be deliberately induced by exposure to carcinogenic agents. Multiple genes tend to be involved in the case of each type of cancer. Such differences in susceptibility may be greatly magnified by intensive inbreeding (e.g., brother–sister mating for several generations).

Different races of man differ considerably in mortality from specific types of cancer, but many of these differences appear to be determined by environmental rather than genetic factors. Between individuals of any one race, provided that there is no inbreeding, genetically determined differences are unlikely to be obvious because of the multiplicity of genes involved and the kaleidoscopic-like heterogeneity of individuals.

Studies on experimental animals also tell us that it is possible to confuse the effects of vertically transmitted cancer viruses (i.e., cancer viruses passed from parent to offspring) with those genes. At present there is no known example either of a human cancer virus or of the vertical-transmission of such.

For the most part, therefore, cancer patients and their families may be told unequivocally that there is no reason to fear that a heightened susceptibility to cancer of the same or other type has been, or will be, transmitted to the next generation. Only in relation to certain rare types of the disease is this liable to happen.

REFERENCE

[1] *Lancet*, 1967, **1**, 935.

Virus Infections and Foetal Malformations

Q.—*Can virus infections, other than rubella, in the first trimester of pregnancy cause foetal malformations, in particular spina bifida? If no relationship exists what is the likelihood that a second child may have a spina bifida or a similar congenital deformity?*

A.—There is no good evidence that any virus infection, including rubella, can cause spina bifida. The recurrence risk of a neural tube malformation in children born after one child with spina bifida is of the order of 4%,[1] though the risk may be a bit higher in the areas where incidence of neural tube malformations is high.

REFERENCE

[1] Carter, C. O., and Roberts, J. A. F., *Lancet*, 1967, **1**, 306.

Pre-oxygenation

Q.—*I believe there is a method of dental anaesthesia in which oxygen is administered initially followed by N_2O alone. Is this satisfactory and can it be used with a Boyle machine?*

A.—The technique of "pre-oxygenation" to which the questioner refers is that described by Mostert[1] as a development of the original work of Neff, Mayer, and Thompson.[2]

Provided that alveolar distribution is not grossly uneven, the inhalation of pure oxygen for two minutes results in the "washing-out" of 98% of the nitrogen in the lungs and a rise in the oxygen gradient across the pulmonary epithelium from about 60 mm. Hg to some 600 mm. Hg. In the average adult some 1,800 ml. of oxygen can then be eliminated or absorbed from the lungs before the oxygen tension in the alveoli falls to the normal level of 100 mm. Hg.

In practice the inhalation of pure oxygen for two minutes is followed by the substitution of pure nitrous oxide for one minute, and this is generally adequate for the production of anaesthesia in the healthy without apparent impairment of the patient's oxygenation. After this oxygen is added to the inspired gas to form at least 20% of the mixture, together with any supplementary agent thought desirable if the surgical procedure is expected to last more than two to three minutes. Subject to this limitation of time available for surgery, the technique is said to be satisfactory for dental and casualty work once proficiency in its use has been acquired.

The technique does not require a flow greater than 10 litres per minute of either of the gases. A Boyle's machine can therefore be used. It should be noted, however, that the two narrow-bore tubes often used to connect an intermittent-flow machine to a nasal mask for dental work are not suitable for use with Boyle's machine. In these circumstances such tubes may impose a high resistance to free inhalation from a reservoir bag, in which the gas pressure is normally only slightly above atmospheric.

REFERENCES

[1] Mostert, J. W., *Brit. med. J.*, 1958, **1**, 502.
[2] Neff, W., Mayer, E. C., and Thompson, R., ibid., 1950, **1**, 1400.

Gaucher's Disease and Pregnancy

Q.—*Does pregnancy occur in women with Gaucher's disease, and how does it affect the condition? What is the risk of the child being affected?*

A.—Gaucher's disease is a metabolic disorder in which the cerebroside kerasin is deposited in the reticuloendothelial system. It occurs as an acute or infantile type and as a chronic or adult type. It affects both sexes and is said to be slightly more common in females.

Women with Gaucher's disease are normally fertile,[1] and when pregnant a normal prenatal course is to be expected. There is no higher incidence of abortion than in the normal population and no undue haemorrhagic complications occur. Gaucher's disease is not an indication for therapeutic abortion, since there is no evidence that pregnancy has a deleterious effect on its course. There is one report of a patient[2] with the disease in whom delivery by caesarean section was required on three occasions because of disproportion due to the involvement of the pelvic bones with Gaucher's infiltration.

The disease may be inherited in three distinct ways.[3 4] In a few families the adult form is transmitted as an autosomal dominant. It would be expected that 50% of the children would therefore be affected. Secondly, and by far the most common, is the inheritance of the adult form as an autosomal recessive. It would be expected that 25% of the children would be affected, but from family studies the incidence would seem to be less than this. Finally, there is a small group in which neurological involvement is associated with an acute illness and poor prognosis. Again this is thought to be inherited as an autosomal recessive.

REFERENCES

[1] Greenwald, J. C., and Fenton, A. N., *Obstet. and Gynec.*, 1959, **14**, 79.
[2] Watov, S. E., and De Sandre, R., ibid., 1964, **23**, 247.
[3] Hsia, D. Y. Y., Naylor, J., and Bigler, J. A., in *Cerebral Sphingolipidoses*, edited by S. M. Aronson and B. W. Volk, 1962. New York.
[4] —— *Inborn Errors of Metabolism*, Part I, 2nd edition, 1966. Chicago.

Inverted Vision

Q.—*What might be the cause in an apparently normal girl aged 8 of fleeting attacks of inverted vision?*

A.—The most likely explanation for this most unusual symptom is the aura of migraine, in which, in addition to objects appearing too large (macropsia) or too small (micropsia), there are many other types of distorted vision—for example, objects appearing more distant (teleopsia).

It would be interesting to know whether the attacks are followed by headache or whether there is migraine in the family. Disturbances of this sort are also seen as an aura of temporal lobe epilepsy, and for this reason the results of electroencephalography would also be interesting.

Pink Staining on Napkins

Q.—*What is the cause of pink staining that appears on napkins on washing and disappears when the washed napkin dries on the line?*

A.—Pink staining appearing on napkins is due to bile pigments. They usually give a green colour, but may cause a pink stain temporarily. A pink colour that turns brown is due to the very rare condition of alcaptonuria and is caused by the excretion of homogentisic acid in the urine.

Notes and Comments

Cold Water for Burns.—Dr. A. WARD GARDNER (Fawley, Hants) and Dr. P. J. ROYLANCE (Kingswood, Surrey) write: We would disagree with your expert ("Any Questions?" 3 June, p. 623) when he states that "immediate application of cold water cannot at present be recommended as a first-aid treatment, except possibly for small burns." Burns and scalds first cause pain and tissue damage, then loss of blood plasma into the tissues surrounding damaged capillaries. The aims of the first-aid treatment of burns are to prevent further damage, to prevent infection, to minimize the effects of loss of fluid from the burned tissues, to reassure the burned person, and to transport the casualty swiftly to hospital.[1]

The work of Ofeigsson[2 3 4] and others[5 6 7] has demonstrated beyond reasonable doubt that immediate cooling not only arrests further thermal injury but minimizes the resultant loss of tissue and skin damage from a heat burn or scald. If clean, cool water is to hand showering or immersion relieves pain drastically and takes less time than producing sterile dressings of the right size and sterility.[8] Ten minutes spent cooling a burn will not significantly affect the hospital treatment of a burn, but it may greatly affect the amount and depth of local thermal injury. Bloch[9 10 11] clearly shows that local cooling is an effective and readily available first-aid procedure, which in fact has been extensively used in the U.S.A., and may be the only means of providing first-aid treatment in the care of casualties.

REFERENCES

[1] Gardner, A. W., and Roylance, P. J., *New Essential First Aid*, 1967. London.
[2] Ofeigsson, O. J., *Brit. J. plast. Surg.*, 1959, **12**, 104.
[3] —— *Postgrad. Med.*, 1961, **30**, 330.
[4] —— *Surgery*, 1965, **57**, 391.
[5] Shulman, A. G., *J. Amer. med. Ass.*, 1960, **173**, 1916.
[6] —— and Wagner, K., *Surg. Gynec. Obstet.*, 1962, **115**, 557.
[7] Courtice, F. C., *J. Physiol. (Lond.)*, 1946, **104**, 321.
[8] *Lancet*, 1967, **1**, 628.
[9] Bloch, M., ibid., 1963, **2**, 249, 791.
[10] —— ibid., 1963, **2**, 1255.
[11] —— Thesis for the Degree of M.D. University of London Library, 1965.

Book Reviews

Modern Forensic Medicine

Modern Trends in Forensic Medicine—2. Edited by Keith Simpson, M.A.(Oxon.), M.D.(Path.), F.R.C.P.(Lond.), F.C.Path., D.M.J. (Pp. 374+x; illustrated. £4 18s.) London: Butterworth. 1967.

This book is not described as a second edition but as a second series, and this is surely true, since its 13 chapters are entirely different from the 12 which appeared in 1953. The subjects dealt with are of equal importance, and these two books together constitute a comprehensive account of recent developments and modern views in forensic medicine. Professor Simpson is himself responsible for two of the chapters. One is on the pattern of traffic accidents, a rather neglected subject in this country, and his study may advance safety designs and precautions in motor vehicles. In his other chapter Professor Simpson deals with the cardiomyopathies, underlining the fact that these diseases, once thought to be extreme rarities, may be responsible for many unexplained deaths.

Professor Simpson has cast his net widely in his selection of authors of the other chapters but has yet kept it within the British Isles, and has managed to persuade the most eminent scientists to contribute to this valuable book. Perhaps one of the most valuable chapters is that by Dr. Keith Mant on the estimation of time of death, which he acknowledges to be still one of the most controversial problems in forensic medicine. Dr. Mant's review of the present situation in this field gives one hope that this estimation will shortly move from the field of intelligent guesswork to that of scientific exactitude.

It is invidious to mention the names of authors of individual chapters without praising all of them, but naturally any individual reviewer is likely to find his interest taken by one chapter more than another, and it is only in this sense that I would mention the value of Dr. Goulding's chapter on side-effects of drugs and of the chapters on forensic immunology by Dr. Pereira and blood-group systems by Dr. Grant. All these three chapters deal with modern problems in an up-to-date manner and are of extreme value to the practising forensic expert.

The present volume appears in a different size and shape from No. 1, and this standard size is certainly more convenient for most library shelves. One must expect to pay 98s. for such an authoritative volume as this nowadays, but the price probably puts it out of the range of undergraduate students of forensic medicine. On the other hand, it must be considered an essential in the library of every practising forensic scientist.

R. DONALD TEARE.

Military Medicine

Radiology in World War II. Edited by Kenneth D. A. Allen, M.D. (Pp. 1087+xliii; illustrated. $8.25.) Washington: Office of the Surgeon General, Department of the Army. 1966.

This is the thirty-second volume published in the history of the U.S. Army Medical Department in World War II. In this huge tome written entirely by radiologists who served in the war, an honest attempt is made to record events so accurately, fully, and candidly that the many radiological errors made during that war will not be repeated in future.

Throughout the book we meet the recurring demand for the appointment of radiological consultants of standing with the Surgeon General and at all operational headquarters, for the placing in hospitals of chiefs of the radiological service, independent of the physicians and surgeons and responsible to the commanding officer only, and for the grading of radiographic technicians on a level at least equal to that allotted to their dental and laboratory counterparts. It is emphasized that the radiologist should always be a better radiographer than his technicians.

The training schedules for turning multitudes of ordinary doctors—mainly paediatricians—into radiologists and enlisted men into technicians were quickly brought into operation. The early "de Lorimier's 8-week wonders" gave place eventually to 12-week graduates at the hands of that brilliant organizer and teacher of radiology.

The story of each campaign and field of operations, from frozen Alaska to sweltering New Guinea, from Normandy to Okinawa, is told in separate chapters, each with operational, mechanical, and minute clinical detail, so there is a good deal of inevitable repetition.

The absence of standard apparatus with interchangeable parts (44 models made by 33 makers), the insufficient tropicalization with resulting deterioration, corrosion, and loss of insulation, and the high rate of cable failure when sets were required to operate therapeutically at voltages never intended by the makers resulted in many difficulties. Sheet lead was always in short supply.

The writers express the opinion that for success morale was always more important than hardware, and one reads with admiration how apparently insurmountable difficulties from moulds, damp, lack of water, and unventilated developing tents were overcome. "Improvisation and scrounging were the order of the day."

The general standard attained on all fronts was high. Myelography, pneumoarthrography, and cholecystography were carried out in the most remote places. The extent to which therapeutic radiology was employed on active service is astonishing, in Europe for plantar warts and clostridial myositis, in the East for jungle sores, fungous infections of the skin, for eczematoid dermatitis, and for cutaneous leishmaniasis.

Excellent relations with the British are reported from all fields and high praise is given to Brigadier D. B. McGrigor and to the staff of the R.A.M.C. College for generous aid afforded. Praise is recorded for help given by native practitioners trained at the Suva Medical School in Fiji.

At the outbreak of the war the cyclotron workers at Berkeley, California, and the staffs of cancer radiotherapy units were among the few persons in the United States who were accustomed to dealing with dangerous radiation.

The appointment of Professor Stafford L. Warren to advise on protection aspects of the "Manhattan Engineer Project" with the pioneering duty of determining and combating the radiation dangers of producing U 235 and plutonium in atomic piles and of disposing of waste and effluents, plus coping with the many medical and psychological problems resulting from isolating a million people in three secret cities, was an outstanding success. The full story of the project is told by Colonel Warren himself with operational and clinical details of the drops on Hiroshima and Nagasaki and of Operation Crossways at Bikini Atoll, where the capacity and deadly aspects of the Bomb were investigated and analysed after the surrender of the Japanese. A new world era started at Alamogordo, New Mexico, on the sixteenth of July 1945.

This big volume is full of interest from start to finish and its editor, Professor K. D. A. Allen, it to be congratulated.

GEORGE R. MCROBERT.

Teaching Human Reproduction

Teaching the Biological and Medical Aspects of Reproduction to Medical Students. Report of a Macy Conference, New York. (Pp. 151+xiii. 44s.) New York and London: Harper & Row. 1966.

In 1955 the Josiah Macy Jr. Foundation set itself to "strengthen the establishment of human reproduction as the basic science of obstetrics, through support of education and research in this field." This book is the report of a conference, held in Princeton, New Jersey, in 1965, to discuss some of the more promising developments in teaching human reproduction.

There has undoubtedly been a serious reappraisal of medical education in recent years, and no department has been under closer scrutiny than that of obstetrics and gynaecology. In training physicians who will practise in a sophisticated, largely urban society we are gradually moving away from the apprenticeship system of acquiring manual skills to an intellectual process of education in reproductive biology. Further, it is accepted that the study of human biology is an important component of a liberal education, that the educated members of society look for a lead in this, and that the physician should be able to provide such guidance. The urgent need for such study has come largely from the world population problem and from recent developments in the field of birth control; but, setting these aside, there is need for a fundamental reorientation of medical education in the direction of positive health, away from the preoccupation with morbid processes, which was essential half a century ago.

In this country we have scarcely begun to think in these terms ourselves, let alone change our syllabus, examination requirements, or teaching methods to take account of this present need. It is therefore of great interest to read of the practical experience of American medical schools with programmes integrating the teaching of departments of anatomy, physiology, pharmacology, psychiatry, and obstetrics. In some centres separate courses in reproductive biology have been instituted, in others the departments of obstetrics have altered their course to place greater emphasis on such topics as the morphological and physiological aspects of spermatogenesis, ovulation, fertilization, the endocrine control of these processes, human genetics, the social and physiological aspects of sex, biostatistics, and population control. Current ideas about the psychology of learning are also illustrated by application. A section of the conference was devoted to the study of methods of teaching reproductive biology outside America. British experience was presented by Sir Dugald Baird, and contributions were made by representatives from Germany and Japan. In both the latter the teaching appeared to have been influenced little by modern thought.

The editing of the papers has been good so far as the main contributors are concerned, but too little of the discussion is presented and one never obtains an impression of the way in which the papers were received. However, brevity in this case has paid some dividends, for the ideas of the contributors are lucidly presented. In all, this is a stimulating book of interest to all teachers of medicine, whether academic, scientific, or clinical.

R. W. Taylor.

Exotic Dermatology

Color Atlas of Dermatology. By Joseph Kimmig, M.D., and Michael Jänner, M.D. (Pp. 304+ix; illustrated. £15 15s.) Philadelphia and London: W. B. Saunders. 1966.

This is the third edition of a well-known *Color Atlas of Dermatology* originally assembled by Friebos and Schönfeld but now completely redesigned and enlarged by Kimmig and Jänner with many new illustrations. The text is also rewritten and in the English and American publication this has been amended by Dr. Goldsmidt.

This is a superb book. The coloured illustrations are truly magnificent and include common, rare, and exotic conditions. It will be of great value to many people. The senior dermatologist may well pick out an unusual condition rarely seen or recognized, and will refresh his memory of eruptions he does not see frequently at the present time. In this respect the collection of syphilitic eruptions is particularly useful. Junior dermatologists and postgraduate students will find this book of great help, as they will see unforgettable pictures of some conditions which they may have missed during their training. Students, preregistration house-officers, and general practitioners could well spend a few hours looking through the atlas and will then appreciate the appearance of some of the conditions they have heard of but not seen. For those dermatologists who have not built up a collection of coloured slides for teaching there is invaluable material available.

Criticism can be made, but only over minor matters. With ringworm fungus infections the dermatologist is now thinking in terms of the actual infecting fungus and the generic term of *Tinea* is not a sufficient diagnostic label. A few photographs are not up to standard and could easily be improved in further editions. The scabies illustration is very poor and the types of cavernous haemangiomata are badly represented. There are also bound to be some omissions and, for example, there is no photograph of orf (contagious pustular dermatitis of sheep).

The book is apparently expensive (£15 15s.), but when consideration is given to the excellent production of over 900 coloured photographs this is not a high price, and it is a book which should be in every large dermatology department, particularly where there is postgraduate training.

R. P. Warin.

Dynamic Psychiatry and the G.P.

Absent. School Refusal as an Expression of Disturbed Family Relationships. By Max B. Clyne, M.D. (Pp. 269+xi. 38s.) London: Tavistock. 1966.

Here is a remarkable example of the work that general practitioners can do when awakened to the potential that exists in their daily work. At the present time Michael Balint may take full credit for this awakening. It is indeed astounding that a general practitioner, while keeping at work, can make this kind of clinical study, dig deeply and wisely into the vast literature, and then find the emotional drive that is needed for the writing up of the data, the ideas, and the theoretical possibilities and suggestions.

Dr. Clyne has taken this one theme, school refusal, neatly and properly dissected out from truancy, and has allowed himself, as was necessary, to look at life through school-refusal-coloured spectacles. In the end he makes a comparative study of theories and then offers a theoretical formulation. The reviewer would like to find this formulation good, because it is based on his own formulation (fully acknowledged) of "transitional objects and phenomena," an area of the mind between subjectivity and the acceptance of the reality principle; but there is no need to jump to final conclusions, for Dr. Clyne proffers his idea with appropriate modesty.

"I have discussed the various aetiological theories of school refusal as described in the literature. I thought that these theories (environmental, sociological, neurasthenia, phobia, separation anxiety, test anxiety, depression, crisis) were insufficient to explain all the features of school refusal. I have put forward a relationship hypothesis according to which school refusal is based on a disturbance of the child's relationship function leading to a regression to the infantile, transitional stage in the development of object relations."

In Chapter 8, of which this has a summary, he has made his meaning clear to anyone who can give some time and thought to what is written, and to the work on which it is based. The main thesis is that it is for the general practitioner to work on these cases, keeping his mind open for all kinds of aetiological factors, and not passing on each case to specialists unless of course he is not temperamentally fitted for the kind of investigation that is needed in each case.

Much that is dealt with in passing should be noted. For instance, the matter of the physical examination, "discovered in the eighteenth century," and now (one would think) in danger of dying out. The patient needs to be physically examined, and perhaps it is the psychoanalyst who knows this best. The theory around all this is interesting and indeed important for medical practitioners.

In the reviewer's opinion the last word has not been said on the theory of school refusal, but this book leads us somewhere nearer to it. It should be read by general practitioners for its side-issues, and as a stimulus to clinical observation, and as an encouragement to those who are in the best position for doing clinical research—provided they are not allergic to dynamic psychiatry and to the idea of unconscious motivation.

D. W. Winnicott.

Proteins and Genetics

Protein Biosynthesis and Problems of Heredity, Development, and Ageing. By Zhores A. Medvedev. Translated by Ann Synge, B.A.(Physiology), M.B., B.Chir. (Camb.). (Pp. 584+xxi; illustrated. £5 10s) Edinburgh and London: Oliver & Boyd. 1966.

It is a pleasure to welcome a Russian textbook translated into English which deals with modern genetics and protein biosynthesis. The Lysenko period is now a memory only, and the translator mentions that the earlier copies still contained detailed and strongly worded attacks on Lysenko, which are now replaced by a more general discussion. Medvedev is not the only Russian author in this field whose publications have recently been published in the West. Spirin is studied regularly, and Dubinin's *Molekulargenetik* (in German) is read widely. Medvedev is a gerontologist and this book contains a particularly interesting chapter on changes in proteins and nucleic acids with age, and on the problem of ageing at the molecular level.

The monograph follows the conventional pattern one expects from a textbook in the field of molecular biology. One part deals with the synthesis of proteins in general, and another with special features such as the reproduction of viruses. Yet others describe the specific reproduction of proteins and nucleic acids, and their biosynthesis. The translation (by Ann Synge) is excellent, and there is no indication that this work was not written in English originally. The book was published in Russian in 1963 and must have been written in 1962. A special supplement for the English edition summarizes in 25 pages some of the important advances made in 1963 and 1964. Even so the book is not quite up to date and some speculations which may have been of interest in 1962 are no longer relevant because the facts have been discovered since.

There are numerous illustrations, some original, some familiar, all of them excellent. Each chapter is followed by references and the reader will find them a help in gaining access to Russian as well as to Western original work. An alphabetical index to all references lists some 2,000 names, and refers to many more publications. A subject index is not provided, but the reader is helped by a very full table of contents. There are now a number of textbooks of this nature available, but those who choose this clear and well-written treatise will not be disappointed.

H. LEHMANN.

Dental Caries

Advances in Fluorine Research and Dental Caries Prevention. Vol. 4. Proceedings of Congress, Utrecht, 1965. Edited by P. M. C. James, Klaus G. König, and Hans R. Held. (Pp. 246+viii; illustrated. £6.) Oxford, London, Edinburgh, New York, Toronto, Paris, and Braunschweig: Pergamon. 1966.

Epidemiological studies into the incidence of dental caries and the clinical testing of agents of use in its prevention are being conducted in many countries, and the publication of the proceedings of the symposium on "The Clinical Testing of Agents for the Prevention of Dental Caries" has come at an opportune time. One of the difficulties in this type of work has been that the results obtained in different countries have often appeared to be in disagreement; and, while this may have been due to variables of which we are, as yet, uninformed, it may on the other hand be the result of differences in techniques of observation and recording which could be more precise.

That workers of international repute with experience of epidemiological studies in dental caries in various countries should have come together in order to discuss these matters, and that the results of their deliberations are made available to us in this book, is certainly to be welcomed. In many countries throughout the world postgraduate diplomas in public dentistry or dental public health are being instituted, and it seems probable that this book will be recommended reading for many of them.

In addition to the report on the symposium there are also nineteen free papers by research workers, many of whom are as distinguished as those participating in the symposium. Many of these papers are of considerable interest and value. The paper, printing, and illustrations are of excellent quality, but, even though this publication has apparently been subsidized by industry to a considerable extent, the price of £6 is somewhat expensive. There may be few individuals who will wish to purchase this work, but it should certainly be included in the library of any university with a dental school.

A. D. HITCHIN.

Queen's Nightman

The Story of William Hunter. By Sir Charles Illingworth. (Pp. 134+viii; illustrated. 35s.) Edinburgh and London: E. & S. Livingstone. 1967.

In the past a student of William Hunter would read the lecture by his contemporary and admirer Samuel Foart Simmons (1783), the later memoir by Peachey (1924) which contains much factual information, and the account by Marshall and Burton in the Glasgow Museum catalogue (1962) and other works. He would find some variation in emphasis and some inevitable contradictions in detail. Sir Charles Illingworth has added to these a comprehensive study of the lives of Hunter's contemporaries, the many bundles of letters in the University of Glasgow and in the Hunter-Baillie collection in London, the periodicals current at the time, and the writings of William Hunter.

It was a happy inspiration of genius to combine all this information into an autobiography as it might have been written by William Hunter himself. Instead of a large collection of facts we are given a continuous narrative of surpassing interest, written in a conversational manner without insistent demand on strict chronological order. Such a style gives a more favourable picture than might have been painted by others but it does not exclude mention of any self-admitted imperfections of character.

The influence of William Cullen, his first mentor in medicine, is apparent throughout the story. Hunter relied on him for the care of his ailing relatives and for advice in his undertakings and he remained "his dear friend." Through Cullen's introduction he met another compatriot, William Smellie, who taught him midwifery and sent him to lectures on anatomy by Frank Nicholls and on natural philosophy by Desaguliers; their different styles influenced his subsequent teaching. In the exuberance of youth he soon thought himself superior to Nicholls and wished to succeed him. James Douglas of the "pouch," a skilled anatomist and an experienced obstetrician, invited him to be his resident assistant, and despite the reluctance of his father who was ill William accepted. Youthful ambition again prevailed and he found no reason to make any sacrifice of his own interests. Douglas played a major part in framing his career.

William determined that the teaching of anatomy must include practical dissection. His rise in obstetrics culminated in his appointment as Queen's Nightman; he learned diplomacy from dealing with the labours of the aristocracy.

William's attitude to his brother John was kind but at first condescending; he was surprised to discover his manual dexterity and inquisitive spirit and his outlook changed to one of pride in his skill and reliance on his help, which he acknowledged generously during the fruitful years of their co-operation. John's tribute to William is not mentioned. The famous quarrel is dismissed briefly with "John was ever hot headed and is now getting more quarrelsome, or so I am told." It is put in its proper perspective in the final scene—"Our little feud is over."

This entrancing story tempts one to assess William's character. His simple tastes were not altered by his rise to fame. He was ambitious, perhaps jealous and a little selfish, but he was compassionate and generous albeit thrifty. Blessed by a good education he became a man of erudition as well as a skilled anatomist and obstetrician.

The thanks of all Hunterians are due to Sir Charles for this most attractive and readable book. The production is excellent but it is worthy of a fuller index. The appendices are useful; reference 169 should be for Chapter 18, not 16.

ERIC RICHES.

Books Received

Review is not precluded by notice here of books recently received.

Atlas of Human Anatomy. Originally devised by Werner Spalteholz. 16th edition. Revised and re-edited by Rudolf Spanner. (Pp. 904+xii; illustrated. £13.) London: Butterworth. 1967.

Cold Spring Harbor Symposia on Quantitative Biology. Vol. 31. The Genetic Code. (Pp. 762+xxii; illustrated. $15.00.) New York: Cold Spring Harbor Laboratory of Quantitative Biology. 1966.

The British Postgraduate Medical Federation. The First Fifteen Years. By Sir Francis Fraser, M.A., M.D., F.R.C.P., LL.D. (Pp. 69+vii. 15s.) London: Athlone. 1967.

A Fortunate Man. The Story of a Country Doctor. By John Berger. Photographs by Jean Mohr. (Pp. 158; illustrated. 30s.) London: Allen Lane The Penguin Press. 1967.

Progress in Nucleic Acid Research and Molecular Biology. Vol. 6. Edited by J. N. Davidson and Waldo E. Cohn. (Pp. 430+xvii; illustrated. £6 12s.) New York and London: Academic Press. 1967.

Zoonoses of Primates. The Epidemiology and Ecology of Simian Diseases in Relation to Man. By Richard Fiennes, M.A.(Cantab.) Nat. Sci., M.R.C.V.S.(Edin.). (Pp. 190. 55s.) London: Weidenfeld and Nicolson. 1967.

Plastic Surgery in the Tropics. By R. J. Maneksha, F.R.C.S.(Eng.). (Pp. 307+xiii; illustrated. 85s.) London: J. & A. Churchill. 1967.

A Textbook of Hospital Catering. By Ann T. M. Harris. (Pp. 306+x. 32s.) London: Barrie & Rockliff. 1967.

The Natural History of Viruses. By C. H. Andrewes. (Pp. 237+viii; illustrated. 55s.) London: Weidenfeld and Nicolson. 1967.

Maxillo-Facial Injuries. Etiology, Clinical Features and Treatment. By Otto Tokvam, B.D.S.(Oslo), L.D.S.(Bris.), L.D.S.R.C.S.(Eng.), B.A.(Paris). (Pp. 193+xii; illustrated. 52s. 6d.) London: J. & A. Churchill. 1967.

The Adrenal Cortex. Edited by Albert B. Eisenstein, M.D. (Pp. 685+xiv; illustrated. £8.) London: J. & A. Churchill. 1967.

Clinical Anesthesia Conferences. Edited by Lester C. Mark, M.D. (Pp. 326+xii. £5 5s.) London: J. & A. Churchill. 1967.

Middle Articles

MEDICAL EDUCATION

Need for Integrated Training Schemes*

P. W. R. M. ALBERTI,† PH.D., M.B., F.R.C.S.

Brit. med. J., 1967, 3, 101–102

It is my aim today to look ahead and see how the National Health Service might evolve to prevent further disillusionment among hospital junior staff. Doctors the world over have been notorious for their lack of forward planning, a lack which is only second to their universal cries of dismay when Governments plan for them. I feel privileged to participate in this break with tradition, in what I believe is to be the start of a constructive attempt by the profession to influence the evolution of the Health Service.

I would like to examine two major grievances of the hospital junior staff and suggest some possible remedies. These are the long and uneven training, and the total uncertainty of a future in the hospital service.

Postgraduate Training

There is growing feeling that postgraduate training, with certain noteworthy exceptions, is frighteningly haphazard: its quality is uneven, its length variable, and its diplomas multitudinous and often misleading.

In view of the increasing shortage of doctors in all branches of the profession the question today must be: "What is the shortest period of training required to fit a man for a consultant post?" If this is accepted, then formal instruction inevitably follows. I believe training programmes in the specialties must come to Britain if we are to continue to produce well-trained consultants for the N.H.S.

The implications of such a change in policy are enormous and would lead to a major reorganization within the hospital sphere. Training schemes must be based on large units or departments, for it is both difficult and uneconomical to provide formal instruction for two or three people, while it is perfectly feasible for 20 to 30. Tuition must be continuous, and practical training well supervised. There are few departments which can undertake formal academic instruction of the postgraduate and at the same time provide facilities for plentiful clinical experience. Some degree of rotation is inevitable. This should be continuous throughout the training period, in and out of the academic unit, revisiting the same hospital at a higher level. Rotation should never imply need for changing residence, for virtually all conurbations large enough to support training programmes have sufficient hospitals close together to allow easy access one to another.

This sort of scheme is possible only if much closer liaison exists between teaching hospitals and regional boards, though it seems difficult under present financing and administrative regulations to adopt a sufficiently flexible attitude to make progress. In my view it is possible to plan on a regional basis only if all parts of the team are working together, and in order to do this the boards of governors and the regional boards might well be combined as they are so successfully in Scotland and Northern Ireland. They must, so far as training is concerned, make regional estimates of needs for hospital staff and plan training posts accordingly.

It will never be possible to establish training for more than a handful of people if it has to be centred on a 30-bedded teaching hospital unit; all that seems to happen is that more and more staff are employed (indeed attracted by the kudos and genuine academic advantage) gaining less and less practical experience, while there may be regional hospitals close by cutting their work loads because of inability to obtain juniors, though they would provide ample experience. The two surely are complementary. The advantage of formal academic training allied to plentiful practical experience would quickly attract juniors.

Regional Centres

What I have said here applies in particular to the specialties: anaesthesia, psychiatry, ophthalmology, otolaryngology, dermatology, and the like, where there is already an incipient staffing crisis, but the same problem will apply to general medicine and surgery in the years to come.

Funds must be put aside for the establishment of one or more regional centres in each specialty large enough to provide the ancillary facilities which are increasingly needed. The Newcastle Region has shown a fine example in some instances, as its neurological, neurosurgical, and radiotherapy services demonstrate, but these are only faint glimmers in an otherwise Stygian gloom. It is the lack of such centres, with their allied training programmes and research facilities, just as much as financial pressures which precipitate emigration among those seeking a future in the hospital service.

The implications of such training schemes are considerable for the Health Service. They would simultaneously provide more consultants and drastically alter the peripheral scene. The most recently available figures of consultant age distribution indicate that it is uncommon for individuals to be appointed to consultant posts before the age of 35. If by swifter and more comprehensive training men were ready at 32 or even 30, the number of consultants would increase by 8 or 13% without any increase in numbers of practising doctors, and would thereby help to eliminate a growing shortage.

A word of warning to juniors is needed at this stage: if they wish this sort of scheme to be introduced, and I believe they do, then they must also realize that it means more and harder work, not more time off and more holidays. One thing is fundamental to training: experience must be gained and there is a limit to spoon-feeding. Any observer of the North American training scheme is immediately impressed by two things: the shorter but more organized training programmes, and the very much longer hours and harder work put in by the residents.

---

* Based on a paper read at the Conference on "The Future of British Medicine" held at Newcastle upon Tyne on 10 and 11 March, organized by the North of England Branch of the B.M.A. (See *B.M.J.*, 18 March, p. 693.)

† First Assistant, E.N.T. Department, University of Newcastle upon Tyne.

If training is to be centred about large institutes, then inevitably there will be no juniors in the periphery. This need not be a bad thing, and in many instances will only stabilize an already current situation.

Some services will be centralized: the large institutes will siphon off patients from the periphery, and as communications improve so the need for small isolated units will diminish. The funds thereby released will help finance the central departments. Hospitals might therefore be built where they can be manned, rather than where political pressure dictates.

Where hospitals survive without training programmes consultants and general practitioners will have to work much closer together. This is one way in which the cry from general practitioners for hospital participation may be answered: they would be employed as integral members of the team in consultant-staffed units, after suitable training. This is quite different from general-practitioner-run cottage hospitals, pleasant though they be, for it enables practitioners to participate in expert first-class units.

Here we must turn to the relations between the Government and the Royal Colleges, and to politics in relation to the social services and the profession. The nation must be persuaded that its funds are better spent in such a hospital structure than they are at present; the Royal Colleges that their examinations and training are most efficiently conducted in defined programmes.

Higher Qualifications

The Fellowship and Membership seem to be inefficient ways of sorting out future consultants. It is my opinion that, by and large, the standard of these examinations is not set too high: if so, it follows that candidates are ill prepared. Much greater note must be taken of the candidates' training before entry. This implies, firstly, sitting later, and, secondly, greater supervision of centres. I think that it is in this latter task that the Colleges can be most faulted. Approved posts for Fellowship and Membership are so variable as to imply a lack of supervision. It is noticeable that nothing so speedily improves the calibre of a training programme in North America as the threat of withdrawal of approval; for once this happens no junior will be recruited. The inspection should be of training programmes, not of posts, and they should be regularly and strictly reviewed. Surgically, I favour the submission of operative experience by candidates, which if small would not jeopardize them, but which if repeatedly small from one unit would jeopardize its programme.

The standard of the further examinations appears to put the cart before the horse. At present the Colleges are reviewing their role in postgraduate training, and, if I read it correctly, the College of Surgeons is suggesting that specialist training be given only after admission to Fellowship, for four years as a senior registrar. The combined pass rate in both parts of the English Fellowship as at present constituted is so low that it is a considerable hurdle in itself. If it is used as an entrance challenge to specialist training in its present form it will both diminish recruitment and unnecessarily lengthen the training period. Genuine confusion also exists at present about the meaning of further diplomas. The Colleges state that they indicate fitness to be trained, but appointment committees assume that they are an indication of training completed and hence of professional competence.

There is obviously a need for some sort of weeding-out examination: it is wrong to think that all those who attempt to specialize are sufficiently able or suitable for training. The selection should be made within three years of qualification, and should carry a fair pass rate. It might take the form in all the specialties of a test in appropriate basic sciences. Thereafter those who continue training should be reasonably certain that after a predetermined period of between two and at the most six years, depending on the specialty, they have a good chance to attain specialist status, possibly with dual standards similar to the Canadian certification and Fellowship, with each major subspecialty having its own examination.

Uncertainty

Already the N.H.S. somewhat grudgingly accepts that senior registrars are career hospital doctors; in the new scheme let it accept this fully. The uncertainty about the most important move in the life of a young hospital doctor, that from senior registrar to consultant, must be unequalled elsewhere in the world, and this fact alone must account for much emigration. Regional boards must know years ahead what posts are to fall vacant by retirement. These could be advertised, and indeed appointed, months or even a year before the candidate finished training and the post fell vacant: this would allow better future planning by doctors and boards alike. The situation would be eased further if retirement was not implemented on reaching the 65th birthday, but at the end of the academic year. At the same time, as in North America, all junior posts could be filled on the same date. A register could be kept of all posts available at the year's end, and, with plenty of warning, juniors and hospitals could plan their future.

CONTEMPORARY THEMES

Memorandum on the Management of Accidents in Childhood*

Prepared by the Standing Committee on Accidents in Childhood of the British Paediatric Association

Brit. med. J., 1967, **3**, 103–105

Children are more liable to accidents than adults because they are immature physically and mentally, lack experience, and are unable to foresee danger and the possible consequences of their actions. Hitherto there has been too little recognition of the facts that children are injured in large numbers, that their injuries differ from those of adults, and that they have special needs related to age and development. The consideration of special provision for children is important now that so much thought, time, and money are being devoted to the planning of hospitals and to the organization of accident and emergency services.

Review of Present Situation

Mortality

Nearly 10% of all accidental deaths in males and 7% of those in females occur in children under the age of 15.† The main causes in the first year are recorded by the Registrar General as inhalation of food, etc., and suffocation, though some of these "cot deaths" may be infective or allergic in origin.

As the toddler begins to explore his environment other causes of death increase in importance: drowning, poisoning, burns and scalds, falls, and traffic accidents. Accidents are the commonest single cause of death among schoolchildren; in 1963 40% (612) of the 1,528 deaths in boys aged between 5 and 15 in England and Wales were due to accidents. The corresponding percentage in girls was 24.7% (224 deaths out of a total of 909).

Morbidity

Rowntree (1950) estimated that about 35,000 injuries in children under 2 years of age were treated annually in the United Kingdom—3,000 by admission to hospital, 11,000 in accident and casualty departments, and 21,000 by family doctors. Children under 15 years of age constituted 22% of patients attending "casualty" departments in England and Wales in one sample week (Platt Committee's Report on Accident and Emergency Services, 1962, Appendix II, Table III).

In Liverpool about 2,000 children (approximately 1% of the childhood population) are admitted to children's hospitals each year as a result of accidents; 1,200 go to surgical wards (over a quarter of all admissions to these wards) and 600 to orthopaedic wards (half of the total admissions to these wards) (Forshall, personal communication).

In 1959 10,907 children and 69,765 adults were seriously injured in road accidents (Interim Report of Accident Services Review Committee, Osmond-Clarke Committee, 1961, Appendix I, Table IV).

Of all poisonings (other than barbiturate), 43% in males occur in boys under 5 years of age, while 53% of all burns in females and 48% of all burns in males occur in children (Hospital In-patient Enquiry for 1959, quoted in Platt Committee's Report on Accident and Emergency Services, 1962, Appendix III, Table III).

A high proportion of accidents involve very young children. According to the British Medical Association's Report on Accidents in the Home (1964), 40% of all home accidents occur in those under 5 years of age: accidents to boys aged 1 and 2 years make up 22% of all reported accidents to males. Of home accidents in Aberdeen, more than half were among children below school-leaving age, though children composed less than one-quarter of the population (MacQueen, 1960).

It should be noted that not all injuries to young children are accidental. Deliberate, serious, and often fatal injury to children by adults seems to be more common than formerly (*Brit. med. J.*, 1966).

Management of Accidents

I. Introduction

Family doctors and casualty officers deal with the majority of minor accidents to children. Serious injuries may be treated by consultant surgeons, while paediatricians are concerned with medical emergencies and acute poisoning. Should an accident cause complicated or multiple injuries many specialists may become involved: the orthopaedic surgeon will deal with the fracture; the plastic surgeon the burn or the dog-bite of the face; and the paediatric or general surgeon the ruptured internal viscera. Thus, though each injury and every complication is expertly dealt with, there may be divided responsibility, fragmentation of care, perhaps overlap of treatment, and failure of total assessment. Because many different specialists are concerned the importance of accidents in childhood, and the size and complexity of the subject, both nationally and locally, may not be sufficiently appreciated. The result will be failure to arouse the public and the professional conscience.

Two general principles should underlie care of the injured child. Firstly his injury should have the best treatment, and secondly his visit to hospital, whether as inpatient or outpatient, should cause him and his parents as little distress as possible. These principles determine the kind of provision that should be made for the hospital care of injured children.

II. Inpatient Arrangements

(a) General Aspects

All children should be admitted to children's units and not to adult wards or to the side-wards of adult units. This important principle is supported by the Accident Services Review Committee (Osmond-Clarke Committee) but is not yet generally accepted, for there are still many children in adult wards. We therefore state our reasons for endorsing it.

Technical.—The emergency resuscitation and treatment of infants and children call for special medical and nursing experience and skills. These include administration of intravenous fluids, collection of blood and other samples for analysis, and understanding of fluid and electrolyte balance in young children. The nursing of infants and young children presents no difficulty in children's wards geared to the daily practice of the specialized techniques used. The best results are obtained by people who are familiar with these methods and with the technical problems presented by emergencies in small children, and who have the right sort of equipment immediately available. These conditions obtain only in large children's hospitals and in large children's units in general hospitals.

---

* Abridged version. Copies of the full memorandum can be obtained from the Secretary, British Paediatric Association, 30 Guilford Street, London W.C.1.

† Throughout this memorandum the word "accident" includes accident, poisoning, and violence.

Psychological.—Children, especially those under 6 years of age, are particularly liable to emotional upset as a result of admission to hospital, and everything possible should be done to minimize this and to promote quick recovery. Only with the special experience and skills mentioned above are the necessary technical procedures likely to be carried out with the minimum of disturbance to the child. The medical, nursing, and auxiliary staffs in a children's unit are expert in dealing with children and acutely aware of their needs, both physical and emotional. Ward routines and arrangements are suited to the needs of children, visiting by parents is encouraged, and mothers can be admitted with their children. Play facilities are available and children have the companionship of others of their own age. Schoolteachers play an important part in preventing the educational handicap which might otherwise develop during a long stay in hospital.

In order to provide the necessary experience and to attract enough doctors and nurses of the right calibre, a children's unit must be large. Spence (1947) thought that the minimum size for a children's unit should be 60 beds, while the Nuffield Foundation report on children in hospital stated that 40 beds should be the minimum, but that where the local population is large enough there should be at least 60 beds (Duncum, 1963).

(*b*) *Inpatient Services in District General Hospitals*

The majority of injured children needing admission to hospital will in the future be treated in children's units in district general hospitals. These units should consist of 60 beds or more and provide for a wide variety of medical and surgical cases. In areas with more than one district general hospital it may prove advisable to concentrate the inpatient facilities in one of them in order to achieve the size necessary for an efficient unit. Obviously it will be more satisfactory if the paediatric unit is in the same hospital as the main accident and emergency department.

In some units, medical, surgical, and orthopaedic cases are nursed together, whereas in others they are in separate wards. Whatever the arrangement, there should be the closest possible liaison between the consultant paediatrician and his surgical colleagues.

(*c*) *Inpatient Services in Regional Paediatric Centres*

There is a definite need for a large paediatric centre in each hospital region to which the more difficult and complex cases can be referred, either directly or by transfer from a district general hospital. The regional paediatric centre should be a children's hospital closely associated with the main regional teaching hospital. The centre should include specialties such as children's orthopaedic surgery, neurosurgery, otolaryngology, ophthalmology, plastic surgery, dermatology, etc., as well as paediatric medicine, surgery, and psychiatry. Such comprehensive provision cannot be effectively made in hospitals of fewer than 200 beds. The services available in the centre would enable a children's accident unit to be established, to serve the surrounding district and to act as the regional reference centre for the more complex problems of accidents to children.

It may be argued that such a children's accident unit should be associated with the adult accident centre rather than with the regional paediatric centre (whether the latter be a children's hospital or a large children's unit in a teaching hospital). A major advantage, however, of associating the regional children's accident unit with the regional paediatric centre is that specialists expert in the paediatric aspects of their subjects will be immediately available. The advantage of having, for example, consultant anaesthetists experienced in the management of small children can scarcely be overestimated, and the same applies to paediatric biochemists, radiologists, and other specialists.

A reason sometimes advanced against the establishment of regional centres for children is that parents will have to travel further when visiting them. This difficulty can be reduced by allowing unrestricted visiting and providing accommodation for mothers to stay in hospital. Furthermore, children in the regional centre are there because of the severity or nature of their injury, and their parents accept the inconvenience in the knowledge that their children are getting expert treatment not available nearer home.

Two special types of injury need further consideration: burns and scalds, and head injuries. Many of these can be dealt with locally, but others must go to the regional centre because of the specialized surgical and nursing techniques required. Severely burnt children need medical and surgical supervision throughout the whole 24 hours, with precise biochemical and haematological control. Renal dialysis may be needed. Infection may be a complication. The child-psychiatrist may help to prevent or deal with the withdrawal symptoms which frequently occur, and the services of the physiotherapist, dietitian, and medical social worker may all be required.

For these reasons special units for children with burns or head injuries should usually be provided in the regional paediatric centre. If such units are not practicable, the closer the children's centre is to the wards where the children with burns or head injuries are cared for the better will be the liaison between paediatricians and surgeons, which is the key to satisfactory care.

III. Accident and Emergency Services
(Casualty Departments)

The arrangements for injured children in outpatient departments are generally less satisfactory than those for inpatients. Children's hospitals—that is, general hospitals catering solely for children—are often too small to have casualty departments well-enough staffed to be efficient, while, on the other hand, few accident and emergency departments in general hospitals provide the necessary special facilities for children, nor do they usually have medical and nursing staff with paediatric experience.

The aim of outpatient care, as with that for inpatients, should be to provide the best medical attention with the minimum of emotional upset to the child. To achieve this:

(*a*) The medical, nursing, and auxiliary staff who deal with children should be trained and experienced in paediatric techniques. This should apply throughout the 24 hours and seven days a week.

(*b*) Paediatric advice and help should always be available at both consultant and registrar level.

(*c*) Unnecessary delays should be avoided. When the child arrives at the hospital, treatment, or admission if indicated, should be immediate and not after a long, tiring, and perhaps harmful delay. The reception area should be near to the children's unit, and thus minimize the time seriously injured patients have to travel.

(*d*) Children should be shielded from unpleasant sights and sounds, such as severely injured, noisy, or drunken people.

In the district general hospital the accident and emergency department should have a separate entrance and separate waiting space for children so that they will not come into contact with seriously injured adults; there should also be children's examination and recovery rooms, appropriately furnished. The paediatrician should work very closely with the surgeon in charge of the department, and should be consulted about the planning and organization of the department.

The children's accident unit associated with the regional paediatric centre should provide a full accident and emergency service for children. In those regions where the centre is part of the main hospital campus it will sometimes be convenient to place the children's accident unit close to the adult accident unit so that operating-theatres and other services can be shared. If a choice has to be made, however, it is preferable to site the children's accident and emergency service close to the children's inpatient unit. In view of the high proportion of poisonings which occur in children, the regional poisons bureau might well be sited at the children's accident unit.

As in all units, whether medical or surgical, the quality of the work done in the children's accident unit will depend on the degree of supervision by senior staff. The consultant in administrative charge should be responsible for ensuring that the junior staff have adequate teaching, supervision, and support, and that an experienced doctor is always available to receive the seriously injured child. Jones *et al.* (1966) have published a report on the work of a children's casualty department, and their conclusions about the advantages to children of such a department strongly support our own.

Research

The cost to the nation of accidents in childhood must be enormous, yet surprisingly little co-ordinated research is being carried out.

Aspects requiring further investigation include the following: (*a*) accurate estimation of the size and nature of the problem, particularly in relation to non-fatal accidents; (*b*) the family and community relationships of accidents in childhood (Backett and Johnston, 1959); (*c*) the physical, psychological, and educational antecedents and sequelae; (*d*) the biochemical and pathological effects of trauma in childhood, together with the day-to-day management of injured children; and (*e*) "operational research"—that is, a critical evaluation of methods and techniques and their results, and of the organization and efficiency of accident services.

The regional accident unit should act as a centre for the dissemination of information about accidents. It should also maintain a close liaison with statutory bodies and voluntary societies, both national and local, that are interested in the whole problem, and particularly in accident prevention. The large subject of accident prevention is at present being considered by the Medical Commission for Accident Prevention, and is not discussed in this memorandum.

Conclusion

Too little thought has been given to the special needs of the injured child. In 1962 the Standing Medical Advisory Committee of the Central Health Services Council produced a report on the Accident and Emergency Services. This important blueprint for the future did not consider services for children, and indeed only once mentioned the special needs of children. The President of the British Paediatric Association wrote to the *British Medical Journal* (Harris, 1963), drawing attention to this omission and the disparity between the report and that on the Welfare of Children in Hospital (1959). In reply, Sir Harry Platt, who had been the chairman of both committees, stated: "The Report on Accident and Emergency Services presents no challenge to the now widely accepted recommendation of the Report on the Welfare of Children in Hospital." He went on to say, "It is important, therefore, that the paediatricians should support their colleagues (in particular, the orthopaedic surgeons) in seeing that separate accommodation (both inpatient and outpatient) for children is provided in all such plans" (Platt, 1963). We hope that Sir Harry Platt's advice will be acted on, and in this memorandum we have tried to show how it can best be done.

REFERENCES

Accident and Emergency Services: Report of the Subcommittee of Standing Medical Advisory Committee of the Central Health Services Council (1962). London.
Accidents in the Home (1964). British Medical Association, London.
Accident Services Review Committee of Great Britain and Ireland: Interim report (1961). British Medical Association, London.
Accident Services of Great Britain and Ireland: Second report of the Review Committee (1965). Ibid.
Backett, E. M., and Johnston, A. M. (1959). *Brit. med. J.*, **1**, 409.
Brit. med. J. (1966), **1**, 601. Memorandum by the Special Standing Committee on Accidents of the British Paediatric Association: "The Battered Baby."
Duncum, B. M. (Ed.), (1963). *Children in Hospital: Studies in Planning.* London.
Harris, C. F. (1963). *Brit. med. J.*, **1**, 1157.
Jones, P. F., Karmody, A. M., and Galloway, J. M. D. (1966). Ibid., **2**, 819.
MacQueen, I. A. G. (1960). *A Study of Home Accidents in Aberdeen.* Edinburgh.
Platt, H. (1963). *Brit. med. J.*, **1**, 1672.
Rowntree, G. (1950). *J. Hyg. (Lond.)*, **48**, 323.
Spence, J. C. (1947). *Brit. med. J.*, **1**, 125.
The Registrar General's Statistical Review of England and Wales for the year 1963. 1965. London.
The Welfare of Children in Hospital (1959). Central Health Services Council. London.

RESEARCH IN PROGRESS

M.R.C. Rheumatism Research Unit

On 26 June the Medical Research Council's Rheumatism Research Unit held an open day for the press. The unit, whose honorary director is Professor E. G. L. BYWATERS, is housed at the Canadian Red Cross Memorial Hospital at Taplow in Berkshire, and was opened in 1947; it was taken over by the M.R.C. in 1958. Much of its work is concerned with studying and treating chronic rheumatism and other connective diseases in children and adults, while the research programme is largely orientated towards related immunological problems.

Juvenile Rheumatoid Arthritis

Dr. BARBARA M. ANSELL described some of the problems of treatment of juvenile arthritis, pointing out that this aimed to leave the patient with a minimum of residual damage once the activity of the disease had died down. Three main principles were involved: the overall management of the patient and the prevention of deformities; the intelligent use of drugs; and co-operation between the various medical and social organizations concerned.

In treatment serial correction of deformities by splints might be necessary, and various plastics for making the latter were being tried out. Hydrotherapy played a valuable part in treatment, as did physiotherapy, which had to be individually planned for each child. Dr. Ansell considered that salicylates were still the safest and the most effective drug available, while if corticosteroids had to be used the aim should be rapidly to try to get the dose down to a minimum level, possibly by adding salicylates as well. Failure to grow in height had been found to be a major problem of long-term corticosteroid therapy. This was not reversed by the addition of either human growth hormone or anabolic steroids, though there was some suggestion that giving the total corticosteroid dosage on one occasion every two days might overcome the failure of growth. Cataract formation had been found to occur in about 10% of all patients treated with corticosteroids, and a trial was in progress to see if this regressed once treatment was stopped.

Concluding, Dr. Ansell emphasized that a large number of social services might be called in to help patients with juvenile rheumatoid arthritis, both when they were in hospital and when they returned home. These included special schools, suitable training for employment, and modifying equipment in the home.

Studies in Autoimmunity

Discussing recent work on autoimmunity, Dr. L. E. GLYNN pointed out that conditions resembling human thyroiditis or allergic encephalitis could be produced in laboratory animals. In rabbits immunized against human fibrin the injection of human fibrin into the knee joints produced a condition with many features similar to rheumatoid arthritis in man, including loss of cartilage and the formation of pannus with lymphofollicular cellular aggregates. A similar lesion could also be produced in about 5% of animals immunized against their own fibrin. This reaction might persist for six to nine months, a finding that suggested that the animal had become immunized to the inflammatory exudate itself, so that the process became self-perpetuating. This hypothesis had been supported by finding that chronic arthritis could be produced by the injection of inflammatory exudate into the joints of animals already immunized against the exudate.

Allergic Orchitis

With Dr. P. C. BROWN, Dr. Glynn had also studied the mechanism of autoimmune damage, using allergic orchitis in guinea-pigs as an experimental model. This could be produced by immunizing the animals with guinea-pig testis and Freund's complete adjuvant, and was characterized by the appearance of delayed sensitivity on the fifth day, of circulating antibody on the seventh to the ninth day, and of histological lesions on the tenth day. If, however, the nature of either of the immunizing agents was changed orchitis did not result, and subsequent work had suggested that this would occur only if both delayed hypersensitivity and circulating antibody were present.

Autoimmune Haemolytic Anaemia

Another experimental model, which had been studied by Dr. E. J. HOLBOROW and Dr. A. M. DENMAN, was the autoimmune haemolytic anaemia that occurs spontaneously in New Zealand black mice. Their findings suggested that an abnormal antigen in the tissues of these animals was providing an autoimmune stimulus to the lymphocytes, the plasma cells, and the tissue cells. Recently electronmicroscopic studies had shown the presence of particles resembling murine-leukaemia virus in the tissues of these animals, and it was possible that these were producing the antigenic stimulus. Antilymphocyte globulin given to young animals had been found to suppress the occurrence of the haemolytic anaemia, though it did not affect the established condition in older animals.

Immunofluorescent Methods

The diagnostic use of immunofluorescent methods in patients with autoimmune disease was discussed by Mr. G. D. JOHNSON. For example, these methods had been used to distinguish between patients with systemic lupus erythematosus, whose sera contained antinuclear factor, and patients with " lupoid hepatitis," whose sera contained, besides antinuclear factor, antibodies directed against renal glomeruli, smooth muscle fibres, and bile canaliculi. One problem that was being tackled at the present time was the international standardization of immunofluorescent methods for diagnosis.

Fluorescent-antibody techniques had also been used by Dr. G. LOEWI to demonstrate the presence of chrondromucoprotein in tissues. Strongly positive results had been obtained in cartilage taken from foetuses and the newborn, but only slight fluorescence had been found in adults.

Collagen and Mucopolysaccharides

Because of its large molecular weight and complex structure collagen would be expected to be a powerful antigen, but, as Dr. J. A. KIRRANE and Dr. GLYNN pointed out, the reverse was true, possibly because of its low content of tyrosine. Nevertheless, the antigenicity of the collagen molecule was greatly increased if it was enriched with tyrosyl or acetyl residues, and this treatment enabled an antibody to collagen to be prepared. They intended to use this to study the normal metabolism of collagen and to see whether it was affected in diseases such as rheumatoid arthritis.

Dr. J. E. SCOTT had studied the distribution of mucopolysaccharides in human cartilage. In infant cartilage virtually no keratosulphate was present around the cells, but its content increased with age, replacing chondroitin sulphate. He suggested that in older subjects this change might lessen the capacity of cartilage to act as a " shock-absorber."

NEW APPLIANCES

Suction Holder for Insertion and Removal of Contact Lenses under Visual Guidance

Dr. J. DALLOS, medical officer in charge of contact lens department, Western Ophthalmic Hospital, London N.W.1, writes: Some persons are unable to handle their contact lenses manually. The first device to help these was introduced in the early 1930s by O'Rourke, and this was adroitly modified by Ruben to suit corneal lenses. However, both instruments are bulky and of use only for insertion of the lenses. A device as small as the ubiquitous rubber sucker, but which accords visual guidance to the contact-lens wearer—both for the insertion and for the extraction of corneal lenses—is now available for the handicapped; in particular, for aphakics and hypermetropes, and also for some other high ametropes who cannot see the lenses once their glasses are removed for insertion; for those who lose control of their direction of sight without firm fixation (one-eyed people, and many others); and for people with clumsy fingers, with small space of lids, etc.

Loose and flabby lids and deep orbits may make routine manual removal of corneal lenses difficult if not impossible, and the often unmanageable difficulties with the blind rubber sucker are resolved by this new instrument. Its size and shape are no different from those of the established sucker, so it is easily carried in any contact-lens case in the space provided. The difference is a rigid transparent collimator rod inserted in its axis, loose at the business end so as not to interfere with suction, and with a hermetically closed opposite club end formed into a lens, which is just jutting out to collect enough illumination from a bright object to maintain a spot of light for guidance, whether the instrument is held loose or is squeezed for suction. Occlusion of the companion eye is automatic, as the other hand is held across the face and spreading the lids apart for action.

WITHOUT PREJUDICE

I suppose that any medical man who has given any thought to the problems of the N.H.S. will be biased in his conclusions on any one of them. There have been so many rapid changes of scene—social, economic, political, national, as well as changes in the development of medicine. Often enough the problems of today are viewed with the prejudices of yesterday. I am sure, for example, that much of the controversy over the payment of G.P.s has arisen because it has related to conditions of practice that are rapidly becoming outmoded by the advance of medicine and the expectations of an informed public.

Unfortunately other elements enter that confuse, and often exacerbate, the issue—and it doesn't really matter what the issue is. The socialist doctor will go all out for a salaried service because of his political beliefs. The fact that socialists like it and advocate it doesn't mean that it is wrong. The Conservative doctor will favour a free-enterprise approach based on payment of fees and competition. The fact that Conservatives like this system doesn't mean that it's right. Their motives are as much political as the motives of the socialist doctor, as much political as medical. They will both assert that what they advocate is in the interests of "good" medicine. The Liberal will try to steer a mid-way course, with a strong political bias against the usurpation by the State of the duties and responsibilities of the individual.

* * *

As we are all political animals, it is therefore not possible to take "politics," that is party politics, out of medicine. Those who protest loudly that politics should be taken out of medicine really mean the other man's politics. Orthodoxy, said F. E. Smith, is my doxy and heterodoxy is other people's. Politics is about power, and, as there is no power so powerful as money, then what doctors are paid and how and by whom is bound to be a political matter. So doctors in this respect have to play politics, medical politics. If the B.M.A. as a medico-political organization did not exist it would be necessary to invent it. Its job is to do the medico-political work for the medical profession. It is in fact, if not in constitution, the medical trade union. Aneurin Bevan knew this. He may have meant to make a bit of mischief when he said at a fork luncheon with the B.M.A. Council, years ago, "I have just come from the Royal College of Surgeons, where everyone is too polite to talk about money. How nice it is to meet people like you who are not ashamed to mention such an indecent subject."

I admit that the medical profession has at times been too obsessed with the subject. Unfortunately obsession, a natural obsession, with money has often determined the attitude of doctors to new ways of doing work that some people think are an improvement on the old. I have often thought that if only methods of work could be examined objectively first, without reference to money, then payment and its methods would in the end sort themselves out. The intensive care for, say, a case of coronary thrombosis has been introduced on the basis of what the proper care is. If this has to be provided in a specially equipped unit such matters as the rights of the doctor as an individual contractor in this context are irrelevant.

Having watched a great friend of mine come successfully through a severe cardiac crisis and a close relative through a pretty desperate status asthmaticus, both as a result of the intensive care available through the efforts of a group of skilled persons, I can have no doubt of the correctness of the verdict of the Association of American Medical Colleges, under the direction of Dr. Lowell T. Coggeshall in 1965. "There is no clear alternative to the organization of the modern practice of medicine as a team effort—and the doctor must be trained specifically to function as leader."

* * *

The evidence piles up, but the English voice is still confused. I find it easier to clear my own mind by looking at the American scene. First of all they are mentally far more adventurous than we are. They are less hide-bound by outdated preconceptions. I have a feeling too that what they do today we shall do tomorrow, as we are much less revolutionary than we like to believe. Nevertheless, I got quite a shock when I read a leading article in the *New England Journal of Medicine* for 25 May which in effect sounded the death-knell of general practice.

"It is probably true," the leader states, "that the physician can function no longer as a general practitioner able to provide total care for his patients under all circumstances." The leader criticizes the suggestion in the report of the Citizens' Commission on Graduate Medical Education that there be a "specialty in comprehensive care" as "somewhat at variance with the concept of elimination of general practice." The leader goes to the heart of the problem with a home-truth everyone is doing his best to ignore: "A role whereby the physician will care for the patient between illnesses and during convalescence is unlikely to appeal to medical students no matter how vigorous the propaganda."

The *New England Journal of Medicine* sees teamwork—group practice—as the proper and efficient way of medical life in a technologically advanced community. "Medical teamwork and close co-operation with paramedical workers leaves little place for the physician specialized in comprehensive care. Much of his work, in fact, may be assigned to a physician's assistant, or to the public-health nurse or social worker." Any scheme for the reform of general or other form of practice must, to my mind, stand or fall by one criterion: Does it afford a fully qualified medical man TIME to do his work efficiently —TIME to examine his patients ? If it doesn't it is almost worthless, even dangerous.

* * *

In the House of Lords debate in February this year Lord Platt made a strong and effective plea for the generalist, and saw the G.P. working in a group practice after the end of his training. So Americans and Britons both agree that group practice, or health-centre practice, is the necessary sequence to strictly individualistic work. Lord Platt went a bit further in the American direction when he said, "Within the group there will be some kind of specialization. A man who has done paediatrics in hospital will take most of the children's work." And I hope the group will include someone thoroughly trained in psychiatry.

We shall move more slowly than the Americans, but I believe that the logic of the situation will mean groups of specialists working in group practices or health centres, with other health workers acting as responsible partners with them. The *New England Journal of Medicine* considers it an error to look upon "specialists [as] somehow incapable of viewing the whole patient, but instead must focus only on a specific organ system. Any good physician is aware of all the ramifications of illness in his patient, and this is continually emphasized in the education of medical specialists."

I suppose Lord Horder was one of the last of the great general practitioners. It is becoming almost impossible for any one man, save the occasional genius, to do the comprehensive work of a general physician—a G.P. There is just not enough available talent of the order required. It is much easier to be a specialist. But a specialist has to study one subject in depth, and when we go to the repair shop we want to have the works put right by a man who really knows what he is doing, by an expert. And this is what the patient will demand. Doctors, after all, exist to look after patients. So I hope that general practitioners in particular will concentrate on the efficient ways of providing medical care in our advanced society, and *then* and only then go into the modes of payment, as the house agents say, subject to contract.

PERTINAX

Correspondence

Letters to the Editor should not exceed 500 words.

Common Market—a Challenge, Not a Danger

Sir,—In his report on a meeting with the General Medical Council about the implications for the British medical profession of United Kingdom entry into the European Economic Community (*Supplement*, 13 May, p. 85) Dr. Derek Stevenson said that "the General Medical Council was fully alive to the dangers that faced doctors if Britain entered the Common Market," and later Dr. A. V. Russell commented: "Mr. Kenneth Robinson may be able to encourage into this country a number of doctors from countries in the Common Market, accept them into the N.H.S., and use them to bring pressure to bear on us in the general medical services field."

What dangers, I would like to ask ? Perhaps the danger that a certain number of European doctors would come to Britain for their postgraduate education and stay there if they wished to, without the difficulties they usually have to obtain a permanent registration, and which graduates from Commonwealth universities with comparable skill, experience, and command of the English language never encounter ? Is there something so inaccessible, almost of metaphysical quality, in British Commonwealth qualifications that the holder of a Makerere, Madras, or Saskatchewan medical degree is automatically eligible for permanent registration, whereas the mere thought of extending the same privilege to a Paris, Heidelberg, or Padua medical graduate raises an outcry and is defined as a danger by the G.M.C. ?

I also find disturbing Dr. Russell's suggestion that Common Market doctors might be used as blacklegs by your Ministry of Health in order to weaken the bargaining power of British general practitioners. It may be interesting for your readers to know that general practitioners in Italy—namely, the poorest country among the six—have an average monthly income of £400 to £500. I am quite sure that there is only one incentive which might draw a number of doctors from Europe into Britain, and this is the high scientific standard of your medicine, though I fail to see why their absorption in your medical services, and particularly in your hospital establishment, should present more problems than in the case of Commonwealth doctors.

Moreover, one should not underestimate the possibilities of a movement from the United Kingdom to Europe. Why should British doctors emigrate to Australia and Canada and not to Cannes or Cortina ? The fact that there was no uniformity of clinical and scientific standards between the medical professions of the six was never described by any of the national medical bodies as a danger for the professions they represent but as a problem to be solved. They solved it once they decided to face the question realistically from a European perspective. This meant a gradual and progressive application of the Treaty of Rome to the practice of medicine in Europe.

I hope that the attitude of the General Medical Council and of some of the speakers at the B.M.A. Council does not reflect the views of British public opinion. If it does one has to conclude, rather reluctantly, that General de Gaulle is not altogether wrong.—I am, etc.,

S. R. SCAGLIOLA.

Ospedale Civile,
Brescia, Italy.

Enzyme Activity and Cervical Carcinoma

Sir,—The conclusion of Dr. J. T. Boyd and his colleagues (24 June, p. 785) that cytological examination of the vaginal secretions is a much more reliable method for diagnosing pre-invasive cervical carcinoma than measurement of pentose pathway enzyme activity is one with which we are in complete agreement. In fact, this is no more than a repetition of what many workers[1-8] on both sides of the Atlantic have repeatedly emphasized, and that since ". . . increased glucose metabolism via the pentose route and consequently increased activity of its enzymes occurs in many physiological processes as well as in non-malignant pathological conditions . . . it is not possible to relate the degree of activity of the dehydrogenase enzymes to a specific aspect of the biochemical process. Furthermore, since many other factors may influence activity of these enzymes, a test of this nature could not be of diagnostic value in neoplasia."[2]

6-Phosphogluconate dehydrogenase activity in vaginal secretions is, admittedly, not the only topic discussed in this article, but the development of a quantitative enzyme test, as a practical alternative to cytology, provided the impetus and was the authors' stated *raison d'être* of a survey undertaken in over 4,000 women.

Large series and detailed statistics should not obscure the fact that prior consideration of biological variation would have both predicted this outcome and proved the point with many fewer cases.

Alas, the large numbers have failed to drive home the point, for the authors still conclude that ". . . a final assessment of the role of biochemical tests in cervical screening must await further clarification of the natural history of carcinoma-in-situ."—We are, etc.,

CHARLES P. DOUGLAS.
JEAN GINSBURG.

Department of Obstetrics
and Gynaecology,
Royal Free Hospital,
London N.1.

REFERENCES

[1] Beaconsfield, P., and Ginsburg, J., *Lancet*, 1965, 1, 324.
[2] —— —— *Brit. med. J.*, 1966, 1, 737.
[3] Nerdrum, J. J., *Scand. J. clin. Lab. Invest.*, 1964, 15, Suppl. 76, 71.
[4] Muir, G. G., Cantl, G., and Williams, D. K., *Brit. med J.*, 1964, 2, 1563.
[5] Hoffman R. L., and Merritt, J. W., *Amer. J. Obstet. Gynec.*, 1965, 92, 650.
[6] Bell, J. L., and Egerton, M. E., *J. Obstet. Gynaec. Brit. Cwlth*, 1965, 72, 603.
[7] Lawson, J. G., and Watkins, D. K., ibid., 1965, 72, 1.
[8] Brooks, P. C., and Muir, G. G., ibid., 1967, 74, 111.

Haematomas of the Abdominal Wall

Sir,—Your leading article (17 June, p. 716) reminds us of the case histories of two young, hard-working bowlers, both of county status.

Both initially complained of vague discomfort over the left rectus abdominis muscle, but there were no clinical signs. Both after periods of some weeks developed visible and easily palpable hard swellings in this region. Both were treated surgically. In one the haematoma was evacuated and the muscle tear demonstrated through the fleshy fibres of the lower medial half only of the muscle, the lateral half being undamaged. This bowler, a slow spinner, gave up professional cricket for other reasons and his functional end-result as a cricketer could not be assessed.

The other, a fast bowler, presented with the same symptoms, but again without signs, and after an interval of many weeks developed a haematoma. Again only the medial half of the left lower rectus was torn apart. A repair of the divided muscle was attempted but was technically unsatisfactory, for the divided fibres were inturned and adherent, so that a gap of 1 in. (2.5 cm.) had to be "cobbled." This bowler has now reached test-match status and has since bowled very hard for several years. In both men the rectus sheath was intact—hence the hard rock-like nature of the swelling, which may suggest an alternative and more serious diagnosis.

Two lessons we have learnt may be of interest to others. Firstly, the body's back swing of a bowler as he winds up just before delivery puts a great strain on the leading rectus abdominis muscle—that is, both were right-hand bowlers and in both the left rectus was involved. Mr. Alec Bedser has advised us that the "wind up" of the trunk in young bowlers should be very slowly and progressively developed with a smooth rhythm in their approach to the wicket—and he should know. Secondly, bowlers, particularly six-days-a-week professionals, presenting with vague discomfort over the rectus abdominis should be completely rested from bowling until all discomfort goes.—We are, etc.,

A. L. D'ABREU,
WILLIAM GISSANE,
Hon. Medical Officers,
Warwickshire County Cricket Club.

Accident Hospital,
Birmingham.

SIR,—I would like to comment on the leading article (17 June, p. 716) "Haematomas of the Abdominal Wall."

One meets this condition from time to time in general surgical practice, and it is, I think, important to try to make this diagnosis whenever possible, thereby avoiding laparotomy. In my experience this condition is frequently associated with cough, and it is a fallacy to believe that the mass remains palpable after contraction of the abdominal muscles. This only occurs if the haematoma should extravasate through the rectus muscle and lie anterior to it. In my experience this has not occurred, and the haematoma remains strictly localized to the rectus sheath posterior to the rectus abdominis. The mass may not become palpable until an examination is conducted under general anaesthesia. Indeed, the condition may not be recognizable until an incision is made, because of the extreme mobility of such a mass under general anaesthesia with relaxants. However, usually the condition can be diagnosed because it is associated with attacks of coughing. I agree that bruising does not appear for at least ten days.—I am, etc.,

P. L. BERGER.

Good Hope General Hospital,
Sutton Coldfield, Warwicks.

Experiments on Man

SIR,—I too was pleased that you chose a physician of great intellectual honesty and moral integrity, in the person of Professor L. J. Witts, to review Dr. M. H. Pappworth's book *Human Guinea Pigs* (10 June, p. 689).

I also firmly believe that these qualities apply equally to Dr. Pappworth himself, and, while many might not agree with everything he says (or perhaps the way in which he chooses to say it), let us not deceive ourselves—for most of us know that only too much of what he says is, regrettably, only too true.—I am, etc.,

B. W. ROPER.

Queen Elizabeth Hospital,
Birmingham.

Ophthalmic Graves's Disease

SIR,—We were interested in the letter of Mr. K. C. Wybar (24 June, p. 836) describing the abolition of lid retraction by hexamethonium iodide. Local application of guanethidine eye drops has produced considerable improvement in lid retraction in more than 60 thyrotoxic patients whom we have studied. In our original paper[1] we described the use of 10% guanethidine, but recently have found that a 5% solution is equally effective and produces little if any conjunctival injection.

The role of sympathetic activity in producing lid retraction is indicated by the widening of the palpebral fissure seen following instillation of sympathomimetic amines into the eye.[2] The effect of directly acting amines such as phenylephrine and adrenaline is potentiated by pretreatment with local guanethidine, while indirectly acting amines such as ephedrine or hydroxyamphetamine fail to produce a widening of the palpebral fissure following such pretreatment. Local propranlol fails to influence the width of the palpebral fissure,[1] which suggests that it may depend on α- rather than β-receptor activity.—We are, etc.,

PAUL TURNER.
J. M. SNEDDON.

St. Bartholomew's Hospital,
London E.C.1.

REFERENCES

[1] Sneddon, J. M., and Turner, P., *Lancet*, 1966, 2, 525.

[2] —— —— *J. Physiol.*, 1967, 189, 20P.

Drugs and Driving

SIR,—The letter by Dr. D. V. Foster (24 June, p. 836) raises important issues and prompts me to record the recent experiences of one of my patients:

Aged 30, she had suffered from a neurotic type depression for two years. I had been giving her tranylcypromine 30 mg. and trifluoperazine 3 mg. (Parstelin) and chlordiazepoxide 30 mg. (Librium) daily for a year as an out-patient which enabled her to hold down a job for which she required a car. She was involved in an accident and considered that her reactions had been depressed by these preparations. On her own initiative she disclosed to her insurance company that she was receiving anti-depressant and sedative tablets. All insurance was promptly suspended unless she could obtain a medical certificate stating that her driving would be unimpaired while receiving these drugs. Since she was unable to get to work by public transport, I was obliged to certify that she had discontinued all medication to enable her cover to be restored. Under these circumstances, should she become depressed again it may be necessary to administer E.C.T.

Insurance companies probably have many similar cases on their records. Thousands of drivers are receiving these and similar drugs on their doctor's prescriptions; but on her proposal form with a major insurance company my patient was only required to testify that she was not suffering from any "*physical* deformity." Perhaps there should now be additional safeguards.

I fully endorse Dr. Foster's conclusion that if we inform our patients that they should not drive while taking the drugs we have prescribed it might cause considerable alarm and would certainly tend to vitiate the "rapport existing between the doctor and patient."

Is there a practical solution? Powerful psychotropic drugs are now available; are there any that are generally regarded as safe to take and drive, and if so in what dosage? Should the popular slogan now be amended to "Don't drink *or take drugs* and drive?" If so most of our patients will have to be passengers.—I am, etc.,

J. C. BARKER.

Shelton Hospital,
Shrewsbury, Shropshire.

Choledochoduodenostomy

SIR,—This valuable paper by Mr. J. N. Burgess and Mr. H. A. Kidd (3 June, p. 607) is really directed towards the management of two conditions: choledocholithiasis and chronic relapsing pancreatitis.

We personally do not regard choledocholithiasis *per se* as an indication for the operation; pigment stones particularly may exist in a healthy blue thin-walled duct with apparently normal function. We consider that the operation is definitely indicated when the common duct contains infected bile in addition to stones, is dilated, and has thick white fibrosed walls, probably the result of long-standing increased intraductal pressure and infection. Appetite and a sense of well-being rapidly return and bloating and heart burn will usually disappear. The operation is also of value if it is not certain that all stones have been removed, especially where the cholangiogram has revealed stones high up in the hepatic duct. We have two cases where a retained stone can be seen on x-ray but the patient is completely symptom free, possibly owing to the presence of the fistula. A small stoma is almost certain to give rise to retention of debris and must be studiously avoided. Except in one case, we have not seen any trouble in over 200 cases where such a stoma was made.

This case was a male aged 56. Within eight weeks of a choledochoduodenostomy for pigment stones in a dilated duct in association with a large spleen, the patient developed recurrent rigors which were only controlled by ampicillin. At re-operation the stoma appeared to be perfectly satisfactory, but in view of the persisting symptoms the integrity of the common duct was restored. The rigors have ceased.

Pancreatitis as we see it in this country may be sharply divided according to the presence or absence of biliary disease. In the former case, gall stones must be comprehensively eradicated. We have found choledochoduodenostomy most satisfactory when indicated in this respect. In contrast we have been unable to find proof that it is specific in the treatment of non-calculous pancreatitis; indeed, we have one certain and one probable case where pancreatitis has relapsed in the presence of an adequate choledochoduodenal fistula. If bile does pass into the pancreatic duct there is no good evidence that this is in any way harmful.[1] We would certainly agree with Burgess and Kidd that sphincterotomy is rarely indicated. It is a procedure with definite mortality and it should be reserved for those cases where pancreatography reveals an obstructed system with a hold-up at the ampulla.

In general we consider that acute or chronic relapsing pancreatitis should not be considered as a single disease entity but that it should always be related to underlying aetiological factors if these can be elicited, as their elimination will often produce a remission in the patient's symptoms. We should abandon the view that any one operation can be a panacea. It is becoming more and more apparent that the exact surgical procedure employed, where duct obstruction is present, will depend upon the site and extent of the blockage.—We are, etc.,

W. M. CAPPER.
J. E. TRAPNELL.

Southmead Hospital,
Bristol.

REFERENCE

[1] Anderson, M. C., and Trapnell, J. E., *Surg. Gynec. Obstet.*, in press.

SIR,—While heartily endorsing the conclusion of Mr. J. N. Burgess and Mr. H. A. Kidd (3 June, p. 607) that choledochoduodenostomy is the treatment of choice for choledocholithiasis, we would like to comment on their technique. In our series of more than 60 such operations (for several indications) we have not found a two-layered anastomosis necessary, a single layer of interrupted or continuous 00 chromic catgut being used.

We are surprised that in the majority of their cases the common bile duct was sufficiently dilated to allow a 2-cm. transverse incision (producing about a 1.5-cm. stoma after two-layered anastomosis) and also surprised that with a stoma that size they had no cases of cholangitis. On preliminary review, our experience is that a 2.5-cm. stoma is advisable, as recommended by Capper,[1] and this can be obtained in most cases only by a longitudinal incision in the common bile duct and a transverse (or, preferably, longitudinal) incision in the duodenum. The importance of the larger stoma seems to be to allow free return of duodenal contents from the common bile duct rather than to prevent stenosis, but we are investigating these points further.—We are, etc.,

A. E. Stevens.
A. G. Johnson.

Redhill General Hospital,
Redhill, Surrey.

Reference

[1] Capper, W. M., *Brit. J. Surg.*, 1961, 49, 292.

Swiss-type Agammaglobulinaemia and Achondroplasia

Sir,—The letter from Drs. R. B. Lowry and J. R. Miller (24 June, p. 842) criticizing the genetic counselling given to the parents of the baby with achondroplasia and Swiss-type agammaglobulinaemia, described in a Clinicopathological Conference published from Hammersmith Hospital (3 December, 1966, p. 1371), calls for a reply. At the time the conference was held it was thought that the agammaglobulinaemia was acquired and that the baby was suffering from classical achondroplasia with little risk of recurrence, but it is now clear that the association is not a chance one (the writer knows of at least four further instances of this combination) and that we are dealing with a new syndrome which is not true achondroplasia nor the usual form of Swiss-type agammaglobulinaemia. In the absence of consanguinity in parents or familial occurrence there is no circumstantial evidence that the condition is due to the expression of a recessive gene, and it is just as likely that it is due to a new and lethal mutation with small risk of recurrence. In the absence of such evidence I feel that it would have been wrong to advise the parents that there would be a 25% risk of further affected children, though they were told that we had not excluded the possibility that this might be the case.

Regarding the previous letter from Dr. V. A. Fulginiti and colleagues (22 April, p. 242), commenting on the same Clinicopathological Conference, I would like to take this opportunity of thanking the authors for their helpful suggestions and for their report of a further case of the syndrome. We had considered the possibility of a runt disease, but this would leave the progressive anaemia that led to the first transfusion unaccounted for, whereas a stem-cell hypoplasia would explain the whole picture. This further example of the concurrence of genetically determined disease of both the bone and bone marrow is of some interest and it would be useful to have the comments of an embryologist on the association.—I am, etc.,

J. A. Davis.

Institute of Child Health,
Hammersmith Hospital,
London W.12.

Treatment of Drug Addiction

Sir,—In the current discussion about the treatment of addiction (20 May, p. 498) there has been little mention of the use of narcosis during the withdrawal phase. It is a regimen which appears to have few advocates, but it seems to have several advantages, especially where opiates are involved. If my small but encouraging experience of it is typical it should perhaps be more widely used. Some of the most seriously handicapped addicts, and those most inaccessible to treatment, either cannot contemplate any reduction in dosage, or, having been persuaded to make some reduction, are so distressed by the withdrawal symptoms that they withdraw from therapy instead. They may simply leave the therapeutic arena, or they may sabotage the treatment by lying about their dosage. In withdrawing this group of addicts narcosis may be the treatment of choice. While compulsory detention might enable more of them to complete their withdrawal, it is not really legal, and, as Dr. P. A. L. Chapple points out (20 May, p. 500), it is not conducive to a good relationship in the more difficult second stage of treatment —keeping the addict off his drugs.

An addict who is withdrawn under narcosis can be assured that withdrawal symptoms will be non-existent, or at most minimal and transient. When he finds that this is so his gratitude and faith may prove useful therapeutic tools later on. Addicts are not noted for their co-operative attitude to treatment; apart from the initial consent, narcosis requires no co-operation. Once begun, it is not at the mercy of his precarious resolve, and since he needs no visitors there is no risk that some of his friends might smuggle drugs to him. Finally, it is perhaps less likely than other methods to deter him from returning for further treatment if he should relapse, as so many do.

Narcosis seems a simple and effective way of managing what is often a difficult and frustrating phase in the treatment of addiction. It has its risks, of course, but they cannot compare with the appalling mortality and morbidity of opiate addiction. It can, and perhaps should, be done in a general medical ward, or in the psychiatric unit of a general hospital with good laboratory facilities.—I am, etc.,

Colin L. Brewer.

The Churchill Clinic,
Princess Alexandra Hospital,
Harlow, Essex.

Lyell's Toxic Epidermal Necrolysis

Sir,—On 21 June a child 18 days old was seen at her home in Coventry. She had a mild form of this condition. The first sign noticed by the mother had been an infected lesion on the face 4 to 5 days previously, and widespread peeling followed later. A swab was taken that evening and the culture examined on 23 June, by which time Dr. J. Jefferson's article (24 June, p. 802) had been seen by us. The organism isolated was *Staphylococcus aureus* (coagulase positive), which was submitted to the cross infection reference laboratory of the P.H.L.S. at Colindale, where phage-type determination showed that it was also type 71. In view of her age the child was admitted, not because she was seriously ill, but because we were afraid she might become so. Local and systemic antibiotic treatment was given and the child has already improved sufficiently to go home.

There was no history of contact with persons from Northern Ireland.

We are indebted to Dr. B. T. Thom for his report on the phage-typing result.

—We are, etc.,

J. G. Holmes,
A. C. Kendall,

Coventry and Warwickshire
Hospital,
Coventry.

J. E. M. Whitehead.

Public Health Laboratory
Service,
Coventry.

Sir,—In his article (24 June, p. 802) Dr. J. Jefferson mentions that Holzel and Jacobs,[1] among others, have suggested that haemolytic staphylococci may play a part in the aetiology of the scalded-skin syndrome. He then goes on to say that phage type 71 *Staphylococcus aureus*, which was isolated in nine of his recorded 31 cases, was in his view the cause of the disease. Dr. Jefferson omits to acknowledge that phage type 71 *Staphylococcus aureus* was the organism found by us and regarded as the aetiology of the scalded-skin syndrome. Furthermore, Dr. Jefferson reports that seven of his patients were aged 4 weeks or under.

It has been customary to honour the man who first recognized the condition in the newborn period 90 years ago by calling it von Ritter's disease, or dermatitis exfoliativa neonatorum Ritter. The aetiological association of phage type 71 *Staphylococcus aureus* with Ritter's disease has been previously recognized by Howell and Jones,[2] Parker and Williams,[3] and Benson *et al.*[4] Precisely because of our awareness over the past decade of the special effect of phage type 71 *Staphylococcus aureus* in the newborn did we investigate our older patients for this organism. The problems involved were fully discussed in our paper.—I am, etc.,

A. Holzel.

Booth Hall Children's Hospital,
Manchester 9.

References

[1] Holzel, A., and Jacobs, S. I., *Schweiz. med. Wschr.*, 1966, 96, 427.
[2] Howell, C. H. L., and Jones, H. E., *Arch. Dis. Childh.*, 1961, 36, 214.
[3] Parker, M. T., and Williams, R. E. O., *Acta paediat. (Uppsala)*, 1961, 50, 101.
[4] Benson, P. F., Rankin, G. L. S., and Rippey, J. J., *Lancet*, 1962, 1, 999.

Health Week in Rural Practice

Sir,—I was a little disturbed to note the figures for prevalence of undiscovered glaucoma quoted in the article (17 June, p. 756) "A Health Week in Rural General Practice." In this it was observed that the prevalence of glaucoma was "slightly" higher in the authors' survey than were the figures of Luntz and of Wright as quoted[1] in the account of a symposium held in June 1965.

A more careful study of this account will reveal that the prevalence quoted by Luntz (1.5%) is in no way comparable to that given by Wright (1.1%). The "glaucomas" in the Luntz series are in fact cases listed in Wright's account under the headings " Ocular Hypertension " and " Possible Early Glaucoma," with a combined prevalence of 3%. The Luntz series clearly excluded any cases of true glaucoma, and indeed all patients with any history of previous eye disease. As the authors give no criteria for their diagnosis of glaucoma, it is impossible to say to what extent their findings can be compared with either survey. They certainly cannot be compared with both. The literature of glaucoma abounds in such comparisons of incompatible data.

It is depressing also to note that the deficiencies of a single measurement of ocular pressure as a means of detecting glaucoma still do not appear to be fully appreciated. This aspect of the problem is discussed in the same symposium and more fully in the account of the Royal Society of Medicine's 1966 Annual Symposium on Presymptomatic Screening.[2] It would be interesting to know if the authors have read these papers and are aware of the objections to tonometric screening.—I am, etc.,

P. A. GRAHAM.

Medical Research Council,
Epidemiological Research Unit
(South Wales),
Cardiff.

REFERENCES

[1] Luntz, M. H., *et al.*, *Glaucoma*, ed. L. B. Hunt, 1966. Edinburgh.

[2] Graham, P. A., *Proc. roy. Soc. Med.*, 1966, **59**, 1215.

" Swallowed " Endotracheal Tube

SIR,—I write to endorse heartily the warning and advice communicated by Mr. J. A. S. Dickson and Mr. G. C. Fraser (24 June, p. 811). I have personally heard of the occurrence of 11 cases of " swallowed " endotracheal tube in recent months—including those dealt with at Great Ormond Street. The accident occurs usually when the resuscitator is relatively inexperienced. The tube slips down the oesophagus either when the proximal end is released preparatory to connecting a supply of oxygen (as suggested by Dickson and Fraser), or when mouth-to-tube intermittent positive pressure respiration (I.P.P.R.) is planned and there is therefore no adapter at the end of the tube. Under the latter circumstance, if the oesophagus is intubated, a sudden movement by the infant, or distraction of the resuscitator's attention, can apparently lead to the mishap. I suggest that the most satisfactory precaution would be for the manufacturers to build a solid plastic hook into the posterior wall of the tube, about one inch (2.5 cm.) from the proximal end. Until a tube modified in some such manner is obtainable it would be preferable that the tube be fitted with an endotracheal adapter as part of the normal preparation of the resuscitation equipment. The presence of an adapter interferes somewhat with the ease of performing mouth-to-tube I.P.P.R., but the safeguard is obviously necessary until a modified tube becomes available.

It always takes time for mishaps of this description to become common knowledge, and one can speculate on the grave implications of this instance. The increasing (and laudable) readiness of residents to intubate a depressed neonate has obviously led to an increased number of times that a tube is advanced down an infant's oesophagus. Has there indeed been an increase in the incidence of perforation of the oesophagus, and of rupture of the stomach due to sudden distension with oxygen or air ? It is important that the occurrence of each of these mishaps does not encourage opposition to the full and proper use of endotracheal intubation in the scheme of neonatal resuscitation, but rather that it helps to promote greater effort in the organization of tuition of residents in the manœuvre.—I am, etc.,

J. SELWYN CRAWFORD.

Research Department of
Anaesthetics,
Royal College of Surgeons of England,
London W.C.2.

SIR,—Mr. J. A. S. Dickson and Mr. G. C. Fraser (24 June, p. 812) have performed a valuable service in drawing attention to the ease with which a neonate may swallow an endotracheal tube that has been placed in the oesophagus. They state, " Where junior staff are to be responsible for resuscitation of the newborn it is essential that they should be trained in endotracheal intubation by practising on stillborn infants." I think that all will agree that practice of this kind is highly desirable, but it is sometimes difficult to bring trainee, instructor, and a cadaver together in the same place and at the same time.

For the past six months we have had a Resuci-baby made by Laerdal, of Norway, in use in this department (available in this country from Oxygenaire Ltd.). This model simulates a large baby with a fair amount of muscle tone. It has proved to be most useful in teaching the art of neonatal intubation to anaesthetists, paediatricians, general practitioners, and midwives. Anyone who has become proficient in intubating the model will experience little difficulty in intubating a neonate which is really in need of intubation.—I am, etc.,

REX BINNING.

Department of Anaesthetics,
Royal Sussex County Hospital,
Brighton 7.

Renal Potassium Wasting in Hypercalcaemia

SIR,—We were most interested to read the paper by Dr. P. H. Sanderson (18 March, p. 679) in which he deals with the uncommon occurrence of renal potassium wasting in hypercalcaemia.

A major cause of hypercalcaemia in childhood is vitamin-D intoxication. Ferris and colleagues[1] have described a case of vitamin-D intoxication complicated by renal potassium wasting and tubular acidosis, and reported only two other cases of vitamin-D intoxication mentioned in previously published works . . . " in which unexplained hypokalaemia was associated with an elevated serum calcium. . . . "

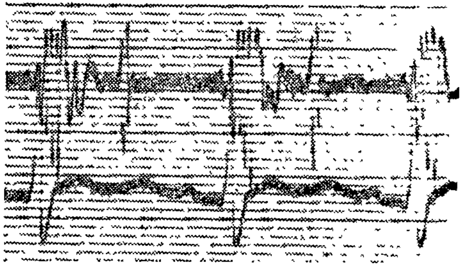
Our experience suggests that renal potassium wasting with hypokalaemia in hypercalcaemia probably occurs more frequently in childhood than is generally realized. In connexion with this we should like to point out some of the cardiographic features which we have noted in a number of cases of the syndrome under discussion. The data obtained from our patients are summarized in the Table below.

Cases 1 to 3 are part of a total of 13 severe cases of vitamin-D intoxication observed in our clinic over the period 1959 to 1964. In all but one of the patients (Case 4) the data were obtained during the first few days of their admission to our clinic, and after a variable period of anorexia, vomiting, thirst, and polyuria.

Case 4 is uncommon for the aetiology of hypercalcaemia and for the evolution of the renal tubular dysfunction syndrome: hypokalaemia with chronic excessive renal potassium loss is still present six years after the severe transient episode of hypercalcaemia. Renal biopsy showed interstitial calcification, tubular changes, and calcification throughout the distal portion of the nephrons.

The electrocardiographic records in Cases 1 and 2 showed the combination of the well-known manifestations of hypokalaemia (prominence of the U wave) together with those of hypercalcaemia (absence of the S-T segment, dome-shaped T waves with shortening of the Q-T). This combined electrocardiographic pattern (see Fig.) is not reported in the published literature on the electrocardiographic changes in electrolyte disturbances.

In Case 1 the phonocardiographic record (see Fig.) also showed the shortening of the dynamically effective mechanical systole identified by the graphically recorded second heart sound (0.18 sec. against 0.22 sec. for the same R-R period in controls). The standard value of the duration of the mechanical systole for the various R-R intervals was deduced from the study of 645 normal children.



The shortening of the mechanical systole was absolute, and was not relative only to the electrical systole identified by the end of the T-wave. The data thus obtained were consistent with the diagnosis of energetic-dynamic cardiac insufficiency (Hegglin syndrome),[2 3] a factor rarely considered in paediatric cardiology.[4]

Case No. and Sex	Diagnosis (Vitamin-D Doses U./day)	Serum Calcium (mg. %)	Serum Potassium (mEq/l.)	Plasma Total CO_2 (mEq/l.)	Urinary *p*H	Urinary Potassium (mEq/24 h)
1 F	Vitamin-D intoxication (300,000) ..	18·6	2·8	26	6·5–7	25
2 F	Vitamin-D intoxication (160,000) ..	16	2·8	24	6·5–7	15
3 M	Vitamin-D intoxication (30,000) ..	15·5	3·1	28	7	21
4 F	AT_{10} overdosage in hypocalcaemic tetany	16	2·5	—	6–7	—

In Cases 3 and 4 the electrocardiographic changes were peculiar to hypercalcaemia and to hypokalaemia respectively, in spite of the combination of the two biochemical disturbances in both of the patients.

Finally, it seems noteworthy that in some cases of hypothyroidism with mild hypercalcaemia, or with a hypercalcaemic pattern of the electrocardiographic record,[5] we failed to note the presence of hypokalaemia and/or an associated electrocardiographic picture of the hypokalaemic type.—We are, etc.,

C. ROMANO.
R. PONGIGLIONE.
G. GEMME.
E. RAFFAELLI.

Department of Paediatrics,
University of Genoa,
Italy.

REFERENCES

[1] Ferris, Th., Kashgarian, M., Levitin, H., Brandt, I., and Epstein, F. H., *New Engl. J. Med.*, 1961, **265**, 924.
[2] Hegglin, R., *Cardiologia (Basel)*, 1943, **7**, 145.
[3] Holzmann, M., L'année cardiologique internationale, *Exp. Scient. Franç.*, 5, 1956.
[4] Romano, C., and Pongiglione, R., *Minerva pediat.*, 1960, **12**, 526.
[5] —— Gemme, G., and Raffaelli, E., *Pediatrics*, 1966, **38**, 694.

Autotransfusion

SIR,—I am glad to note that the safe and life-saving measure of autotransfusion has been duly recognized and emphasized in the leading article entitled "Autotransfusion" (13 May, p. 393). No side-effect has been encountered in a series of 332 cases of ectopic pregnancy reported in the *Singapore Medical Journal*.[1] The response of the patients has been found to be satisfactory, gratifying, and oftentimes most dramatic.

I would like to point out, however, that it is not necessary to put any sodium citrate in the sterile collecting flask. The amount of 3.8% sodium citrate solution advocated in your leading article (1 part of solution to 9 parts of auto-blood) is unnecessarily large and may interfere with the blood-clotting mechanism in a patient who requires a massive amount of auto-blood transfusion.—I am, etc.,

DONALD P. C. CHAN.

Department of Obstetrics
and Gynaecology,
University of Malaya,
Kuala Lumpur, Malaysia.

REFERENCE

[1] Chan, D. P. C., *Singapore med. J.*, 1965, **6**, 23.

SIR,—We would like to endorse the great life-saving value of autotransfusion in the acute ruptured ectopic pregnancy as described in the leading article (13 May, p. 393). For 10 years in a small mission hospital in the West Indies, where ectopic pregnancies are common, we always used autotransfusion. A sterile pack was kept ready for immediate use. It contained two galleypots, a funnel, and a blood-giving bottle together with routine surgical towels, instruments, etc., for a laparotomy. The sterile sodium citrate was purchased in ampoules. On opening the abdomen blood was collected in the gallipots, and using gauze as a filter poured through the funnel into the bottle containing the citrate. Frequently 3 pints (1.7 l.) of blood and sometimes more were returned.

In countries where there is no blood bank and relatives are asked for blood for the patient there is often considerable superstition in donating for the urgent case. The method of autotransfusion is simple and safe and does not require laboratory backing or finances to pay the donors. This method was also used in Government hospitals where the blood bank had but limited supplies.

We do not recall losing one patient with a ruptured ectopic pregnancy, and the number of cases must be well over 100 during the 10-year period.—We are, etc.,

DAVID BULL.
DOREEN BULL.

Leamington Spa,
Warwickshire.

Successful Treatment of Cyanide Poisoning

SIR,—In reporting (17 June, p. 763) the successful treatment of cyanide poisoning with Kelocyanor (cobalt ethylene diamine tetra-acetate), Drs. J. T. B. Bain and E. L. Knowles commented on "the risks involved" in the accepted method of treatment[1] with intravenous nitrite and thiosulphate. We doubt whether there is significant risk in using the accepted method, even in a case where coma may actually be due to cerebrovascular accident rather than to cyanide poisoning. The danger of nitrite-induced hypotension would seem to be more of theoretical than of practical significance. Cases of cyanide poisoning treated in this way usually show a marked improvement in blood pressure, even though the thiocyanate which is produced by the therapy is itself a hypotensive agent. Moreover, the recommended dose of sodium nitrite (0.3 g.) probably[2] produces less than 10% methaemoglobinaemia, and the majority of Chen and Rose's patients recovered with one such dose. They suggested that further amounts may be necessary in severe poisoning, and that up to 1.5 g. could be given without serious ill effects. The fatal dose[2] seems to be about 2 g.

Our experience of one such case has convinced us of the value of Chen and Rose's therapy, and of the dramatic speed with which it takes effect.

A 46-year-old employee in a works where cyanides were used was found unconscious, having been seen well 10 minutes previously. An "egg" of sodium cyanide was found near by. Intravenous nikethamide was given, and he was admitted to the poisoning treatment centre 35 minutes later.

On examination the man was deeply unconscious and not responding to painful stimuli. His breathing was deep and stertorous at a rate of 6 to 8 per minute. He was cyanosed, with a cold clammy skin and a whitish lividity of both feet. The conjunctivae were suffused and cyanosed and the radial pulse rapid and feeble. The blood pressure was unrecordable. No cyanide odour was detected.

His clinical condition was so grave that it was considered necessary to treat him for cyanide poisoning despite the fact that there was only circumstantial evidence for this diagnosis. While a blood specimen was obtained he was given amyl nitrite to inhale. A cuffed endotracheal tube was inserted, without response, and ventilation with oxygen started. This was immediately followed by the intravenous injection of 15 ml. of 3% sodium nitrite during three minutes. When this was completed the respiratory rate had risen to a point which made positive pressure unnecessary. Fifty millilitres of 50% sodium thiosulphate was injected over the next five minutes, by which time the patient was feeling for the endotracheal tube. Ten minutes later it was necessary to remove the tube. Gastric aspiration and lavage were then carried out, and sodium carbonate and ferrous sulphate solutions were left in the stomach. At the completion of this procedure (50 minutes after admission) the patient was fully conscious and orientated. No further injections of nitrite or thiosulphate were necessary.

The man later admitted having attempted suicide by licking a cyanide egg. Rapid absorption of cyanide through the buccal mucosa was consistent with determinations[3] of cyanide and thiocyanate[4] by microdiffusion. Cyanide could not be detected in the gastric aspirate. The plasma level of HCN at admission was 6.1 mg./l.; one hour later this had fallen to a normal basal level (<0.5 mg./l.), but the plasma thiocyanate had risen to 32 mg./l., and remained at a high level for several days. The urinary excretion of thiocyanate reached a peak of 11 mg./l. after four days.

We conclude that until further experience really establishes the efficacy of Kelocyanor there should be no hesitation in using intravenous nitrite whenever there is any possibility at all of cyanide poisoning in an unconscious patient.—We are, etc.,

A. T. PROUDFOOT.

Poisoning Treatment Centre,
Royal Infirmary,
Edinburgh.

S. S. BROWN.

University Department of
Clinical Chemistry,
Royal Infirmary,
Edinburgh.

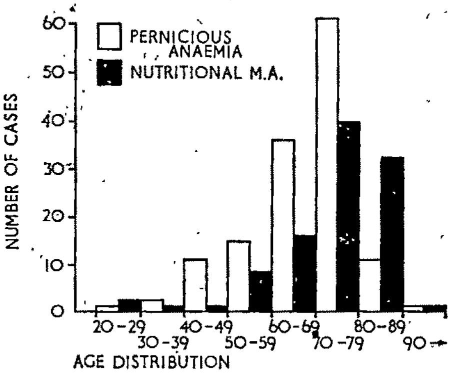
REFERENCES

[1] Chen, K. K., and Rose, C. L., *J. Amer. med. Ass.*, 1956, **162**, 1154.
[2] Bodansky, O., *Pharmacol. Rev.*, 1951, **3**, 144.
[3] Higson, H. G., and Bark, L. S., *Analyst*, 1964, **89**, 338.
[4] Guatelli, M. A., *Meth. forens. Sci.*, 1964, **3**, 233.

Folate Deficiency in the Elderly

SIR,—The recent articles in the *B.M.J.* (10 June, pp. 652, 667, and 670) prompt us to report our own observations.[1]

Since 1961 in every case of megaloblastic anaemia we have routinely performed both serum vitamin-B12 and folate assays. We found the absolute incidence of both pernicious and nutritional megaloblastic anaemia to be highest in the eighth decade, after which nutritional megaloblastic anaemia (M.A.) was more frequent than pernicious anaemia (see Figure). There was no clinical evidence of malabsorption in any of the cases of megaloblastic anaemia due to folic acid deficiency, and in the vast majority a dietary deficiency was found to be the most likely cause. In a small group of the folate deficiency anaemias a folic acid absorption test[2] was performed, with normal results; following folic acid treatment and dietary improvements no recurrence was observed. We feel, therefore,



that there is a good case for the nutritional origin of these megaloblastic anaemias. The high incidence of pregnancy megaloblastic anaemias in our district, 272 over the same 71-month period, would also support the mainly dietary origin of folate deficiency megaloblastic anaemias.

While in some areas it holds true that pernicious anaemia is the predominant megaloblastic anaemia in the elderly, this does not appear to be the case in our patient material. This does not subtract from the importance of the recommendation contained in the last sentence of your leading article, but underlines at the same time the necessity of an exact diagnosis of the deficiency involved in megaloblastic anaemia in any age group—even in the elderly.—We are, etc.,

S. VARADI.
A. ELWIS.

Department of Haematology,
Northern General Hospital,
Sheffield 5.

REFERENCES

[1] Varadi, S., Elwis, A., and Reed, E. R., *XIth Congress of the Internat. Soc. of Haematology*—Abstracts, 1966, 215.
[2] Chanarin, I., Anderson, B. B., and Mollin, D. L., *Brit. J. Haemat.*, 1958, 4, 156.

Problems of Antenatal Care in the Tropics

SIR,—I enjoyed Mr. S. Haroon's excellent paper "Problems of Antenatal Care in the Tropics" (3 June, p. 617). I feel, however, that the section headed "Admission to Hospital" deserved a more prominent place in his thesis. I should like to comment on two aspects of this problem.

Workers in developing countries must constantly remind themselves that, however much they improve their own local practice, they have a responsibility to the often greater part of the population which so far has not been reached by the maternity services, and for whose confinements there will not be enough hospital beds in the foreseeable future. Thought must be given to a programme that will reach this group and will include mobile antenatal clinics, a domiciliary service, outlying delivery units, and, above all, contact with and upgrading of the indigenous midwife. She will continue to be the only source of aid for village women in many parts of the world for a long time to come, and to dismiss her as a "quack" is not to face reality.

In the second place, when it has been decided that a patient is at special risk and must at all cost be delivered in a hospital, experience has shown that for those whose homes are far from hospital and who for various reasons, often quite beyond their control, cannot be relied upon to attend for admission at the onset of labour a maternity "waiting area" or "village" can be very successful. These need not be elaborate institutions; they are effective when no more than simple structures which may be erected by local community effort near a maternity hospital, at little or no expense to the local authority. Patients may stay here for the last two to three weeks of their pregnancy, cared for by a younger relative who shares the simple accommodation and cooks for the expectant mother. During this vital period the patient is available for antenatal care, for education in health and nutrition, and for immediate admission at the very onset of labour, or earlier should complications supervene.

I feel that at the present stage of communications in the rural areas of many rapidly developing countries, to which Mr. Haroon refers, where the pressure on hospital beds is great and will increase, the provision of such waiting accommodation would do as much as any one other single factor to reduce maternal and foetal mortality.—I am, etc.,

R. R. TRUSSELL.

Department of Obstetrics
and Gynaecology,
Makerere University College,
Kampala, Uganda.

Suppository Treatment of Haemorrhoids

SIR,—I was most interested in the article under "Today's Drugs" referring to the suppository treatment of haemorrhoids (13 May, p. 425). While I agree with your contributor that the use of analgesics should be restricted because of the danger of sensitization, I am somewhat surprised that one of the preparations recommended should contain amethocaine, which is a derivative of para-amino benzoic acid, when it is well known that this group of local analgesic agents is the most likely to produce such sensitization.

I think it might be brought to the attention of your readers that there are two preparations which contain lignocaine as the analgesic agent, a local analgesic which does not produce allergy when repeated with anything like the frequency that happens with the ester group. These agents are Xyloproct Plain and Xyloproct H suppositories.—I am, etc.,

VICTOR GOLDMAN.

Department of Anaesthesia,
Eastman Dental Hospital,
London W.C.1.

Muscle Stiffness and Vitamin C

SIR,—Dr. I. H. Syed has described his experiences in using massive doses of vitamin C to prevent or greatly reduce muscular pain following unaccustomed physical exertion (30 July 1966, p. 304). We have carried out a double-blind trial to assess the effect of vitamin C on 47 volunteer oarsmen from two Oxford colleges, one London school, and from one club crew.

The trial covering 11 days consisted of two periods of four days each separated by three "free" days. On the first day of each four-day period strenuous circuit training was performed and five tablets containing 500 mg. of vitamin C or a "dummy" identical in size, colour, and shape were taken, three during the day with meals and one before and after the "circuit." On the second day three further tablets were taken similar to those on the first day. On the third and fourth days no tablets were taken and no "circuit" undertaken. The two treatments were allocated to the subjects randomly, half taking vitamin C in the first period and the other half having the dummy treatment in the first period. Following the three "free" days the procedure was repeated with the other treatment. The subjects and clinician were unaware of the order in which the treatment was allocated. A questionary was completed by each participant daily (except for the "free" days), indicating the degree of muscular pain experienced, any ill effects, the time since last training, and whether or not the rower felt he had benefited from taking the drug.

Analysis of the results showed no detectable difference between vitamin C and the dummy in the relief of severity of pain irrespective of the order in which the treatments were given. The tentative conclusion drawn from the trial was that vitamin C did not prevent or reduce muscular pain after unaccustomed physical exertion, but possibly the design of the trial was not sufficiently sensitive to detect small differences. One complication was that the first half of the trial affected the second half regardless of the order in which the drug and dummy were taken. There was also some bias due to the length of time since the subjects had last trained. Perhaps the major difficulty, however, is the inherent problem of comparing individual assessments of pain.

We are grateful to the oarsmen and their coaches who assisted in this trial, to Dr. J. M. K. Spalding for advice, to Mr. Breffit and Miss C. Witton-Davies, of the Pharmacy Department of the Churchill Hospital, for assistance, and to Roche Products Ltd. for providing us with "Redoxon" and "dummy" tablets.

—We are, etc.,

J. L. CORBETT.

Department of Neurology,
Churchill Hospital, Oxford.

A. BARR,
Chief Records Officer and Statistician.
Oxford Regional Hospital Board.

Neuro-anatomy

SIR,—The department of anatomy at University College London proposes to introduce courses in neuro-anatomy. It is suggested that two levels are needed:

(1) For those anxious to work in some other field of neuro-biology (for example, neurochemistry); such a course might be for three months.

(2) For those with some knowledge of biology wishing to make serious investigations involving neuro-anatomy; this would be a longer course, perhaps one year.

It would help greatly in planning such courses if anyone interested in either direction would be so kind as to write to me. Such a communication would of course in no way constitute a commitment, but it would be of help to the subject to know how many were likely to be interested, say during the next two years. It is intended to approach the Science Research Council for provision of support for suitable applicants, and it would be pointless to do so without an indication of the level of demand and interest.

May I, through your columns, ask anyone who is interested to write to me at the address indicated?—I am, etc.,

J. Z. YOUNG.

Department of Anatomy,
University College London,
London W.C.1.

Phenylketonuria

SIR,—A working party set up by the Medical Research Council is conducting a trial of different diagnostic techniques for phenylketonuria. So far, most helpful information has been obtained by studying the newborn siblings of known cases of phenylketonuria, and we are grateful to those who have helped us in this. We are anxious that this work should continue and we would ask any general practitioner, paediatrician, or obstetrician who knows of the expected birth of a sibling of a known case of phenylketonuria to get in touch with: Dr. L. I. Woolf, Department of the Regius Professor of Medicine, Radcliffe Infirmary, Oxford.—We are, etc.,

ALAN MONCRIEFF.
O. H. WOLFF.
F. P. HUDSON.
L. I. WOOLF.

Radcliffe Infirmary,
Oxford.

Principle of Merit Awards

SIR,—Sir Ronald Tunbridge (24 June, p. 844) states that in any specialty there must be varying degrees of professional competence and skill. This no one will deny, but Sir Ronald goes on to infer therefrom that the rejection of merit awards implies that there are "no differences in the quality of medical practice among general practitioners," and that "23,000 general practitioners are equal in all respects professionally."

With respect, the rejection of merit awards makes no such implication, and surely no one in their senses believes that all general practitioners are equal. What many who oppose merit awards believe is that these awards would do nothing to raise the standard of general practice, but that they would raise the standard of a host of undesirable activities in general practice. For this reason they have been quite rightly rejected by the great majority of general practitioners, and the Representative Body is almost certain to follow the example of the Conference of Local Medical Committees in confirming this rejection.—I am, etc.,

W. B. S. CRAWFORD.

Bath.

SIR,—Sir Ronald Tunbridge (24 June, p. 844) suggests that the country's 23,000 general practitioners imply by their rejection of the proposed merit awards that they believe they are all of equal merit. Any doctor who rejects the proposal on those grounds must be lacking the capacity of self-examination.

It is my belief that the general practitioners have rejected the proposed awards for two reasons:

(1) We do not accept the principle of secrecy in making the awards. If a doctor is considered by any adjudicating committee to have outstanding merit his name should be published within the profession, together with a statement of the grounds on which the award is made. In this way others would be encouraged to emulate his example, and the standard of practice would thus be raised.

(2) Nobody has yet proposed criteria for awards which the general practitioners as a whole consider would, if so emulated, lead to a general improvement in standards among the many different types of general practice conscientiously and effectively carried out in this country.

If secrecy is removed, and satisfactory criteria are drawn up, merit awards will be accepted and welcomed.—I am, etc.,

J. L. RILEY.

Yeadon,
Nr. Leeds, Yorks.

SIR,—As one who voted against the principle of merit awards, I would like to explain my action to Sir Ronald Tunbridge (24 June, p. 844), who believes that the majority of general practitioners are behaving in a ridiculous manner over this. Unfortunately this issue is becoming clouded, and I can understand the wrong conclusions reached by the learned gentleman.

I personally—and I believe many others also—am not against rewarding merit, but if one can clearly define it in general practice it is clear to me that all who are meritorious should receive the same reward. What I and the others voted against was "the principle of merit awards as proposed by the Review Body, and elaborated by the Working Party of the G.M.S.C." To have accepted this would have been to accept that out of 23,000 general practitioners there are 2,600 alone who are worthy of special monetary awards, and that it is possible to select these doctors on a perfectly fair basis.

I cannot accept this, and moreover I do not see how such a scheme could help to raise standards in general practice; there are certainly many better ways of doing this. I *do* see, however, that by a strange coincidence the acceptance of the merit award scheme would satisfy the theory of the Royal Commission that there should be a sufficient variation of incomes in general practice, and this seems to be its main purpose.

The merit award scheme for consultants does not look very satisfactory to me. Is it fair? Has it improved standards? Have we got too many fourth-rate consultants?—I am, etc.,

B. E. COOKE.

Padiham,
Lancs.

Public Health Dispute

SIR,—Your issue of 13 May contained much of significance to public health medical officers. May I make a few comments on one theme? Dr. J. J. A. Reid (p. 432) appears to play down the significance of poor salary rates as a factor in the present decline of morale in the public health service. But in a whole-time service status is closely and overtly related to salary. I remember when the Askwith agreement (1929) was reached the public health doctors were the objects of envy of the other local government chief officers, not excluding the clerks. Since then the salary position of the doctors has deteriorated badly—for which the B.M.A. cannot be held altogether free from blame. At a time when the B.M.A. black-listing appeared to be on the verge of success, in 1949, as soon as the local authorities, being by then in real difficulties about medical staffing, offered to negotiate (at a time they had already agreed the salaries of town clerks and other chief officers) the B.M.A. immediately gave away their most effective weapon, black-listing.

The Ministry of Health's present attitude betokens a sympathy with the local authorities and, it seems to me, a disregard for the welfare of the local health service; a disregard which has been manifest in other ways—namely, (*a*) no support for the suggestion that, when appropriate, medical officers of health should be made honorary members of staffs of hospitals (Guillebaud Report), (*b*) inadequate support for the amalgamation of welfare services with health services, (*c*) inadequate support for medical-officer-of-health membership on executive councils and regional hospital boards, and (*d*) denigration of medical administration.

The salaries of local government departmental medical officers with a maximum of £2,130 are derisory, even in terms of many other local government staff, who have certainly not had their training nor experience nor responsibilities. The salaries of deputy medical officers of health in the smaller authorities are very little better; only in the largest cities and counties does the medical officer of health himself get a salary commensurate with his training and experience. If the B.M.A. wants to protect the living standards of doctors generally it will have to fight hard for public health medical officers. If good doctors are discouraged from entering the service then the organization of preventive health services will decay—to the certain disadvantage of the public.—I am, etc.,

E. D. IRVINE.

Health Department,
Exeter.

Disincentive to Acquisition of Special Skills

SIR,—I wish to call attention to a further disincentive to good general practice and the acquisition of special skills by family doctors.

In 1961, some considerable time before a hospital cytology service in this area was established, I underwent six months' training at King's College Hospital in my spare time so as to be able to screen our own patients for cervical carcinoma. I also did six weeks' intensive study in the gynaecological department there and have since done a refresher course in cytology. With the aid of the Medical Research Council a long-term study of the cytology and sequelae of cervical erosions was begun. A yearly cancer check-up was offered to all women who wished it in our practice, which included a careful clinical examination and cytological screening. Records have been carefully checked and all slides stored against future need for research purposes. The service was free to patients and no payment was received for the work involved. In April 1967 a fee of 7s. 6d. for taking smears from women over 35 once every five years was instituted. This small sum was at least a token acknowledgement that this service was in the public interest.

Two days ago we received a directive to the effect that no fee would be paid unless the slides were examined at the hospital pathology service. One is therefore paid for *not* doing work which has in the past provided a welcome service to some 800 patients a year. The hospital service in turn will suffer from an influx of slides to swell its already overburdened resources. The absurdity of a situation where one is paid not to acquire special skills is self-evident.

Admittedly only a few family doctors will be affected by this decision and one might have expected that those who wanted to continue cytology should produce a certificate of competence in cytology from their training centre, but it is disheartening to realize that bureaucratic regulations can effectively stifle enthusiasm for learning and skill in general practice.—I am, etc.,

UNA M. P. KROLL.

St. Pauls Cray,
Kent.

Democratic Efficiency at the A.R.M.

SIR,—Consideration of the agenda for the Annual Representative Meeting for this year (*Supplement*, 10 June, p. 149) with its nearly 600 items, and the reports one has had of the meetings of recent years, makes one wonder how effective our medical democracy is at present. With a programme of this size it is impossible to hold proper discussions or make useful decisions, even though organization is efficient, the acoustics and weather favourable, the speeches as short as the fashionable mini-skirts, and any blitzkrieg from the junior hospital doctors not too formidable. It is surely time we realized the value of Sir Winston Churchill's oft-reiterated advice "to put all the facts down on half a sheet of notepaper."

There are two changes which, I suggest, might improve things—to ration the number of motions a Division can send up, and to empower the Agenda Committee to prune the programme more ruthlessly. It is well known that some Divisions are more loquacious than others. Study of the agenda shows that at least 29 Divisions, including, I must admit, my own, have submitted more than one motion, with an average of seven, and that nine Divisions have submitted 10 or more motions. In our process of modernization it would surely not be unreasonable to limit each Division to one motion—quality and enthusiasm might improve inversely to diffuseness and prolixity.

At present the Agenda Committee groups together motions on similar subjects and stars one of them. Might it not be better for only the main subjects which could be satisfactorily dealt with in the time available to be listed? More simplification on these lines could cut down enormously the verbosity of the agenda, decrease the great clerical work and expense involved, and decrease the chances of mistakes and overlapping.

Democracy is on trial in many parts of the world. Surely a learned profession in this home of democracy can show an example of modern efficiency in the conduct of its affairs, which are of such importance to every citizen.—I am, etc.,

BRYAN WILLIAMS.

Middlesbrough.

Health Centres

SIR,—I must take issue with Dr. T. D. Richards (10 June, p. 703) on the second paragraph of his letter. If the N.H.S. is to continue providing an unlimited service then this should be the most economical in available manpower. The present system of single-handed or partnership practices does not economize in manpower. Particularly in urban areas there are many "rival" general practitioners, serving the same districts and even the same family. In my view, if an efficient and economic system is to be devised, the alternative to limiting the service available is to provide centres from which a team of general practitioners serve a specific "district." This of course removes the patients' free choice of doctor, and probably means a salaried service.

The remainder of Dr. Richards's letter is most pertinent. The one factor which will save the profession from a salaried service oriented on health centres is the astronomical cost. Undoubtedly the centres would become similar to hospital outpatients, with all the staff working on a shift system. But to talk of collecting evidence to find out if doctors or patients desire health centres is nonsense in the present situation. The problem is not what is desired, but what can be provided for the least money, and in these circumstances the present system is cheapest. When enough practices have organized themselves no doubt the Government will take over, as in 1948, and use suitable premises as centres, which will be cheaper than providing them ab initio.

I must point out that this is not a defence of health centres or a salaried service. Both were envisaged in the original Act, and I believe that the N.H.S. is moving steadily, if slowly, in that direction. The encouragement of group practice is really helping to set up private health centres; machinery for a salaried service is included in the Charter. I personally believe that the patient wants to remain an individual with his own doctor. Much of the present trouble of general practice stems from the attempts to give this service to the public on unlimited demand and free at the time. Nothing could be further from the truth than the premise on which the N.H.S. is founded. It is not an individual's unalienable right to enjoy good health and the best medical care; it is a privilege, and as such must be paid for.—I am, etc.,

H. CAIRNS.

Cardiff.

SIR,—Dr. T. D. Richards writes (10 June, p. 703) that "it is time we started collecting evidence from the patients" about "what proportion . . . in the country prefer health centres to the personal service the good family doctor can now provide in his own consulting-room."

What sort of choice is it that anyone—patient or doctor—makes between something one has experienced and something one has not. Surely only a choice founded on prejudice. The only realistic way of arriving at Dr. Richards's ratio is to ask patients who have sampled both sorts of practice, not "all the patients . . . in the country." Such an opinion poll must of course include not only the patients who have remained in health-centre practices but those who have left such centres to return to orthodox practices, either because they did not care for health centres or because they moved to a district where no health centre existed. Allowance would also have to be made for the fact that there are, I suspect, good and not-so-good health centres, just as there are good and not-so-good practices. Most patients will prefer a good doctor in a well-run practice to a poor doctor in a badly run health centre. In my opinion centres which become "institutions similar to hospital outpatients" *are* badly run.—I am, etc.,

D. S. RACTLIFFE.

Westbury-on-Trym,
Bristol.

East Yorkshire's Memorandum

SIR,—Exception has rightly been taken to an error in our Memorandum on the Constitution (*Supplement*, 3 June, p. 143). The phrase, "The Representative Body, the national forum, is not representative of hospital junior doctors, but the ratio of general practitioners to consultants is approximately correct," should read:

"The Representative Body, the national forum, is not representative of hospital junior doctors but the proportion of consultants is approximately correct."

Consultants form 12% of the home membership of the Association (6,000 in 50,000) and in a Representative Body with 500 members should have 60 seats. In fact they occupy 77.—We are, etc.,

R. L. LUFFINGHAM.
S. T. LUNT.
Joint Secretaries.

Hull, Yorks.

Medical Practice Freedom Fund

SIR,—You were kind enough to grant space in your columns[1, 2] for the publicizing of the above fund. This you may remember was launched in Birmingham, with the object of supporting those doctors who had resigned from the National Health Service. The support was generous; indeed, many of our N.H.S. colleagues are still contributing to the fund.

However, we feel that the fund has now served its purpose, and some restitution must be made to the contributors. Accordingly, a meeting was held at Berrow Court, in Birmingham, on 28 May, of the trustees, committee members, and donors, in order to formulate future policy. Details of the resolutions will be sent to each donor, but, briefly, the proceedings may be summarized as follows:

(1) Contributions by subscribers should be terminated by the end of July 1967.

(2) The borrowers from the fund will shortly be asked to commence repayment over a period of two years.

(3) All subscribers, who have not yet received repayment of their loans to the fund, will be paid an initial 25% of their total contribution, in September 1967.

(4) A further meeting of the trustees, committee, and subscribers, will take place in one year's time, to reassess the financial position.

(5) No more loans are to be granted after July 1967.

In conclusion, Sir, may I express the hope that this letter and subsequent action by their committee will assure the doctors who have subscribed so generously to the fund that the financial position is being regularly reviewed.—I am, etc.,

P. G. JONES,
Secretary to the
Medical Practice Freedom Fund
and Birmingham Action Group.

Birmingham.

REFERENCES

[1] Wainwright, A. J., *Brit. med. J.*, 1965, 2, 424.
[2] Ibid., 1965, 2, Suppl., p. 27.

Points from Letters

Dispensing in Rural Areas

Dr. K. T. BROWN (Pebmarsh, Essex) writes: I too wish to protest against the mischievous Memorandum on Rural Dispensing. Rural doctors are performing a vital function. . . .

We have here scattered villages served by one bus on a Tuesday and another on a Thursday. Many patients have no cars. However, immediate medical attention is the rule, and often the required drugs are handed over by the rural doctor to the patient in his home. Our patients enjoy so prompt a service that so far I have met nobody who has one good word for the Memorandum. That most certainly includes local members of our Women's Institute.

Obituary Notices

Sir CLAUDE FRANKAU, C.B.E., D.S.O., M.S., F.R.C.S.

Sir Claude Frankau, consulting surgeon and emeritus lecturer in surgery to St. George's Hospital, died at his home near Saffron Walden, Essex, on 29 June. He was 84.

Claude Howard Stanley Frankau, the youngest son of F. J. Frankau, a barrister, was born on 11 February 1883. He was educated at Rugby School and studied medicine at St. George's Hospital medical school. In 1907 he qualified with the Conjoint diploma and the following year became a Fellow of the Royal College of Surgeons of Engand. In 1909 he graduated M.B., B.S. at London University, and also gained the William Brown exhibition. He had gained the Herbert Allingham surgical scholarship in 1908. After the usual house appointments and surgical registrarship he was elected to the surgical staff of St. George's Hospital. When the first world war broke out he volunteered for service and was put in charge of a forward casualty clearing station, where he showed his surgical skill and initiative by operating successfully on many gunshot wounds of the abdomen, performing one of the earliest successful resections of the colon for damage by gunshot. His obvious ability was noted, and he was promoted to the position of consulting surgeon to the Fifth Army with the rank of colonel (temporary). He was thrice mentioned in dispatches, and was honoured by the conferment of the D.S.O. in 1918 and the C.B.E. the following year. In 1921 he took the M.S., and was awarded a gold medal.

Frankau was a general surgeon, but at different times he was in charge of the genito-urinary and the fracture departments of St. George's Hospital. He was for several years lecturer on surgery in the medical school. He was also consulting surgeon to the Waterloo Hospital for Women and Children, Queen Charlotte's Hospital, Woodford Hospital, and the King Edward VII Convalescent Home for Officers at Osborne. In addition, he served as adviser in surgery to the Ministry of Health. Frankau examined in surgery for the University of London, and from 1926 to 1934 was a member of the court of examiners of the Royal College of Surgeons. His high reputation among his professional colleagues was shown by his being elected president of the Association of Surgeons of Great Britain and Ireland in 1937–8 and by his being chosen president of the surgical section of the Royal Society of Medicine in the following year.

In the second world war Frankau was appointed to the very responsible post of director of the Emergency Medical Services for London and the Home Counties. In this position his promptitude, resource, and general administrative ability were outstanding, and it was largely owing to him that the thousands of casualties resulting from the bombing were so smoothly and adequately provided for. In 1945 his outstanding services were recognized by his being knighted.

Claude Frankau was tall, dark, and distinguished-looking. He had a caustic wit, and was adept at deflating pompous persons. Though essentially good-natured and willing to help where help was needed, his outward manner did not always reveal his inward generosity and kindness. While not a prolific writer, he published several valuable articles, including the chapter "Wounds of Joints" in the *Medical History of the First World War*.

Frankau was twice married, firstly in 1914 to Edith Lorne MacDougall (died in 1934), by whom he had two sons and a daughter; and secondly to Isabella, widow of Gordon Cunningham. She died last May.

Lieutenant-Colonel S. R. PRALL
B.A., M.D., I.M.S.(RET.)

Lieutenant-Colonel S. R. Prall, formerly of the Indian Medical Service, died suddenly at his home in Sutton Valence, Kent, on 2 June. He was 76.

Samuel Reginald Prall, son of the late Lieutenant-Colonel S. E. Prall—a well-known "character" in the East, and for many years port health officer in Aden—was born on 18 February 1891. He was educated at Tonbridge School and Emmanuel College, Cambridge, where he held an open scholarship in the natural sciences. After graduating B.A. with honours he entered St. Bartholomew's Hospital, London, for his clinical studies, which were interrupted by the outbreak of the first world war. He spent some months on the North Sea as a surgeon-probationer R.N.V.R. before returning to qualify with the Conjoint diploma in 1915, graduating M.B., B.Chir. the following year. He then took a temporary commission in the R.A.M.C. and served in France and India until 1921, when he received a permanent commission in the Indian Medical Service, in which he remained until the transfer of power in 1947. He proceeded M.D. in 1931.

The last sixteen years of his service were performed on the civil side in the Bombay presidency. He held charge of many civil district hospitals and enjoyed high repute as a good all-round physician and surgeon. As a senior civil surgeon he held charge of St. George's Hospital in Bombay, and he ended his service with four years as civil surgeon, Poona, superintendent of the Sassoon Hospital with its attached medical school, lecturer in gynaecology and obstetrics, and personal surgeon to the Governor of Bombay. A much-respected clinician, he bore an overwhelming clinical and teaching burden through the years of the second world war.

Prall retired to South Africa in 1947, but returned to England after two years and entered into general practice in Kent. He conducted a large and varied practice for ten years, and his vast experience and all-round competence were greatly appreciated. In 1954 he was run over in a road accident and sustained very severe injuries, including a ruptured spleen and colon, a fractured pelvis, and dislocated shoulder, but his brave spirit enabled him to make a good recovery and to return to work, though his competence as a first-class golfer was permanently impaired. He retired to Sutton Valence after ten busy years. In 1918 he married his wife, who survives him with one daughter and an adopted son, to whom our sympathy is extended.—G. R. McR.

H. S. W. writes: I worked under and with Lieutenant-Colonel S. R. Prall for several years in Bombay before and during the second world war, when he had to carry out the duties not only of physician, surgeon, and obstetrician for the men of the old Indian Services and their families but also to administer the large European hospitals, first in Bombay and later in Poona. He was always a sound clinician and an excellent practical and unflurried operator, but above all one was impressed by his great kindness to all those who came in contact with him, from those of the highest rank to the humblest sweeper and his family.

He was a natural games player in his early days, a first-class golfer, and an excellent host and companion. His many friends will always be thankful to have known him and his cheerful family, and will sympathize with them now in their sad loss.

T. PRICE, M.B., M.CH.

Mr. T. Price, formerly consultant orthopaedic surgeon to the Bath clinical area, died at his home in Heswall, Cheshire, on 18 June. He was 53.

Tom Price was born on 2 May 1914 at Connah's Quay, Flintshire, and was educated at Hawarden Grammar School, after which he entered the University of Liverpool for his medical training. He qualified M.B., Ch.B. in 1939, and the same year took the Conjoint diploma. After holding resident posts in Liverpool he joined the R.A.M.C. in 1941, and in spite of the disability of congenital hip trouble he served with distinction for four years, of which he spent three and a half years in India. After demobilization in 1946 he returned to Liverpool, and took the M.Ch. in orthopaedic surgery in 1947. Shortly after this he was appointed to the Bath and Wessex Orthopaedic Hospital, where much of his time was devoted to the children's clinics of Somerset and Wiltshire. When the National Health Service was established in 1948 he was appointed consultant orthopaedic surgeon to the clinical area, and he fulfilled this post with great enthusiasm and efficiency. In 1957 his health began to fail, but in spite of this additional disability he continued to work heedless of the cost to himself. He insisted on sharing the emergency work and the routine with his colleagues, and put his patients' interests above everything else. Eventually in 1964 he was forced to give up and was prematurely retired. He was a member of the British Orthopaedic Association, and was chairman of the Bath Division of the British Medical Association in 1954–5.

Tom Price was a quiet, competent surgeon with a great love for his work and for his patients. He particularly enjoyed " cold " orthopaedics, and with his own disability he established a close relationship and mutual regard with his patients. His name will long be remembered in the counties of Somerset and Wiltshire and by his many friends, young and old alike, in the city of Bath. He died in sight of his beloved Welsh mountains and the beautiful Dee estuary. He leaves a widow, Mary, whose devoted care and companionship enabled him to enjoy his short retirement.—A. E. B.

Ll. RHYS-JONES, M.R.C.S., L.R.C.P.

Dr. Ll. Rhys-Jones, a general practitioner in Aberystwyth, Cardiganshire, died in hospital on 29 May. He was 73.

Llywelyn Rhys-Jones was born in 1893 in Treorchy, South Wales. Before taking up medicine as a career he had intended entering the church, and with this in view he gained a scholarship to St. David's College, Lampeter. From Lampeter he gained a further scholarship to Jesus College, Oxford. His education was interrupted by the outbreak of the first world war, and he was commissioned first in the Royal Welch Fusiliers and later in the King's African Rifles. He served in France and East Africa. After demobilization he returned to Oxford. He had, however, then made the vital decision to abandon his theological training and to qualify as a doctor. Becoming a student at Guy's Hospital, he qualified with the Conjoint diploma in 1925. His first practice was in Brixton, South London, but in 1948 he returned to Wales to practise in Aberystwyth.

His early training in theology and the arts marked him out from among his fellow practitioners. Apart from his work as a doctor his main interest throughout life remained in Welsh literature. He was himself a poet and was proud of his relationship to Ben Bowen, a promising Welsh bard who died when he was a very young man. Dr. Rhys-Jones derived great pleasure from his membership of the Bedol, a small group in Aberystwyth whose primary interest has been in the cultivation of Welsh literature. Yet his main concern rested in his endeavours to relieve suffering. His first thought was for his patient and his family, and nothing was too much trouble for him. His kindness, sympathy, and conscientiousness endeared him to all his patients.

He is survived by his widow, a son, and a daughter.—J. A. W.

J. R. B. RUSSELL, M.B., CH.B.

Dr. J. R. B. Russell, formerly in general practice at Chester, died in Chester Royal Infirmary on 13 May at the age of 79.

John Russell Brodie Russell was born in Edinburgh on 3 May 1888, and was educated at Denstone College. After leaving school he studied law for a year in Edinburgh, but finding it too detached from human contact he went to Manchester University to study medicine, graduating M.B., Ch.B. in 1914. After resident posts at Manchester Royal Infirmary he joined the R.A.M.C. in the same year, serving with the Lancashire Fusiliers, and saw active service at Passchendaele and Vimy Ridge. He attained the rank of major, and was invalided in 1916. After demobilization he came to Chester, where he was initially in charge of St. James's Hospital (now Chester City Hospital). At that time he carried out most of the operations in the surgical and maternity departments. A few years later he joined Dr. J. L. Browne in practice in Chester, continuing with some surgical work at St. James's Hospital for another ten years. When Dr. Browne died in 1935 Dr. Russell continued the practice with the help of assistants until he was joined by his son in 1951. His kindly manner coupled with a quiet humour endeared him to his large number of patients, who were helped by the courtesy and patience with which he listened to their problems. His work was his principal interest, and he kept his knowledge of medicine up to date by diligent reading.

When failing health led to his retirement in 1964 his friends were concerned that he might find it difficult to develop new interests. However, he took up painting with the same energy he had previously devoted to medicine, and rapidly achieved a consistently high standard of production in his own particular manner. His representational style is not now generally popular, but many would have been pleased to emulate his work after a lifetime of application. Although increasingly handicapped physically, he had great happiness from his few years of retirement, which he shared with his daughter, who looked after him devotedly after his wife's death.—A. C. C. H.

JANIE H. McILROY, M.A., D.SC., M.B., CH.B., D.P.H.

Dr. Janie H. McIlroy, formerly honorary senior clinical assistant at the Royal Westminster Ophthalmic Hospital (now Moorfields), London, died at her home in Ayrshire on 21 May. She was 87.

Janie Hamilton McIlroy was born in 1880, daughter of the late Dr. James and Mrs. Anne McIlroy, of Ballycastle, Northern Ireland. After graduating M.A. at Glasgow in 1898 at the early age of 18 she took the B.Sc. in 1901 and the M.B., Ch.B. in 1904. She then embarked on a distinguished scientific career, winning several research scholarships, and becoming D.Sc. in 1911. The following year she took the D.P.H. But her interest now turned to ophthalmology, and after an appointment as assistant medical officer and full-time oculist to the Education Authority, Glasgow, she went to India as lecturer in diseases of the eye at the Lady Hardinge Medical College, Delhi. On her return to Britain she continued with ophthalmic work, and was appointed clinical assistant at the Royal Westminster Ophthalmic Hospital, London, in 1926, becoming chief clinical assistant the following year. Here it was that she worked happily for many years in conjunction with an ophthalmic post in the L.C.C. medical service, retiring with the advent of the National Health Service in 1948. Her cheerful presence and willingness to help made her a most popular member of the clinic in which she worked, and her scientific background showed in the logical way in which she attacked all problems.

Her good humour, patience, and tact endeared her to the patients, and when she retired and left London she was much missed by all. But she is not forgotten by her friends.—G. G. P.

W. H. PARKINSON, M.B., CH.B.

Dr. W. H. Parkinson, a senior assistant medical officer in charge of the maternity and child welfare services in Northampton, died suddenly on 5 June. He was 53.

Wilfrid Hampson Parkinson was born on 15 April 1914, and was educated at the Royal School, Edinburgh, and Edinburgh University, graduating M.B., Ch.B. in 1941. He entered general practice in 1947 and succeeded as principal in January 1949 at Byfield, near Rugby, where he remained the sole practitioner until he was obliged to retire from general practice in 1966 on account of ill-health. In December of that year he entered the field of public health as senior assistant medical officer in charge of the maternity and child welfare service in Northampton, and his sudden death was a tremendous loss to the department. In his short term of office he had shown himself to be an extremely able and competent colleague, scrupulous and diligent in the pursuit of his new responsibilities, to which he had adapted himself with enthusiasm and success. His calm, quiet, and charming manner not only endeared him to all in the department who worked with him but quickly earned him the respect of his colleagues.

His untimely death is a sad and tragic blow, not only to the department, but more particularly to his wife and three children, to whom we extend our deepest sympathies. —W. E.

D. B. STEPHEN, M.B., CH.B.

Dr. D. B. Stephen, formerly in general practice at Enfield, Middlesex, died suddenly at his home in Enfield on 16 June. He was 57.

David Bishop Stephen was born in Aberdeen on 17 March 1910, and received his medical education at Aberdeen University, graduating M.B., Ch.B. in 1937. He first entered practice in Coventry, but his practice was blitzed in the second world war, and he went to Enfield as an assistant to Dr. R. Adam to succeed his twin brother, George, who had been called up. Shortly afterwards he joined the R.A.M.C. and served in Italy, where he was graded as a dermatologist. After demobilization he returned to take up a partnership with Dr. H. P. Warren, while his brother returned to take up partnership with Dr. J. E. Carpenter, both in general practice in Enfield. David later entered into partnership with Dr. P. McCulloch, and became medical officer to the Small Arms factory. His twin brother died some three years ago.

He is survived by his widow, to whom we extend our deepest sympathy.—H. R. S.

News and Notes

EPIDEMIOLOGY

Coroners' Verdicts in Greater London

The seven coroners in Greater London have given the Greater London Council the following information about their verdicts on the 3,641 inquests held in Greater London in 1966. Comparable figures for the previous year exist only for the nine months from 1 April.

Verdict	1966	1965 (Nine Months Only)
Murder	18	9
Manslaughter	3	8
Suicide	992	814
Self induced or attempted abortion	4	4
Lack of care or self neglect	6	6
Chronic alcoholism ..	45	46
Addiction to drugs ..	9	10
Want of attention at birth	2	3
Industrial diseases ..	32	23
Accident or misadventure	2,007	1,381
Stillborn	6	4
Natural causes	90	55
Open verdicts	249	161
Adjourned	178	119

Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available.

	Week Ending 16 June	Week Ending 23 June
Dysentery		
Bedfordshire	9	**15**
Biggleswade R.D. ...	0	**10**
Durham	8	**20**
Gloucestershire	25	**23**
Bristol C.B.	25	**21**
Greater London	70	**58**
Southwark	10	**13**
Lancashire	107	**126**
Blackpool C.B. ...	5	**15**
Liverpool C.B. ...	10	**10**
Preston C.B.	11	**21**
Eccles M.B.	10	**11**
Prestwich M.B. ...	5	**10**
Preston R.D.	1	**14**
Northumberland ...	15	**29**
Ashington U.D. ...	13	**16**
Morpeth R.D.	2	**10**
Dysentery (contd.)		
Warwickshire	49	**58**
Birmingham C.B. ...	13	**14**
Coventry C.B. ...	19	**28**
Rugby M.B.	17	**15**
Yorkshire West Riding ...	74	**47**
Bradford C.B.	39	**14**
Leeds C.B.	18	**17**
Edinburgh	40	**36**
Glasgow	32	**26**
Food-poisoning		
Greater London	28	**58**
Hillingdon	0	**29**
Lancashire	20	**25**
Liverpool C.B. ...	12	**20**
West Lothian County ...	0	**11**
Measles		
Lancashire	446	**455**
Liverpool C.B. ...	110	**136**
Leicestershire	316	**242**
Leicester C.B. ...	170	**106**
Nottinghamshire ...	280	**187**
Nottingham C.B. ...	133	**104**
Warwickshire	352	**325**
Birmingham C.B. ...	180	**121**

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **17 June** (No. 24) and corresponding week 1966.

Figures of *cases* are for the countries shown and for Greater London. Figures of *deaths* and *births* are for the whole of England and Wales (London included), Greater London, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ...	0	0	0	0		0	0	4	0	
Dysentery ..	486	70	95	23	5	520	114	78	18	9
Encephalitis, acute ..	0	0		0		1	0		0	
Enteric fever: Typhoid ..	3	1	0	0		1	0	1	0	
Paratyphoid	0	0	0	0		6	1	0	0	
Food-poisoning	94	28	5	49		318	37	13	3	
Infective enteritis or diarrhoea under 2 years				23	52				23	56
Measles* ..	7,254	511	55	136	241	6,574	714	93	138	266
Meningococcal infection ..	6	0	1	2		9	3	2	0	
Ophthalmia neonatorum	8	0	2	0		17	2	1	0	
Pneumonia† ..	83	11	63	0		60	11	60	7	1
Poliomyelitis, acute: Paralytic ..	0	0	0	0		0	0	1	0	
Non-paralytic	0	0	0			0	0	0		
Puerperal fever§	60	22	3	0		76	27	3	0	
Scarlet fever ..	417	56	21	13	9	347	71	21	21	8
Tuberculosis: Respiratory ..	216	54	38	4		238	66	44	7	
Non-respiratory ..	60	8	15	1		49	13	9	4	
Whooping-cough	556	69	99	7	50	320	55	41	6	19

DEATHS	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0		0	0	0	0		0		0
Dysentery ..	1	0		0		0	0			
Encephalitis, acute ..					0					0
Enteric fever ..	0	0	0	0		0	0	0		
Infective enteritis or diarrhoea under 2 years	4	0	0	0	1	6	2	1		1
Influenza ..	2	1	0	0	0	3	2	0		0
Measles ..	0		0	0	0	0		0		
Meningococcal infection ..			1					0		
Pneumonia ..	573	71	14	14	7	485	69	18		6
Poliomyelitis, acute ..	0	0		0	0	0	0			0
Scarlet fever ..	0		0	0	0	0		0		0
Tuberculosis: Respiratory .. Non-respiratory ..	38	6	3	0	1 0	40	9	4		1 0
Whooping-cough	1	0	0	0	0	0	0	1		0
Deaths 0-1 year	241	47	17	13	10	278	49	23		8
Deaths (excluding stillbirths)	9,575	1476	544	117	130	8,839	1408	472		148
LIVE BIRTHS	16,685	2784	890	269	490	16,759	2944	896		469
STILLBIRTHS	239	29	18			235	39	9		

* Measles not notifiable in Scotland, whence returns are approximate.

† Includes primary and influenzal pneumonia.

§ Includes puerperal pyrexia.

PARLIAMENT

Abortion Bill in Jeopardy

The report stage of the Medical Termination of Pregnancy Bill was unfinished after 12 hours' debate that ended about 10 a.m. on 30 June. Over 200 M.P.s, stayed throughout the night, a measure of the Commons' interest in abortion reform. It must now be considered doubtful if the Bill will get on the Statute Book this session. Even if the Government provides more time and the Bill goes through the Commons, it has still to be conducted through all its stages in the House of Lords.

During the debate the significant change was made of removing from Clause 1 the contentious "well-being" condition. This was done at the instance of the sponsor of the Bill, Mr. D. STEEL (Roxburgh, Selkirk and Peebles, Lib.), and received the approval of the Home Secretary, Mr. R. JENKINS, who has regarded the Bill as a worthwhile and reforming measure that should be acceptable "to a good deal of moderate opinion both inside the House and outside."

With some other related amendments Clause 1, subsection (1)(a)(i) now reads: "That the continuance of the pregnancy would involve risks to the life of the pregnant woman or any existing children of her family."

Questions in the Commons

[FROM OUR PARLIAMENTARY CORRESPONDENT]

Treatment of Drug Addiction

Mr. W. DEEDES (Ashford, Con.) asked the Minister of Health on 26 June what consultations he had had with the London teaching hospitals about future arrangements for treating drug addiction in London.

Mr K. ROBINSON: "General principles of treatment of heroin addiction were considered at two medical conferences of the consultant psychiatrists concerned. Separate discussions took place with each hospital individually. Informal discussions on points of practical application will continue with a group representative of interested London hospital boards."

Mr. DEEDES said that at least one London teaching hospital had grave misgivings about certain aspects of this scheme and doubted whether it would work. Was the Minister sure he was proceeding on the right lines ?

Mr. ROBINSON replied that as far as he was aware there was no general dissent among those primarily concerned about the way they were proceeding. Outpatient facilities were available at nine hospitals in central London, and other clinics would be opened in due course. About 30 hospitals in the London area already provided facilities for inpatient treatment of addicts of all types.

Health Centres

The Minister of Health stated on 28 June that since July 1948, when there were 10 health centres in existence, 36 more had been opened in England and Wales, 30 more were under construction, 28 had been approved, and plans for 48 were under consideration. Present evidence suggested that the 10-year plans of local health authorities for 300 centres by 1976 might be greatly exceeded.

Alcoholism in Scotland

Mr. W. HANNAN (Glasgow, Maryhill, Lab.) asked the Secretary of State for Scotland on 28 June how many patients suffering from alcoholism or alcoholic neurosis were admitted to mental hospitals in 1956, 1961, and 1966 ; and what proportion of the total bed accommodation such patients occupied in those hospitals.

Mr. B. MILLAN, Under Secretary: "The numbers admitted were 732, 1,350, and 2,755 respectively, which constituted 7.1%, 9.9% and 13.6% of the total admissions to such hospitals. For 1966 these figures include admissions to psychiatric wards in general hospitals. I regret that figures are not available for the proportion of total bed accommodation in these hospitals occupied by alcoholic patients. On average, however, their length of stay is shorter than that of other patients in these hospitals."

Mr. HANNAN wanted him to include alcoholism in the considerations of the committee on drug addiction. Mr. MILLAN thought this impracticable, but told him that regional boards had been asked to set up special units to deal with alcoholism and some were already being established.

General Practitioner Service in Scotland

The Secretary of State for Scotland gave the following figures on 26 June showing the total number of doctors working the general practitioner service in Scotland since October 1964:

	Principals	Assistants	Total	Trainee Assistants
1964 October	2,684	106	2,790	44
1965 January	2,680	109	2,789	45
April ..	2,671	116	2,787	44
July ..	2,651	105	2,756	50
October	2,638	90	2,728	46
1966 January	2,618	100	2,718	36
April ..	2,610	105	2,715	26
July ..	2,615	90	2,705	23
October	2,597	78	2,675	33
1967 January	2,594	89	2,683	35
April ..	2,601	85	2,686	39
June ..	2,606	92	2,698	40

Breath Alcohol Tests

Mr. GRESHAM COOKE (Twickenham, Con.) asked the Home Secretary on 22 June what study he had made of the evidence sent to him tending to show that breath alcohol tests could give spuriously high results for as long as 30 minutes after the consumption of alcohol ; and whether arrangements would be made to instruct the police fully about this aspect of the matter.

Mr. ROY JENKINS: "Authoritative investigations have shown that traces of alcohol in the mouth do not ordinarily persist after 20 minutes from the time of drinking. I shall advise the police that this is the minimum time which should elapse between a roadside test and the offer of a second test at a police station."

New Fulham Hospital

Mr. IVOR RICHARD (Barons Court, Lab.) asked the Minister of Health whether he was satisfied with the speed of the development of the new Fulham Hospital.

Mr. J. SNOW, Parliamentary Secretary: "Yes. Initial site works are in progress. The main works, costing some £10 million, will begin this autumn, and the final phase is likely to start in 1972-3. The whole of this major project to rebuild the Charing Cross Teaching Hospital and Medical School and to replace a number of other scattered hospitals is scheduled for completion by 1976."

Emigration of Doctors

Mr. J. BIFFEN (Oswestry, Con.) asked the Minister of Health on 3 July what study he had made of the evidence about emigration of doctors contained in a survey conducted by the Junior Hospital Doctors Association.

Mr. ROBINSON: "This survey was, I understand, undertaken in a single hospital region in order to obtain experience for a wider one, and the results quoted can only be preliminary. I expect to publish shortly the results of my department's work on the emigration and immigration of doctors during the period 1962 to 1964, which will describe in considerable detail the general features of this movement."

The Sexual Offences (No. 2) Bill passed the report stage in the House of Commons and was read a third time on 4 July.

The National Health Service (Family Planning) Act was given Royal Assent on 28 June.

Questions in the Lords

Lead in Water Supplies

LORD DOUGLAS OF BARLOCH asked the Government on 27 June what advice, if any, had been given to water undertakers about the necessity of correcting water supplies that are liable to dissolve lead.

LORD SORENSEN said no general advice had been given, since the normal remedy, treatment of the water with alkali, was simple and well known.

LORD DOUGLAS OF BARLOCH pointed out that a recent survey carried out by the department of civil engineering at Liverpool University showed that in county boroughs with a population of 20m. 95% had water supplies that were liable to dissolve lead. Did not that require attention ?

LORD SORENSEN said his information did not cover that point but added that the use of lead pipes for water was declining and in many parts of the country the practice did not exist.

MEDICO-LEGAL

Court Orders Blood Test

[FROM OUR LEGAL CORRESPONDENT]

A judge of the Probate, Divorce, and Admiralty Division of the High Court has ordered that a child should undergo a blood test with a view to determining paternity (*The Times*, 2 June).

A decision of the Court of Appeal in 1964[1] that the Court had no power to order parties to a suit to undergo blood tests remains unimpaired. The judge in the present case, Mr. Justice Ormrod, in making the order for the test, drew on the jurisdiction of the Court as custodian of the child. He held that the jurisdiction was unaffected by the earlier decision of the Court of Appeal.

The question of paternity arose in June 1965, after a husband had been granted a decree of divorce on the grounds of his wife's adultery with the party cited. There was a child of the wife's who could be the daughter of either the husband or the party cited. The court had ordered that the paternity of the child be tried as an issue. That issue was first argued in June 1966, when it was appreciated that the earlier decision of the Court of Appeal prevented the ordering of a blood test. The husband, wife, and party cited all consented to undergo a blood test, as all wanted to resolve the genuine doubt about paternity. But the Official Solicitor, who was acting as guardian *ad litem* for the child, refused to consent on behalf of the child. In the absence of any other helpful evidence the court would have had to fall back on the presumption of legitimacy and hold that the husband was presumed to be the father. Instead of deciding the matter in this unsatisfactory way the court adjourned the hearing for argument on its custodial jurisdiction.

In the course of argument on the court's powers relative to children in its care, counsel for the Official Solicitor conceded that a Chancery judge in wardship proceedings could order that a ward submit to a blood test but argued that a judge of the Divorce Court did not have those powers. Mr. Justice Ormrod acepted the concession but rejected the argument that a judge in one division of the High Court did not have all the powers of a judge in another division of the court on similar subject-matter. Whether the Official Solicitor's concession was rightly made or not does not appear to have been argued.

Accordingly Mr. Justice Ormrod held that he had the power to order a blood test on the child in the exercise of his custodial jurisdiction, and would exercise it if it was in the interests of the child to do so. On the facts the court considered that in the future the child was bound to wonder who her true father was, and she might suffer great anxiety over the question. Each of the four people concerned in the case would have a better chance of developing a healthy and normal relationship between themselves on the basis of truth rather than on the basis of doubt.

Mr. Justice Ormrod ordered that the child's blood be tested, but only after the three adults concerned had permitted samples of their blood to be taken. On the application of the Official Solicitor a stay was granted on the order, provided a notice of appeal was entered against the court's decision within 28 days.

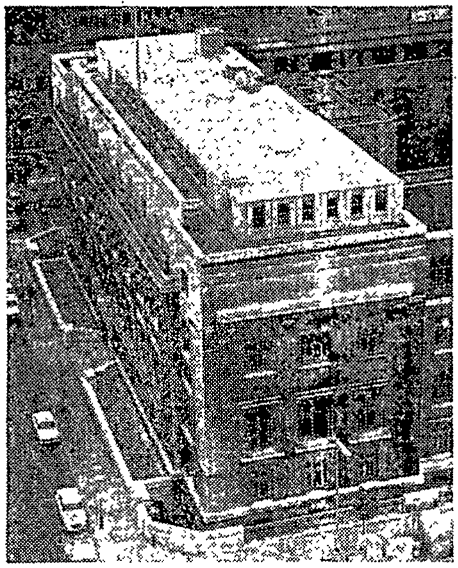
REFERENCE

[1] W. v. W. [1964] P. 67.

MEDICAL NEWS

Extensions at Keppel Street

On 28 June PRINCESS ALEXANDRA opened the new and reconstructed departments at the London School of Hygiene and Tropical Medicine (see *B.M.J.*, 18 February, p. 441). The gains in accommodation include a new refectory, new premises for the departments of human nutrition and entomology, and an extension of the public health department on a new fourth floor built on the roof. A valuable addition, provided by the Wellcome Trust, is an open-access stack for the library. LORD HEYWORTH, chairman of the court of governors, and Dr. E. T. C. SPOONER, dean of the school, also took part in the ceremony.



Postgraduate Tropical Medical Centre

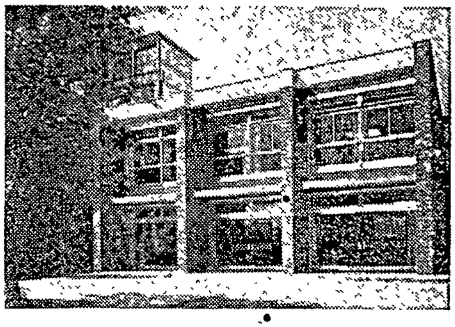
Contributions from Ghana, Uganda, and Zambia in support of the International College of Tropical Medicine were presented at a ceremony held in the Ugandan Embassy in Washington on 1 June, the first anniversary of the incorporation of the college. In accepting the gifts Mr. GEOFFREY MYERS, F.R.C.S., provost of the college, said the council would be deciding later this year where to establish its postgraduate medical centre in Africa (see *B.M.J.*, 1966, 23 July, p. 248). The address of the college is P.O. Box 497, Hamilton, Bermuda.

Medical Research in Scotland

The Scottish Hospital Endowments Research Trust has made a grant of £34,465 over five years to Professor JAMES WALKER, St. Andrews University, for studies of the physiology of pregnancy. Others to receive support for projects are: Dr. MARTIN M. WHITTET, Craig Dunain Hospital, Inverness, study of the epidemiology of alcoholism in the Highlands and Islands, £5,000 over two years; Mr. W. BRYAN JENNETT, Killearn Hospital, Stirlingshire, studies in cerebrovascular disease, £2,950 (supplementary grant); Professor Sir IAN HILL, St. Andrews University, studies in vectorcardiography in heart disease, £1,158 (supplementary grant); Dr. IAN W. B. GRANT, Northern General Hospital, Edinburgh, bronchial asthma, £3,390 (supplementary grant); Dr. STANLEY S. BROWN, Edinburgh University, biochemical study of drug binding in acute poisoning, £6,219 over three years; Dr. ANDREW SNEDDON and Mr. THOMAS HAMILTON, Edinburgh University, ovarian steroidogenesis in relation to human and experimental breast tumours, £4,788 over three years; Dr. D. J. C. SHEARMAN and Dr. D. G. FINLAYSON, Edinburgh University, relationship of gastric carcinoma to pernicious anaemia, £5,104 over three years. The Cruden Medical Research Fellowship for one year has been awarded to Dr. MARJORIE E. M. ALLISON.

Luton Medical Centre

Professor Sir MAX ROSENHEIM, President of the Royal College of Physicians, gave the inaugural address at the Luton and Dunstable Hospital medical centre on 27 June. The centre, which was opened in April, has been built from funds raised locally and with the support of the regional board and the hospital management committee. It consists of two floors, each linked to the main corridors of the hospital. Facilities include a lecture hall with seating accommodation for 160, a lounge, and a medical library. The building and equipment have cost about £40,000.



BRITISH MEDICAL JOURNAL

LONDON SATURDAY 15 JULY 1967

Pointers

President's Address: Mr. Robert V. Cooke addresses the Annual Representative Meeting (p. 129). Leader this page.

Phenylketonuria in Children: Dietetic treatment gives best results when started in early infancy, according to Dr. Barbara Clayton and colleagues (p. 133). Leader at p. 124.

Epidemiology of Tinea Pedis: Miss Mary P. English and colleagues found that infection was transferred by socks in a long-stay hospital (p. 136). Leader at p. 128.

Haemodynamic Response to Squatting: Dr. M. Nellen and colleagues from Cape Town found changes in intensity and duration of systolic murmur an aid to bedside diagnosis (p. 140).

Clotting in Scribner Shunts: Dr. A. J. Wing and colleagues were able to reduce this with long-term oral anticoagulant therapy (p. 143).

Diagnostic Paracentesis: Mr. W. N. W. Baker and colleagues recommend this in blunt abdominal trauma and post-operative complications of abdominal surgery (p. 146).

Stress Incontinence: Mr. Thomas Moore and Mr. P. F. Schofield suggest success of electrical stimulation treatment is due to restoration of pelvic muscle floor tone (p. 150).

Ethacrynic Acid: Hepatocellular damage reported by Professor K. K. Datey and colleagues from Bombay (p. 152).

Case Reports: Sugar consumption related to seborrhoeic dermatitis (p. 153). Biliverdinaemia in indomethacin therapy (p. 155). *Mycobacterium Battey* infection resembling tuberculosis (p. 157).

Today's Drugs: Fenfluramine (p. 159).

Cervical Cytology: Apparatus for automatic preparation and scanning described by Mr. M. M. Beddington and Dr. R. A. Diamond (p. 160)

Is There an Alternative?: Private health insurance prospects examined by Mr. Arthur Seldon (p. 166).

St. Christopher's Hospice: Example of voluntary effort in the Welfare State (p. 169).

Radio Communication: Speed-up in the treatment of urgent cases reported by Dr. M. H. Hall and Mr. R. S. Garden (p. 170).

Pertinax: Without Prejudice (p. 172).

Annual Representative Meeting: First report (*Supplement*, p. 25).

Future President: Dr. J. W. Howie elected President of B.M.A for 1969–70 (*Supplement*, p. 25).

C.C. and S. Committee: *Supplement*, p. 66.

Unity and Service

Concern with each other and concern for the service that medical men and women give to the community is the theme that provided the title " One Profession, One Purpose," chosen by Mr. Robert V. Cooke for his presidential address at this year's Annual Meeting of the British Medical Association at Bristol. It is reproduced at page 129 of the *B.M.J.* this week. Like many other observers of the current scene he has been impressed by the signs of conflict, even disintegration, within the medical profession, and he specially emphasizes the need for " bonds of closer unity " between the family doctor and colleagues in other branches of practice. The twentieth century is indeed a time when, in response to not unnatural impulses, peoples and individuals are everywhere seeking the means to govern themselves. We have all taken to heart Cassius's lesson that the fault is not in our stars but in ourselves that we are underlings, and the remedy is increasingly sought through vigorous political action. But in the righting of old-standing wrongs, old benefits and amities may perish in the ferment. More fortunate than people in many other occupations, medical men and women acquire in their training much besides a technical equipment to do a job efficiently, for the alleviation of an individual's suffering that every member of the profession begins to undertake from the first moment he steps into the wards as a student surely gives all but the most insensitive a deep respect for the human condition—and perhaps its sorrows more than its joys. As the President remarks, the doctor will always be something more than the latest computer, bringing to his job " the highest ethical standards, the deepest sense of personal responsibility, and a readily felt warm humanity."

In calling for unity within the profession Mr. Cooke was making a particularly topical plea, for the Representative Body has lately been much concerned with proper representation in the counsels of the B.M.A. and this year again debated its constitution. Discussion of the details of this debate is beyond our present purposes, but it is worth stressing here that equitable representation lies at the heart of professional unity. The Association has long cherished a reputation for the open manner in which it conducts its affairs and the facility with which any member may put forward his views. Its members are no more restricted to any particular branch of the profession than are its policies the reflection of any particular doctrine. In the much-debated constitution of the autonomous bodies it attempts to reconcile the special needs of certain groups with the obligations that every medical man owes to his membership of one profession. Thus the aim of constitutional change may be thought of as twofold, firstly to provide the means by which true majority decisions are reached, secondly to safeguard the interests of minorities. And the often expressed anxiety that autonomy can go too far if not wisely restricted springs from the ordinary doctor's awareness that membership of a profession entails relationships deeper than those deriving from political self-interest.

© *British Medical Journal*, 1967. All reproduction rights reserved.

Speaking as a surgeon who has devoted his life to this most exacting of crafts, Mr. Cooke has been struck by the real service that a good clinician does his patient by sparing him unnecessary diagnostic investigations and needlessly hazardous remedies. He acknowledges, as any doctor must today, that there are limits beyond which clinical diagnosis cannot go, but "I am sure," he declares, "we should reaffirm our faith in clinical diagnosis, teach it more carefully, recognize that it takes a long time to learn, requiring as it does a great deal of experience, quite apart from a vast amount of knowledge correctly to interpret the story and the physical findings." This is particularly true in relation to the many underdeveloped parts of the world for which British medical schools have taken on educational obligations.

Phenylketonuria

In 1934 A. Følling[1] discovered phenylpyruvic acid in the urine of 10 mentally deficient patients. Ferric chloride reacts with phenylpyruvic acid to produce a greenish-blue colour, and the addition of a small amount of a ferric chloride solution to the urine is the standard method for detecting it. Originally all affected persons were thought to be blond and blue-eyed and to have a very low intelligence, but further experience has shown that some patients merely have less pigmentation than other members of their family and that in some races pigmentation may be normal. It has also been shown that the scatter of intelligence in the untreated state is considerable, a few patients being well within the normal range.

The basic defect in phenylketonuria is the absence of the hepatic enzyme, phenylalanine hydroxylase, which normally converts into tyrosine the dietary phenylalanine which is not used up in the synthesis of protein. In the absence of this hydroxylase phenylalanine accumulates in large amounts in the blood and is partly converted, by alternative metabolic pathways, to phenylpyruvic acid and other metabolites, which are excreted in the urine. Unchanged phenylalanine is also present in the urine.

Phenylketonuria is inherited as an autosomal recessive; the heterozygous parents of affected children are therefore clinically normal, nor does their urine contain phenylpyruvic acid. The heterozygous state can, however, be detected by phenylalanine loading tests. When a child with phenylketonuria is born there is statistically a 25% chance of a similarly affected sib being born to the same parents.

The relationship between this metabolic error and mental subnormality is largely derived from observations on man. Nearly all persons with phenylketonuria have a very low intelligence, but giving a diet low in phenylalanine to affected infants from an early age will usually result in a child of normal or nearly normal intelligence. At page 133 of the *B.M.J.* this week Dr. Barbara Clayton and her colleagues in London describe their experience in the treatment of 57 children with phenylketonuria. They have shown that early diagnosis, with careful dietary and biochemical control, produces excellent results. Eleven children in their series attend a normal school, and 10 children of pre-school age will also be eligible for normal schooling if their present level of intelligence is maintained. In those children in whom the diagnosis was made and treatment started before the age of 6 months the intelligence quotient before treatment was normal, and the effect of treatment was to maintain it at a normal level. In the majority of those in whom treatment was started after the age of 6 months the intelligence before treatment was well below normal, and even with prolonged treatment it was rarely possible to achieve an I.Q. of 80, though substantial improvement was made in just under half of these children.

Several important conclusions can be drawn from this work, which is representative of that done in many other paediatric centres. For an affected child to have normal intelligence the treatment must be started as early as possible, certainly before the age of 6 months. Dietary control is essential and must be combined with repeated estimations of the level of serum phenylalanine as the presence or absence of phenylpyruvic acid in the urine does not afford a sufficiently sensitive test. Some improvement in intelligence and behaviour may result from the dietary treatment of older patients, and another reason why they should be sought is that the discovery of an older child with phenylketonuria will alert the paediatrician to the possibility of similarly affected sibs, born and unborn. An important observation about the adult with phenylketonuria is that when an affected woman becomes pregnant and is not treated by diet during the pregnancy the infant will probably be mentally subnormal, though not suffering from phenylketonuria. This is due to the influence of a raised maternal, and hence foetal, level of phenylalanine on the developing brain. Fortunately the converse of this situation is more commonly seen: the affected infant is normal at birth because the placenta is able to maintain the foetal level of phenylalanine within normal limits.

The best way of ensuring early diagnosis and treatment is by routine screening tests on all young infants. The present method in general use is to test the urine, or more commonly the napkin wet from freshly voided urine, by means of the Phenistix test paper (a modification of the ferric chloride test). This test is not reliable immediately after birth and is usually performed at the age of 3 to 6 weeks. In practice the results of widespread use of this test have been disappointing. Dr. Clayton and her colleagues found that only ten of their series were detected at infant welfare centres, and of these only two were under the age of 6 weeks. A more satisfactory procedure, the Guthrie test,[2] is done on a drop of blood dried on filter paper, which is then sent to a central laboratory. This test can be done as early as the fourth day of life, provided the infant is feeding well and has therefore a normal intake of protein. Suspected cases detected in this way are then investigated by more precise methods. Even so, difficulties may arise in the interpretation of a raised level of phenylalanine, as it has been shown that in some premature infants the serum phenylalanine may be temporarily raised,[3] often with a positive Phenistix test. This is thought to be due to delay in the maturation of the enzyme systems dealing with phenylalanine and tyrosine. Such infants can on further investigation be distinguished from true phenylketonurics, and should of course never be treated as if they had this condition.

Perhaps the most difficult decision, once treatment has started, is when to stop. F. P. Hudson[4] has described four children who returned to a normal diet after treatment for 2½ to 5 years. Observation of them on a normal diet for varying periods has as yet disclosed no deterioration. Dr. Clayton and her group are as yet reluctant to commit themselves on this point.

---

[1] Følling, A., *Hoppe-Seylers Z. physiol. Chem.*, 1934, **227**, 169.
[2] Guthrie, R., and Susi, A., *Pediatrics*, 1963, **32**, 338.
[3] Menkes, J. H., and Avery, M. E., *Bull. Johns Hopk. Hosp.*, 1963, **113**, 301.
[4] Hudson, F. P., *Arch. Dis. Childh.*, 1967, **42**, 198.
[5] Cohen, B. E., Bodonyi, E., and Szeinberg, A., *Lancet*, 1961, **1**, 344.
[6] Wagner, M. G., and Littman, B., *Pediatrics*, 1967, **39**, 108.

The incidence of phenylketonuria in a population of northern European origin is probably about 1 in 10,000 births, but the condition appears to be less common in American negroes and in Ashkenazi Jews.[5] It has been described in Japan and recently in North American Indians.[6] The rate of early detection in Britain could be greatly improved. To make the diagnosis only when mental subnormality is suspected is to make it too late.

Bristol A.R.M.

With the longest agenda in its history the Representative Meeting in Bristol was always in danger of becoming submerged under the mass of business. It did not altogether escape this fate. Although extra time was taken and representatives exercised considerable self-denial, the end was reached only by disposing of many items on the last day without discussion. The Meeting recorded its regret at the shortness of time available for hospital affairs. However, despite all the difficulties the Representative Body dispatched a useful amount of business during its four-days sitting.

A motion from Birmingham urging a delay in legislation on therapeutic abortion until an independent tribunal, such as a Royal Commission, "had collected, scrutinized, and reported" on all the relevant facts was taken early, because of the imminent passage of Mr. Steel's Bill through the House of Commons. The Representative Body had to decide whether to lend the Association's weight to those who wanted the present Bill to fail, or whether it should recognize that Mr. Steel's Bill was, as one speaker said, "probably the best Bill [we shall] ever get." It was one to which the Association together with the Royal College of Obstetricians and Gynaecologists had already contributed much. The Bill now makes the decision to terminate a pregnancy entirely a medical matter, depending on assessment of the risk to life and health of the woman and her existing children or of serious foetal deformity. This is a long way from the purely social indications the Bill once contained. After a lively debate and hearing that the B.M.A. would continue to press vigorously for certain important amendments to the Bill, the Meeting rejected the Birmingham motion by 274 to 98 votes.

One or another aspect of the Health Service formed the subject of a number of motions. Among many of minor importance some that dealt with matters of principle stood out. Asked to revoke the 1945 S.R.M.'s undertaking that the profession would, with certain provisos, accept a health service that was available to the whole population (the "100% issue") the Meeting instead recorded its view "that the profession can no longer accept collective responsibility for the preservation of a standard of medical care which a modern community should expect under the Health Service." This is a warning which the public and the Minister should heed. The tenancy arrangements for doctors working in local authority health centres were seen as a possible threat to the independence of general practitioners. Official interest in building such centres is increasing. Indignation that the patient's signature as well as the doctor's should be required on the form for payment for itemized services such as night visits was voiced. Did a doctor's signature no longer command trust, it was asked.

After an undertaking that the Council would examine alternative proposals from the East Yorkshire Branch and after a thorough discussion, the new constitution emerged from its ordeal by debate amended but recognizable. Proportional representation is to be introduced, but a Division's right to individual representation in the R.B. was successfully championed. Each of the 21 hospital regions will elect to the R.B. a representative of its junior hospital staff. Its future size will be about 538. By its provisions for dealing with the work of the autonomous committees the new constitution should do much to relieve Representative Meetings of the burden of the sort of trivialities which contributed so much to the unmanageable size of this year's agenda. The R.B. will retain its sovereignty, as it must, and be free to consider the report of any committee, but it will normally address itself only to questions of major policy. Perhaps more than any other measure, this will enhance the usefulness of the Association's Annual Representative Meeting, and therefore its prestige.

The Meeting, which was ably chaired by Dr. A. N. Mathias, is reported in the *Supplement* at p. 25.

Chemical Treatment of Skin Cancer

In contrast with other forms of neoplasia, skin cancer is relatively easy to treat. Diagnosis can be made early, the full extent of the lesion can be ascertained readily, complete extirpation by surgery or ionizing radiation is usually possible, and the effects of therapy can be evaluated without difficulty. In the case of basal-cell tumours the fact that distant metastasis is rare also favours a good prognosis, and cure rates of 95% or better can regularly be obtained by the traditional methods of treatment.[1 2] Is there therefore any place for chemotherapy in the treatment of skin cancer ?

In the treatment of internal cancer by chemotherapy the problem is to find chemical substances more toxic to cancer cells than to normal cells. Most of the success of the chemotherapeutic drugs now in use depends on their selective toxicity for proliferating cells. The same property limits their use, because they damage not only proliferating tumour cells but also proliferating normal cells, particularly those of the gut mucosa and blood-forming tissues. Recently attempts have been made to concentrate the effect of chemotherapeutic agents on tumour cells by perfusion or local intra-arterial infusion. Attempts are also being made to develop rapidly destroyed cytotoxic drugs for administration by infusion, the intention being that by the time they have passed through the tumour and into the general circulation their cytotoxicity will have been lost.[3] Yet another approach is to develop cytotoxic drugs which are linked to other molecules—for example, tumour-specific antibodies—which can be expected to "home" on the tumour cells.[4]

In the treatment of skin cancers there is no need to use chemicals with selective toxicity, because agents can be accurately and directly applied to the cancerous tissue, and, provided absorption into the body is limited, exposure of normal tissues can be reduced to a minimum. It is not surprising, therefore, that many relatively simple chemical substances such as sodium bicarbonate[5] and zinc chloride[6] have been shown to be effective in eradicating skin cancers. More elaborate toxins such as colchicine, demecolcine, *N*-desacetylthiocolchicine,[7] and podophyllin[8] have likewise been found effective.

According to E. Klein and his colleagues,[9] 5-fluorouracil, an agent developed specifically for the treatment of cancer, is not suitable for the treatment of basal-cell carcinomas, let alone squamous carcinomas. J. C. Belisario,[7] on the other hand, suggests that agents such as methotrexate and triaziquone, alone or in combination with colchicine or colchicine-like agents, have an important place in the treatment of skin cancer in Australia, where the disease is common.

In general it would seem best to continue to use the well-tried methods of treatment—namely, surgery and radiotherapy—particularly where special considerations discussed by Belisario[7] for using chemotherapy do not apply. But are we failing to make proper use in selected cases of the technique of chemosurgery developed by F. E. Mohs[6] ? In countries other than Britain it has proved to be of considerable value in the treatment of flat, sclerotic basal-cell carcinomas with poorly defined margins, of tumours near important anatomical structures such as the nasal ala or orbital canthus, and of tumours that have recurred after surgical removal or radiotherapy. The special value of the method lies not in the fact that extirpation is accomplished by chemical means (zinc chloride) but in that it is controlled stage by stage by the systematic microscopical examination of tissues removed from the base of the lesion, so that complete removal is achieved with the minimal destruction of normal tissues. Mohs claimed a 95% five-year cure rate for previously treated basal-cell carcinomas and a 99% five-year cure rate for previously untreated lesions. Other surgeons have reported comparably good results.[10-17] N. L. Morgenstern and R. W. Leeper[18] also confirmed the value of chemosurgery and provided a useful brief description of the method and indications for its use. They do not recommend chemosurgery for the small uncomplicated lesion, because the application of zinc chloride may produce severe pain (controllable by analgesics) and oedema. Moreover, the technique is more time-consuming for both the patient and his doctor. However, for the appropriate case these authors[18] regard chemosurgery, which can be performed by any pathologist and dermatologist working as a team, as the method of choice.

It is difficult to believe that any form of local treat
whether by chemical agents or electrodissection
curettage,[19 20] can be as successful in the treatment o
cancer as Mohs's technique unless it includes the same s
of careful histopathological control. Herein lies the rat
for using zinc chloride, since it acts sufficiently well
fixative to permit a flat layer of tissue removed from th
of an ulcer to be examined systematically for the prese
tumour tissue. Precise evaluation of this kind is not p
in treatment with other types of chemical agent
curettage.

In the main, therefore, surgery and radiotherapy r
the best methods for treating skin cancer, though ther
need to introduce the technique of chemosurgery into B
The use of no other form of chemical treatment is just
unless it involves stage-by-stage histopathological evalu
the essential feature of Mohs's technique.

---

[1] Churchill-Davidson, I., and Johnson, E., *Brit. med. J.*, 1954, 1, 1465.
[2] Rank, B. K., and Wakefield, A. R., *Brit. J. Surg.*, 1957-8, 45, 531.
[3] Garai, O. F., Cooling, C. I., and Shaw, H. J., *Annual Report of the British Empire Cancer Campaign for Research*, 1967, 44, 18.
[4] Isliker, H., Cerottini, J. C., Jaton, J. C., and Magnenat, G., in *Chemotherapy of Cancer*, edited by P. A. Plattner. Amsterdam. 1964.
[5] Cameron, D., *Lancet*, 1944, 2, 720.
[6] Mohs, F. E., *Chemosurgery in Cancer, Gangrene, and Infections*, Springfield, Illinois. 1956.
[7] Belisario, J. C., *Arch. Derm.*, 1965, 92, 293.
[8] Chatard, M. H., *Bull. Soc. franç. Derm. Syph.*, 1957, 64, 324.
[9] Klein, E., Stoll, H. L., Milgrom, H., Traenkle, H. L., Graham, S., and Helm, F., *J. invest. Derm.*, 1966, 47, 22.
[10] Beirne, G. A., *Kaiser Fdn Med. Bull.*, 1955, 3, 225.
[11] Lunsford, C. J., Templeton, H. J., Allington, H. V., and Allington, R. R., *Arch. Derm. Syph. (Chic.)*, 1953, 68, 148.
[12] Phelan, J. T., Milgrom, H., Stoll, H., and Traenkle, H., *Surg. Gynec. Obstet.*, 1962, 114, 25.
[13] Shepard, R. A., *J. int. Coll. Surg.*, 1958, 30, 220.
[14] Wilson, C. J., and Mullins, J. F., *Sth. med. J. (Bgham, Ala.)*, 1959, 52, 1241.
[15] Buchwald, H., and Aust, J. B., *Amer. J. Surg.*, 1964, 108, 589.
[16] Phelan, J. T., and Juardo, J., *Arch. Surg.*, 1963, 87, 212.
[17] Tromovitch, T. A., Beirne, G., and Beirne, C., *Cancer (Philad.)*, 1966, 19, 867.
[18] Morgenstern, N. L., and Leeper, R. W., ibid., 1964, 17, 5.
[19] Sweet, R. D., *Brit. J. Derm.*, 1963, 75, 137.
[20] Freeman, R. G., Knox, J. M., and Heaton, C. L., *Cancer (Philad.)*, 1964, 17, 535.

Needs of Pre-school Children

The National Society of Children's Nurseries has re
published a report by Dr. Simon Yudkin of an inqu
a working party which met under his chairmanship t
into the care, outside their homes, of children under
age.[1] The working party of 18 members represent
principal professions closely concerned with the w
health, and education of pre-school children. In her for
Lady Allen of Hurtwood bluntly asserts that the aim
report is "to stir into action the Government, Memb
Parliament, local authorities, and the general public"
regard to what she characterizes as the "chaotic terri
of existing provisions for nursery care and education.
society is supported in its demands for a Government i
by 33 voluntary and professional organizations interes
the social welfare of mothers and children under 5 ye
whom there are more than 4¾ million in the country.
Yudkin marshals considerable evidence to support hi
tention that, "although provision for their physical ca
stand comparison with those of any country, and the
detection and management of handicapped children is in
ing year by year, by contrast, provisions for their soci
emotional development and training are chaotic, inade
and based on no apparent general philosophy."

The report is in three parts. The first section ex
the position of working mothers and reviews the ne
their young children in two main age groups, since t
general agreement that the needs and tolerances of ch
aged up to 3 years and of those aged 3 to 5 differ in
respects. There are also wide variations within these
according to family unity, domestic arrangements, ho
economic circumstances, and, in some cases, physi
mental handicap. The second section, dealing with
minding and with day and residential nurseries, pr
disquieting evidence of the exceedingly unsatisfactory an
dangerous conditions under which many young child
this country are illegally looked after or fostered. The
section offers comment and suggestions. Though o
facts and figures are not available, much useful inform
has been painstakingly collected from various agencie
published reports, which is supplied in the appendix.

---

[1] Yudkin, S., *A Report on the Care of Pre-School Children.* N
Society of Children's Nurseries, 45 Russell Square, London
5s. net.

After 1945 Ministerial policy was directed—and it is only fair to remember, in the conditions then prevailing or expected, with every good intention so directed—towards the closure of wartime day nurseries and the encouragement of family care of young children. At the same time shortage of teachers necessitated a limitation of nursery schools and classes. But social conditions have greatly altered since then. The age of marriage has fallen and the birth rate has risen. The cost of living has soared. The number of mothers, particularly young mothers at work, has increased rather than diminished. The housing situation remains difficult. There has been an influx of coloured immigrants with low earning capacity and large families, and these have tended to congregate in already overcrowded industrial cities such as London, Liverpool, and Birmingham. Though previous lack of foresight in high places may be regrettable, past miscalculation is no excuse for present inaction. The miseries and dangers which unknown numbers of helpless babies and young children are at present enduring in our midst cannot be ignored. The situation calls for urgent investigation and vigorous remedial measures.

While there can be no possible disagreement with the main thesis of this report, for which the National Society of Children's Nurseries is to be commended, there is one serious omission which will immediately strike workers interested in developmental and social paediatrics. There is no mention of one of the most needy of all groups, the children aged under 5 in hospitals for the mentally subnormal, a group which for some inexplicable reason was also omitted from the terms of reference of the Platt Committee on the Welfare of Children in Hospital. Any new inquiry must not be allowed to perpetuate unjustifiable hierarchical distinctions between physically, mentally, emotionally, and socially handicapped children. The quantity and quality of provisions for the care and welfare of all children under 5 years who are cared for outside their own homes should be investigated and remedied where necessary without exception. It is to be hoped that urgently needed legislation will be promptly considered, clearly defined, and thereafter strictly enforced.

Safety of Drugs

The Committee on Safety of Drugs has two main functions. It requires manufacturers of new drugs to submit evidence to establish that it is reasonably safe to start clinical trials, and later requires further evidence on safety and efficacy before the drug is released for marketing ; and it collects and assesses information about adverse effects of drugs in general use. The committee's third annual report,[1] published this week, shows that both functions are working smoothly.

In 1966 there was a small rise in the number of submissions on new drugs (908) made to the committee, which claims that delay in clearing the drug has been kept to a minimum by the use of informal discussions rather than official communications. The committee's policy is that only in the most exceptional circumstances will it release any drug for clinical trial in women of child-bearing age until tests for teratogenicity have been carried out in animals, and the report points out that this policy has led in some cases to populations used in clinical trials being unbalanced. Manufacturers are advised to carry out tests for teratogenicity early in the programme of assessment.

In the three years during which the " early warning system " for reporting adverse reactions to drugs has been in operation twice as many reports of suspected adverse reactions to drugs have been received from general practitioners as from hospital staff. The committee suggests that this may be due to some confusion in the minds of doctors about the nature or severity of reactions that should be reported. The report states:

> " Broadly, doctors and dentists are asked to report all suspected reactions, however trivial they may appear to be, following the administration of drugs introduced on to the market within the past two years: they are asked to report all serious or unusual reactions to drugs which have been on the market for a longer period. When there is doubt about the date of marketing, the doctor or dentist should always report his observations."

The committee proposes to issue more reports in the Adverse Reactions series, and in the case of widely prescribed drugs it will provide on request " extract sheets " summarizing the cumulative reports received on them.

Finally, the report draws attention to the narrow limits within which the committee is concerned with the efficacy of drugs. Clearance of a drug by the committee does not necessarily imply that it thinks the drug is a valuable remedy, but only that it is safe for the purpose for which it is intended to be used. " Thus, a number of products which in the committee's view are relatively worthless, though innocuous, have been cleared for the market."

Bed Rest and Lumbar Disc Protrusions

The results of surgical treatment of protrusions of lumbar intervertebral discs have been well documented. J. E. A. O'Connell[1] reported on his results in 500 patients all of whom had severe or prolonged symptoms before operation. In his follow-up he found that 92% were either completely free of pain or very greatly improved after operation and that recurrence of symptoms severe enough to indicate reoperation was 2%.

The great majority of patients with symptoms due to this condition are treated by conservative measures, but there is surprisingly little factual information on the long-term results. J. Pearce and J. M. H. Moll[2] have recently corrected this in a study of 91 consecutive patients with acute symptoms considered to be due to a lumbar disc lesion, the patients being admitted in the course of 13 years. In all patients there was restriction of spinal flexion and of straight-leg raising and in the majority signs of nerve-root compression. The authors omitted from the series patients with a strong neurotic element and those in which there was any diagnostic doubt. Unfortunately they also omitted patients who were submitted to early operation on account of intractable pain after one to two months of absolute bed rest and those with evidence of compression of the cauda equina and sphincter disturbance. It would be of value to know how many patients come into this category. Treatment was strict bed rest with a fracture board under the mattress and one pillow. If the patient was free of pain after two weeks he was gradually mobilized, while if pain persisted he had a further fortnight's bed rest. When walking was possible without pain he was discharged and returned to work within a few weeks, and he was advised not to bend or lift heavy objects for three months.

---

[1] *Annual Report of the Committee on Safety of Drugs,* 1967. H.M.S.O., London.

[1] O'Connell, J. E. A., *J. Bone J. Surg.*, 1951, 33B, 8.

[2] Pearce, J., and Moll, J. M. H., *J. Neurol. Neurosurg. Psychiat.*, 1967, 30, 13.

The series included 38 patients in their first attack of pain and 53 who had had previous attacks. The follow-up was an average of eight years (range 0–13), but 18 patients could not be traced. Five patients (7%) had developed severe recurrence of symptoms and had been operated on. Of the remaining 68 patients 26% remained completely free of pain, 41% had persisting mild pain, and 32% were still complaining of moderate or severe pain. The authors also analysed the 68 patients' ability to work since the original hospital admission: 57% had not lost time off work, while 43% had had recurrences sufficiently severe for them to have periods off work, some of them for two months or more at a time; 71% were still doing their original type of work but 29% had had to change to lighter work.

It is sometimes thought that if a patient recovers from the acute symptoms of a lumbar disc protrusion with a period of bed rest he is likely to remain free of serious disability, but this valuable study shows that this is not so in more than 30% of the patients. The question arises whether persistence with spinal-extension exercises after recovery from the acute attack might help to prevent recurrent pain. The authors' findings certainly suggest that, when there are repeated episodes of pain sufficiently severe to stop the patient from working, operation needs serious consideration.

Tinea in Hospitals

One of the hazards of community life is the risk of acquiring tinea pedis, and this is well recognized in schools, the armed Forces, coal mines, and elsewhere. Now Dr. Mary English and her colleagues at Bristol report in the *B.M.J.* this week (page 136) their investigations on mentally subnormal patients in a long-stay hospital. The patients lived in numerous separate "lodges," between which there was only a limited interchange. Scrapings were taken from all suggestive lesions on hands and feet, and types of fungus were identified by culture. About 40% of those examined gave positive cultures. Among these *Trichophyton interdigitale* was the commonest (50%) and *T. rubrum* the next (26%), with *Epidermophyton floccosum* a poor third (4%). The incidence of infection was related to the length of the patients' stay in hospital but not to their ages. In the lodge containing the longest-stay patients the incidence rose to 66%, which approximates to that found in coal mines in England[1] and Germany.[2] The authors suggest that the residual 30–40% may represent the proportion of the normal population who have a natural resistance to the infection. The frequency of *T. interdigitale* infections was about the same in each lodge, but in one lodge *T. rubrum* showed a significantly higher incidence both absolutely and in relation to *T. interdigitale* and it caused more severe lesions. A possible explanation of these findings is that, while there was multiple introduction of *T. interdigitale,* the outbreak of *T. rubrum* may have resulted originally from a single case. This is comparable with the findings of J. C. Gentles and J. G. Holmes[1] in coal miners; in some pits there were hardly any cases of *T. rubrum,* while in others its incidence was over 40%. *T. rubrum* was comparatively rare before 1939, but since then it has become increasingly common, and once introduced into a community it may spread rapidly. It was originally one of the most intractable forms of ringworm, but now fortunately can be controlled by griseofulvin. Gentles and Holmes showed that there was an association between the spread of tinea pedis and the use of pit-head baths, but Dr. English and her collaborators could find no relationship between their patients' use of the bathroom and the spread of the infection. On the other hand they were able to culture fungus from socks which had been laundered, a fact of importance because the socks were not the property of individual patients but were reissued indiscriminately after laundering. Furthermore, four out of nine crippled patients who had never walked had ringworm, so that the authors considered that infected socks were probably a more important source of infection in this community than contaminated floors. Football trousers worn indiscriminately after laundering have been known to spread tinea cruris likewise.

How far are these findings relevant to hospital conditions generally? It seems unlikely that there would be much interchange of socks and underlinen between patients in an ordinary acute hospital except possibly for pyjamas. Tinea cruris is less common than tinea pedis, and it must be rare for the former to be contracted in hospital from pyjamas. However, tinea cruris has been spread by contaminated towels used in a physiotherapy department. It seems probable that the chief risk in acute hospitals is in the bathrooms, though whether the risk warrants active preventive measures, such as the provision of disposable slippers, is doubtful. On the other hand, in communities of long-term patients it would seem a simple and reasonable precaution to ensure that each patient should have his own socks returned to him from the laundry. It is debatable how much further one should go in improving preventive measures and the restrictions they necessitate, particularly in a community of patients with a low mentality who frequently walk about barefoot in the dormitories as well as the bathrooms. In this relatively cold country tinea pedis is rarely a disabling disease.

But eastward, look, the land is bright

Following a practice that has already been found fruitful in other fields, the Ministry of Health is to send a team over to the U.S.A. and Canada next October in the hope of persuading medical emigrants to return to practise in Great Britain. An announcement giving the details appears in the advertisement on the inside front cover this week. Among those who have emigrated are many young men and women who could make an outstanding contribution to medicine in the country of their birth. The great majority of them on qualifying had no thought of making their life's work anywhere but in Britain. Why then did they go? This question has evoked a multitude of different answers, but essentially most emigrants are dissatisfied with either the postgraduate training or the professional prospects offered in this country, sometimes with both. If the Ministry team can convince them that real improvement is on the way it may succeed in persuading at least some of these doctors to turn their steps homeward.

---

[1] Gentles, J. C., and Holmes, J. G., *Brit. J. industr. Med.,* 1957, **14,** 22.
[2] Götz, H., Sturde, H. C., and Hantschke, D., *Dermatologica (Basel),* 1965, **130,** 130.

Papers and Originals

British Medical Association

ONE HUNDRED AND THIRTY-FIFTH ANNUAL MEETING, BRISTOL, 1967

President's Address

One Profession, One Purpose

ROBERT V. COOKE,* CH.M., F.R.C.S.

Our beloved Queen, in her most recent Christmas message, spoke of concern for others—in fact this matter of being concerned ran through all that broadcast, in which she paid so many tributes to womankind, generous, but how true. She particularly praised them for their sagacity, tenacity, and loyalty, attributes which we would all wish to possess.

About this time I attended my first B.M.A. Council Meeting. What struck me most was the evident concern of all those present for the plight of two of the smaller groups of our profession. With a long agenda there was no hurry; the most careful consideration was given to the problems besetting these colleagues, in some ways less fortunate than others and standing in need of help.

My attendance at all subsequent Council Meetings has convinced me that that first impression of their concern for minority groups was no mere chance. Since then there has been anxiety and concern for the present position and future of senior hospital medical officers and senior administrative medical officers, Service doctors, and whole-time teachers. On the last occasion there was a prolonged and most sympathetic hearing of the special case of public health doctors. It was the main preoccupation of the meeting, and I have been most impressed. Impressed, too, with the support given to the more junior doctors, who have now achieved substantial representation on important committees, and are playing an active part in negotiations at a time when their needs are great and urgent.

For many months I had been casting about for a subject for this special audience—not too technical and not too inflammatory. At one time I was almost tempted to repeat that memorable address at Oxford four years ago—as brief as it was memorable. Then, as you remember, Sir George Pickering said that he had "felt like a Sunday preacher seeking for a text," which he found in the mottoes of Winchester and New Colleges—"Manners Makyth Man." His captive audience will remember the account he gave of William Wickham, and the theme which followed—"The ethos of medicine is of no less significance than the science" and "that this must not be squandered." "It was manners that makyth man—that character and conduct mattered at least as much as learning," though, of course, we must have both. He spoke of arrogance, selfishness, and alcohol as examples of bad manners and the cause of much injury and grief, particularly in regard to road accidents. This was evidence of lack of concern for others.

So it was that I came to my text or title—based upon concern for each other and concern with the service we give—"One profession, One purpose."

Unity

We hear a great deal about the importance of the unity of peoples, of countries, of the Churches. This oneness is surely imperative for our great profession, and never was it more needed than now. Each of us must have real concern for the whole profession, every branch, every group, however small. It has gladdened the heart to have seen this spirit in operation in your Council and on your Committees. We might with advantage remind ourselves of our own good fortune, of all the help we have received because others have been concerned about us. Maybe it was a parent, a schoolmaster, a particular friend in the profession, or a wife whose concern for us and for others has meant for her a life of selflessness, perhaps taken too much for granted. It may even have been the British Medical Association.

Sir Ian Fraser, in his Belfast address, deplored "this disintegration from which the consultant side of the profession must be saved," referring particularly to divisions into teachers, clinicians, and research workers. After all, the so-called clinicians must be responsible for a great deal of the teaching, and who better able to do so? The clinicians should encourage the researcher and the laboratory man, dependent as they are on their special labours. They should not only receive their meed of praise, but we must see to it that they are properly paid and efficiently equipped. But of greater importance is the development of closer bonds of unity between the family doctor and all the rest of the profession.

William Stokes, Regius Professor of Physic at Dublin, and President of the B.M.A. 1867–8, in his valedictory address at Oxford, said: "So far we have been an united body, working for the benefit of science in the world, with independent local action and a representative on the central executive. How long this strength-giving union may last no man can predict, nor on the other hand can any man say to what amount of influence for good this association may attain.

"But it is plain that its durability and usefulness will depend on its being made the instrument for public good rather than the machinery to advance the immediate worldly interests of the profession."

I could mention many examples showing how in recent months concern for others in our profession has led to active steps being taken and not just pious hopes expressed.

The changes proposed in the composition of the Central Consultants Committee of the special Negotiating Committee of fifteen, which will replace the present one of nine members, were all designed to give the younger men an important say in our deliberations, and not only as regards terms and conditions of service. The committee on training at the Royal College of Surgeons will now from time to time invite representatives of those younger men in training to listen in, as it were, and express their own views on any plans envisaged for their future education and examinations. We look for happy co-operation, not a grudging acceptance of regulations laid down. After all, the younger men are not so young. Anyone attending the last Junior Doctors Forum in Manchester or that special meeting in Newcastle would have satisfied themselves that many are mature, thinking people, capable of adding strength to our discussions, and bargaining with the administration. By integrating these younger men and women into our councils we are at once strengthening and unifying our Association.

---

* Senior Surgeon, Bristol Royal Hospital.

The National Health Service will not make people healthier. But it is a part of our national way of life. It must be made to work. And, as regards the saving of expense, it is my personal view that we are not doing all we could and should to preserve this Service, for it must be preserved. The astronomical expense could be cut. We may not be able to tackle the administrative costs, but we should do whatever we can; for a little here, with a little there, can add up to a considerable sum. It is so easy to be complacent or to feel that our little efforts are of small account. In any case, inevitably we must need more and more to meet all kinds of new expenditure as science advances and many new and expensive procedures are developed. Kidney transplants are now almost commonplace, and other organ transplantations are in the offing. Haemodialysis presents ethical and moral problems, but certainly the cost is going to be great.

The Cost of Life

The recent symposium at the Royal Society of Medicine (under the able chairmanship of Lord Cohen) served to emphasize the price we must pay for these refinements of treatment. Yet we *must* concern ourselves with the tetraplegic, the mongol, the hydrocephalic, the spina bifida, and the serious head injury in particular. To listen to these papers made one realize something of the future developments and demands. The horizons of medicine are limitless and none can foretell how far we may be able to go. But there can be only one standard of treatment. We cannot choose a treatment for one and give something less to another. We may not play God, —we must accept the risks involved and constantly try to improve our results.

As doctors we should never too readily give a certificate of unfitness or for minor ailments. Men and women taken out of industry and kept out of work are paid for doing nothing. Demoralizing for them, it is bad for the country. Convalescence, be it from medical disease or surgical operation, is often so protracted that it has itself to be recovered from. Between us, doctor and consultant together, we must try harder to get patients back to work just as soon as is reasonable. In many conditions the early return to useful activity makes the best possible contribution to full mental and physical recovery.

Governments, at their wit's end to find more and more money, might more readily be persuaded to look again at the Health Service if it was seen that all of us were contributing something in one way or another to eliminate wastage. Many have given much thought to methods of collecting money from other sources, but some such measures suggested might provide a relatively small return for a big outlay in money and manpower. It is said that, unlike other activities, we have no end-product for sale or for export. Surely we have the best of all—positive health. Our great trade unions know this and are alive to the fact that illness and absenteeism account for more loss in working days than all the strikes put together. One cannot at this moment refrain from saying a word against overemployment if only because of its bad effect on real health of mind and body of those insufficiently employed. Standing about on the shop floor is much worse for them than a certain degree of overwork.

Use of Hospital Beds

Another contribution concerns the more careful use of hospital beds, for there is no doubt that bed-stay in various parts of the country varies between wide limits. We should save every single day that is reasonably possible, having regard to the home conditions of the patients about to be discharged. Serving on a regional board I saw something of the work of the geriatrician. Some of them contrived to save the use of hospital beds in a remarkable way—a real contribution, saving money and personnel to be deployed to meet other demands.

Sir George Godber said in Londonderry that the fullest possible use should be made of outpatient departments. With complete collaboration between the family doctor and the consultant, Farquharson, of Edinburgh, has shown what can be done in this respect with regard to operations for hernia, and we are all well aware of Fegan's admirable work in Dublin, where he has re-emphasized and improved the injection treatment of cases of varicose veins as outpatients.

I am glad that for my first fifteen years as a consultant I served in a voluntary hospital, and, brought up in that old school, I have never felt it was right to have a waiting-list for outpatients, or at most a very short one. Though I am prepared to admit that in some specialties it would be difficult to follow this practice, I would just like to say that by using the help of a senior registrar, a senior house-officer, and a house-surgeon we ran an outpatient service with no waiting-list. Sometimes we were in a little trouble with the establishment, overstaying our allotted time, but the service we give to patients in need is all-important. We were saving money, too, because patients waiting for a consultation were only too often put off work in the meantime. The cost of drugs was constantly under review by a watchful subcommittee who found that at the Bristol Royal Infirmary there were wide variations in the use of drugs without noticeable difference in results. I was proud that I was about the cheapest consultant available. Obviously there must be special allowances made for research.

Emigration

A further aspect of the Health Service is the vexed question of emigration, for beyond certain limits this burden may be too heavy to bear. For many years now medical students have received free or greatly assisted education and training by funds ultimately raised from the taxpayer. The Minister was surely right when he pointed out that there was a moral obligation to give something in return to the country. In Egypt there is an enforced period of service wherever there is need, and the scheme works well. There is no doubt that certain countries, badly needing doctors in all but their larger towns, are proudly exporting far too many of their own well-trained young men and women.

The loan method is not a new idea, but the soaring costs of higher education may force the introduction of this alternative in the place of direct public grants. The loans would have to be repaid over a period of years after qualification, when students have started work. Professor Vaizey put the case clearly before an audience at Sussex University as recently as last month.

Now that continuing education in our hospitals is receiving more attention, house-officers are not just regarded as hard-working pairs of hands. Their interests, their futures, are being cared for by special lectures and demonstrations, so that they are more prepared for whatever step they next propose to take. This was one of the things, among many, that we learned from our friends across the Atlantic, and until recently the absence of such concern was one of the causes of emigration and the loss of promising young men from our country.

And thinking of continuing medical education, I feel I must speak for the cottage hospital, which, properly used, is still a means of continuing medical education, both of visiting consultants and of the local family doctors who bring their cases for discussion. Both learn; the consultant learns again to appreciate the doctor's difficulties, and, though expensive in consultant time and labour, this should be shouldered in the interest of service given on the spot, with the saving of patient's time travelling to and fro, perhaps many miles each way. The local community hospital is still a valuable and viable entry. It is up to us, particularly the consultants, to use these lively useful hospitals wisely and well. They will then never disappear.

Purpose

Nothing is better calculated to preserve the unity of our profession than a purpose, a creed, almost a religion if you like. Purposes may be partly or wholly evil; but powerful, even fanatical movements have often solely depended on a unifying sense of purpose.

When we come to reflect on our service to our patients may I refer you again to the Oxford address: "Yet they get stupefied with drugs or afflicted with unnecessary surgery." I would add—tormented by innumerable, tiresome, and often unnecessary investigations, which can be painful, even frankly dangerous, quite apart from the cost to the service in manpower and bed usage, with the inevitable delay imposed on others.

Clinical Diagnosis

To my mind this is largely due to a gradual loss of the science and art of clinical diagnosis. Here is the root cause of the abuse of all these ancillary investigations. Consultants must accept their fair share of blame. With so many laboratory facilities and all manner of superb radiological aids at hand they too readily resort to these and more elaborate methods before they have tried to get as near to the truth as possible without them. Thus the taking of infinite pains with the history, and exquisitely careful and complete examination of the patient, is so seldom seen that when it is it is a cause for special notice instead of being the rule and sheet anchor of diagnostic procedure. I am sure we should reaffirm our faith in clinical diagnosis, teach it more carefully, recognize that it takes a long time to learn, requiring as it does a great deal of experience, quite apart from a vast amount of knowledge, correctly to interpret the story and the physical findings. By emphasizing the importance of these time-honoured methods we are encouraging our family doctors in their work, for of necessity they will always have to rely largely on their powers of clinical diagnosis, even though many of them may have access to pathological and radiological services. The first suspicions of disease must always be their responsibility and concern, even if selective investigations are found necessary either to support a clinical suspicion or to provide a more complete or more precise assessment of the case.

Yet the teaching of diagnosis is not enough. The clinical teacher must all the time be doing his best to explain the scientific method in addition to his efforts to train powers of observation, and thought. In his fine Harveian address in 1963 Dr. Rae Gilchrist used again the words of Bacon: ". . . the desire to seek, the patience to doubt, the fondness to meditate, the slowness to assert, the readiness to reconsider, the carefulness to dispose and set in order; . . . and to hate every kind of imposture." And he went on to say that "One result is that sound judgement can often dispense with multiple diagnostic tests and the battery of biochemical analysis which masquerade as the scientific approach in current hospital practice. The limitations of the scientist tend to be revealed when discrimination, judgement, and wisdom are in short supply."

We must never forget a mistake—we must ponder over it, learn from it; and I mean mistakes of omission as well as those of commission.

In all our efforts toward the education of future consultants or family doctors we must see to it that they are firmly determined to practise the art and science of clinical diagnosis, and encourage this rather than direct their attention to all the tests which are possible and which on occasion may be necessary. This is particularly true for those of us who frequent other less-advanced countries, who need encouragement, and who must not be exasperated by extolling investigations which in the main are beyond their present resources.

Clinical Judgement

But clinical diagnosis of a high order requires a special capacity for judgement, the ability to set aside the unimportant, the irrelevant, and seize upon the important facets of the problem case. In the Usher Hall in Edinburgh, where many medical conferences are held, there is a dome-shaped ceiling—very high up, unhappily not so well seen by the audience, but there for all speakers to read, if they care to look, are the well-known words: "Wisdom is the principal thing, therefore get wisdom, and with all thy getting get understanding."

This kind of wisdom and judgement is attained to only by long years of application, and, with some, never at all. But it is something beyond price and, for those who acquire it, the hallmark of a great doctor, whatever branch of medicine he adorns.

Of course there are limits beyond which clinical diagnosis cannot go, but even then many possibilities should have been ruled out and consequently investigation reduced to a prudent minimum. It is necessary, too, to remember that results from investigations may mislead, giving rise to a false sense of security. It is well to be particularly sceptical when such results conflict with a considered clinical assessment, or even a well-based clinical impression.

It happens that in three of my own special fields of interest—the thyroid, the biliary tract, and the large bowel—the painstaking history coupled with a most careful and complete physical examination more often than not will enable the physician or surgeon to make a confident diagnosis, or at least be able to decide on the wisdom of an exploration without any recourse to special tests.

I must not weary you with example after example to illustrate my point. Suffice it to say that the acute abdomen, the injured abdomen, as well as those many cases where the abdomen can be wrongly incriminated—the actual cause of symptoms being derived from an extra-abdominal cause—these all almost entirely depend for their successful management on sound and maybe rapid clinical judgement, based on clinical diagnosis or reasoned clinical suspicion.

All this of course takes time, but the more the family doctor can do the fewer should be his calls on the hospital service. The doctor will need adequate time to do this efficiently, but if he is not burdened with too many patients he will give the kind of service which will automatically cut down hospital work and outpatient waiting-lists. If, added to this, the consultants relied a little more on clinical diagnosis and a little less on multitudinous tests much labour and expense would be saved. I am sure it is our bounden duty in this and every possible way to have regard to the expense of this National Health Service of ours.

All too often the surgeon or physician is thanked and praised for his promptitude and skill; but maybe it is the family doctor who should get the praise and gratitude, for it was he whose suspicion was first aroused, and the consultant called in may have a relatively easy problem on his hands. A timely operation or a prompt removal to an intensive care unit has been entirely due to his informed mind, his wise judgement. Let us give, and make a point of giving, praise when and where praise is due . . . . One profession—one purpose.

Iatrogenics

Concern for our patients' good must inevitably lead to the study of iatrogenics—that is, the study of disease and disability inflicted or created by doctors.

Our Gold Medallist today in 1965 said: "No remedial agent or measure is without its hazard. Yet to be over-cautious may result in lack of performance." The same caution should be observed if risk of iatrogenic disease is to be avoided when using certain methods of investigation.

Hippocrates, 460–335 B.C., said: "First do no harm."

Bonaparte, 1820, said: "I do not want two diseases, one nature-made, one doctor-made."

Osler, 1894: "But know also that man has an inborn craving for medicine . . . which distinguished him from his fellow animal creatures. It is really one of the most serious difficulties with which we have to contend."

As Sir Stanford Cade, the chairman of our symposium of this afternoon, wrote: "The review of the hazard to which the patient is exposed, never deliberately . . . is a melancholy clinical exercise, but is nevertheless salutary." In the ninth Crookshank lecture Sir Stanford was directing his remarks to some of the iatrogenic diseases which may follow irradiation; most of these are the results of scarring or fibrosis, and well-nigh any tissue may suffer. These effects may be avoided by changes in technique, in timing, in fractionation of dosage, or by using other therapeutic measures—perhaps combined with irradiation.

Positive Health and Leisure

I have spoken of positive health. We all know that this will not come from the National Health Service, which is far more a national disease service. Positive glowing health is much more than a rather negative disease-free state.

At the Saturday evening meeting the subject was "Religion and Health." Speakers set out to show that a state of real health of mind and body may best be reached and kept when we have come to terms with the problems of life and death. The service at the cathedral was an act of unified worship and prayer for the "Hallowing of Medicine," the like of which we have not seen before.

Sir Ian Fraser's last paragraphs were about leisure, the need, and the way to spend it. The maintenance of full health usually requires some form of recreation. Your Thursday afternoon will be taken up by a symposium on this very subject. Well-known experts will be speaking on some of the many ways of pursuing other interests than our work, for, however much we are devoted to that work, we need these outside interests if we are indefinitely to maintain a full service in our profession. We may not yet have a professor of leisure, but universities nowadays provide means and incentives for the enjoyment of leisure, and you will have noticed that in this regard our university is not lagging behind.

The session on vocational practice will indicate that special sense of satisfaction which is derived from devotion to, and a real sense of vocation in, our work, which we intend to *enjoy* not only for our own sakes but for the sake of those who seek our help.

The doctor will always have to be something more than the latest computer. Science will always have its limitations. The doctor must bring to his job the highest ethical standards, the deepest sense of personal responsibility, and a readily felt warm humanity. You will remember the result of a British Medical Association inquiry of some fourteen hundred schoolmasters regarding what qualities they thought important in the boy intending to practise medicine. In a formidable list emphasis was laid on loyalties, perseverance, poise, conscientiousness, resourcefulness, sympathy, patience, compassion, gentleness, and imagination. Some of these are the more intangible things to which Sir George Pickering referred and was so concerned lest we lost these precious assets in our search for science and truth.

To quote again from William Stokes (1867). "When medicine is in a position to command respect be sure that it will be proportionately increased, and its status elevated." And for many decades that respect and regard was ours, sometimes almost automatically. We held an enviable position in society. Now in 1967 how do we stand? Certainly there is no automatic respect or regard today; these must be merited, but they can be won, and kept.

The Written Word

It is customary to publish this address, and there is no escape from tradition. I had many great teachers who taught me to *do* things well, but there is comfort from Keats, who said, "I am convinced that fine writing is, *next* to fine doing, the top thing in the world."

However, it is a duty to publish critical accounts of experiences which may be of far greater value than we may think at the time. As Byron once said: "A small drop of ink, falling like dew upon a thought, produces that which makes thousands, perhaps millions, think." "Written words are dangerous," said Richards, so it behoves us to go into print with caution. What little I have written has never satisfied me. Yet three years ago when, without warning, I visited a surgeon in Colombo he told me that by a strange coincidence only a few days previously he, with his surgical team, had referred to something I had written in 1952, and, as the result, they had proceeded successfully to remove an advanced malignancy of the colon.

You will notice that I have quoted extensively from the works of others—only a few crumbs are my own. It is said that to copy from one book is cheating, to copy from two or more books is research.

At Londonderry someone said that coffee was essential to family practice—referring to the quite splendid medical centres springing up all over the country, where all can meet, family doctors, consultants, and others. There they can chat, learn to know each other, and learn to be concerned for each other. The "happy ship" was mentioned—perhaps a bit wistfully. Surely we should be just that.

Conclusion

In summary, then, free from any threat of disintegration and speaking with one voice, our great and noble profession, unified not only by loyalties and concern for each other but by its one great unifying purpose, will give a service which will still be the envy of every country in the world—the pattern which others will seek to follow.

Perhaps, even unwittingly, as we are more and more concerned for others we shall in fact be following more nearly the pattern of that incomparable life of concern for others. You will remember how our Lord answered the question—

"*When* saw we Thee sick and came unto Thee . . . ?"

"Inasmuch as ye have done it unto one of the least of these my brethren, ye have done it unto Me."

Dietetic Treatment of Phenylketonuria: a Follow-up Study

BARBARA CLAYTON,* M.D., PH.D., M.R.C.P.; ALAN MONCRIEFF,† C.B.E., M.D., F.R.C.P., F.R.C.O.G.
G. E. ROBERTS,‡ M.B., B.CH., D.P.M.

Brit. med. J., 1967, 3, 133–136

This is a factual study of 57 children with phenylketonuria (31 boys and 26 girls) seen during the period 1955 to the end of 1965. Most of them were under the care of one of us (A. M.), but other physicians at the Hospital for Sick Children have allowed us to use their records. With this small number under various physicians, the reasons for not treating some children or terminating treatment in others necessarily varied. Only those who were treated, or at least given a trial of treatment, are included in this report. Some patients born or detected late in 1965 were not included, as the results obtained were too recent for any satisfactory assessment. One patient (Case 55), detected at 6 years and 4 months, had an I.Q. of 105 and is the subject of a special note.

Methods of Treatment

The basis of the dietetic treatment of phenylketonuria is the exclusion of phenylalanine from the diet save for a minimal amount necessary to sustain life and progress. After a positive test for phenylpyruvic acid in the urine, confirmation is sought by examining the phenylalanine content of the blood. Normally this is about 2 mg./100 ml. serum when a chromatographic method of estimation is used, but in affected children it is much higher. The aim of dietary treatment has been to maintain the level below 4 mg. It is generally advisable to admit the child to hospital for "stabilization."

In the early days of the treatment, when affected children mostly past infancy were being discovered and treated, the practice was to eliminate all phenylalanine by using a synthetic "milk" very low in phenylalanine and a careful selection of other items free from or very low in phenylalanine. When a satisfactory low blood level had been achieved—and sometimes this regimen resulted in the complete disappearance of phenylalanine from the blood—ordinary cow's milk (liquid or dried) was added to the diet until the level of phenylalanine rose; but such a rise was restricted to a maximum of 4 mg./100 ml. serum and the amount of milk adjusted accordingly by frequent estimations of the serum phenylalanine level. An early account of experience in this programme at the Hospital for Sick Children has been published (Woolf, Griffiths, and Moncrieff, 1955). Further experience led to a full account of the methods used and the results achieved (Woolf, Griffiths, Moncrieff, Coates, and Dillistone, 1958).

When treatment of quite young babies was started, however, complete exclusion of phenylalanine from the daily diet produced alarming results, which included skin rashes, loss of appetite, and wasting. An account of some of these difficulties was published (Moncrieff and Wilkinson, 1961). Because of these findings it is necessary to add a calculated amount of milk to the diet, the basis of which is one of the special casein hydrolysates. Full accounts of the methods used have been published as a report of a conference to the Medical Research Council (1963). A short, simple account of a method for feeding the phenylketonuric infant was published from the Hospital for Sick Children by Clayton, Francis, and Moncrieff (1965). It can be assumed that all the children whose cases are reported in the present series have been treated according to the methods in the publications cited.

No mention is made here of methods employed elsewhere than at the Hospital for Sick Children, as this is essentially a report of personal experiences. For the same reason no attempt has been made to review the literature.

The main detailed results are shown in Table I, and the patients are arranged in order of the age of detection, beginning with the youngest. The "quality" of treatment

Table I.—*Summary of Effect of Treatment*

Case No.	Age Detected (Weeks)	Initial I.Q.	Duration of Treatment (Weeks)	Quality of Treatment	Last I.Q.	Epilepsy	Placement
1	2	107	37	Good	111	–	Preschool
2	3	119	376	"	79	–	Ordinary school
3	3	74	30	"	104	–	Preschool
4	4	133	16	"	119	–	"
5	5	111	45	"	120	–	"
6	6	108	104	"	95	–	"
7	6	94	52	"	106	–	"
8	6	83	158	Fair	90	–	"
9	8	90	108	Good	100	–	"
10	8	95	104	"	98	–	"
11	17	70	17	"	85	–	"
12	18	65	476	"	82	–	Ordinary school
13	19	83	320	"	78	–	" "
14	26	74	212	"	65	–	Preschool
15	28	102	260	Fair	109	–	Ordinary school
16	28	15	160	"	39	–	Preschool
17	28	18	221	Good	30	–	"
18	37	31	292	"	61	+	E.S.N.
19	38	29	396	"	55	–	"
20	38	65	208	"	73	+	Ordinary school
21	41	41	372	"	51	+	E.S.N.
22	52	8	368	"	27	+	T.C.
23	52	51	87	"	65	–	Preschool
24	55	45	132	Fair	36	+	Hospital
25	57	21	260	Good	23	+	"
26	59	44	360	"	44	+	"
27	61	45	106	"	44	+	T.C
28	62	58	15	"	58	+	Preschool
29	64	36	464	"	33	+	Rudolph Steiner
30	66	32	364	"	27	+	Hospital
31	68	57	520	"	68	–	Ordinary school
32	69	28	416	"	41	+	T.C.
33	70	11	78	"	8	+	Hospital
34	71	33	104	Fair	30	+	Preschool
35	88	57	60	Good	70	–	"
36	88	42	156	Fair	38	–	T.C.
37	104	24	468	Good	20	+	Hospital
38	104	71	520	"	82	–	Ordinary school
39	104	70	296	"	98	–	" "
40	104	34	72	Fair	46	–	Preschool
41	113	36	220	Good	71	–	Ordinary school
42	114	20	104	"	18	+	Hospital
43	122	23	264	Fair	19	+	T.C.
44	122	48	224	"	61	–	E.S.N.
45	124	35	256	Abandoned	26	–	T.C.
46	128	49	212	Fair	53	–	E.S.N.
47	128	70	268	Good	100	–	Ordinary school
48	138	47	288	Fair	67	–	E.S.N.
49	146	40	120	"	61	–	"
50	168	36	184	Good	39	+	Preschool
51	196	92	112	"	105	–	Ordinary school
52	199	67	160	"	70	–	E.S.N.
53	213	64	72	Fair	56	–	"
54	305	38	312	"	53	–	T.C.
55	321	105	16	Good	104	–	Ordinary school
56	450	49	320	Fair	45	–	Preschool
57	496	47	28	Abandoned	49	–	T.C.

Ordinary school indicates placement with the normal educational system.
E.S.N. indicates placement in a school for the educationally subnormal.
T.C. indicates placement at a training centre.
Hospital indicates placement in a hospital for the subnormal.
Rudolph Steiner indicates placement in a special unit.

---

* Consultant Chemical Pathologist, the Hospital for Sick Children, Great Ormond Street, London W.C.1.
† Formerly Nuffield Professor of Child Health, University of London, and Physician, the Hospital for Sick Children, Great Ormond Street, London W.C.1.
‡ Physician Superintendent, the Ida Darwin Hospital, Fulbourn, Cambridge.

was assessed as good, fair, or bad. This assessment is necessarily subjective, but it was made from our knowledge of the parents together with the views of the ward sister and the dietitians. Thus in 40 instances the standard of maternal care was good, in 15 it was fair, and in two the treatment was abandoned.

Intelligence Testing

The assessment of developmental progress and/or intelligence in children of all ages, but especially in the neonatal period, is fraught with difficulty. Nevertheless, in assessing the progress of children being treated for phenylketonuria, some objective evaluation has to be made, though the limitations of such procedures are well recognized. In particular the standard tests used do not measure the more subtle aspects of behaviour and "intelligence" that may result from dietary treatment.

In the longitudinal study various tests have been used, depending on the age of the child. These tests have included the Griffiths, the Stanford–Binet, the Merrill–Palmer, and the Wechsler. For the purpose of this paper the "score," whatever the test, is expressed as "I.Q." for reasons of convenience.

It must be recognized, however, that the determination of an I.Q. in numerical terms is related to placement within the educational system. It may be that in future, for infants and small children, the term "developmental" tests would be more appropriate.

In the early days in the treatment of phenylketonuric children, before screening tests were introduced on a more or less national scale, it was surprising to find such variable levels of intelligence at the initial testing. One child (Case 55), with an I.Q. of 105 at the age of 321 weeks, has already been mentioned, and this case has been fully reported (Coates, Norman, and Woolf, 1957).

Case 55.—A boy, the fourth child of a family of five, was affected by Gowers's muscular dystrophy. At the time of this diagnosis, when he was 6 years old, the urine was examined for amino-acids, and phenylpyruvic acid was detected. The level of phenylalanine in the blood was raised. Other children in the family were given intelligence tests and were all higher in rating than the patient. It is perhaps significant that just over two years after the initial intelligence testing the level in this patient had fallen by an average of 18 points and a low phenylalanine diet, previously abandoned after three months, was reinstituted.

The parents of this child had above average levels of intelligence, especially the mother. Unfortunately, the intelligence level of other parents in the present series was not estimated.

Effects of Treatment

In general terms the best results, as might be expected, were obtained when treatment was started in early infancy, though some surprisingly good results were obtained in older children, with a rise in intelligence level which enabled them to go to a school for the educationally subnormal (Cases 18, 19, 21, 44, 46, 48, 49, 52, and 53) and to an ordinary school (Cases 2, 12, 13, 15, 20, 31, 38, 39, 41, 47, 51, and 55). Some of these results are shown in the Chart. The final placements of all the children are shown in Table I.

Additional Comments

The reasons for referral to hospital are shown in Table II, which illustrates clearly that the patients are by no means always referred because of mental subnormality alone. Table III shows how and where the disorder was initially diagnosed. It was disappointing to find that during the whole period only 10 patients were detected in infant welfare centres and only two of these were under 6 weeks of age. Seven were detected because of the presence of a previous sibling with the condition, five in the first three weeks of life, and these have done well. The majority, however, have been detected because of the presence of mental subnormality, unfortunately only becoming apparent from 6 months of age onwards.

TABLE II.—*Main Reasons for Referral to Hospital*

Mental subnormality		32
Epilepsy (in each case "infantile spasm")		4
Failure to thrive		3
Speech retardation		1
Eczema		2
Muscular dystrophy		1
Asymptomatic	1. From infant welfare centre	7
	2. Known to be "at risk"	7
	Total	57

TABLE III.—*How, Where, and Why the Diagnosis Was Made*

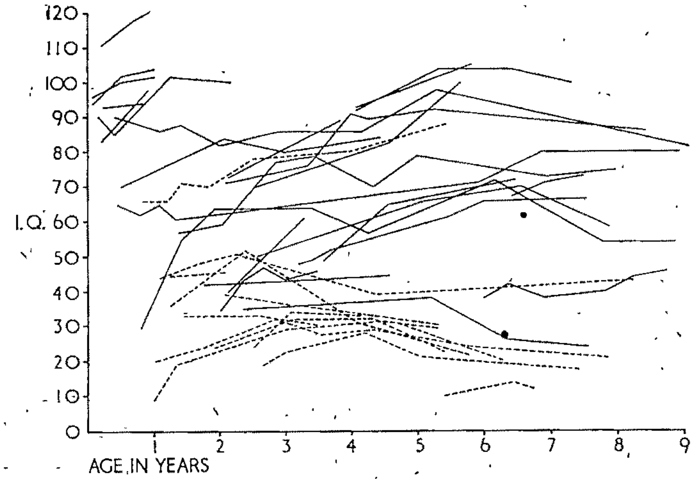
Age	Infant Welfare Centre		Hospital Services			Health Visitor ? M/S	Family Doctor ? M/S
	Routine	? M/S	Routine Investigation	Screened for M/S	At Risk Child		
<3 weeks	1				5		
3–6 weeks	1						
6–8 „	3						
8–12 „	1						
3–6 „	1		1		1		
6–9 months			1	4		1	
9–12 „				3			1
12–18 „		1	1	8			
18–24 „				3			
2–2½ years		2		6			
2½–3 „				3	1		
3–4 „			1	2			
4–5 „				1			
5–6 „							
6–7 „			1	1			
7–8 „							
8–9 „				1			
9–10 „				1			

M/S = Mental subnormality. At risk = Previously affected sibling.

Reasons for failure or partial failure of the treatment are perhaps as important as reasons for success. Several possibilities, or associated phenomena, must be taken into account when assessing the progress of an individual child.

1. *Epilepsy.*—All but three children with epilepsy appear to have responded badly to dietary treatment (see Table I). Eighteen of the 57 children suffered from epilepsy. The progress of some of these is shown in the Chart. A statistical analysis was carried out to see whether the final I.Q. score differed in the two groups of children (epileptics and non-epileptics) after adjusting for initial I.Q., duration of treatment, and age at detection. The results of an analysis of convariance were as follows:

(F-test) $F = 14.6$ (D.F. 1,49)
Very highly significant; $P < 0.001$.
Difference between groups for adjusted final I.Q. = 16.4



Developmental progress of the patients on treatment who had been regularly assessed. ——— Denotes non-epileptics. - - - - - Denotes the presence of epilepsy.

Hence the results indicate that the final I.Q. is higher in non-epileptic children after allowance is made for initial I.Q., duration of treatment, and age at detection. The type of epilepsy and the ages of onset are shown in Table IV. The high incidence of infantile spasms is noteworthy.

TABLE IV.—*Type of Epilepsy and Age of Onset*

Type of Epilepsy	Age of Onset (Months)						Total No.
	5	6	7	8	9	12–18	
" Infantile Spasms "		2	1	1	4	2	10
Grand mal	1				2	3	6
Petit „						2	2

2. *Infection.*—Because the blood phenylalanine level is found to rise temporarily during acute infections, it was thought that the presence of chronic infection—for example, chronic tonsillitis or discharging ears—might militate against the success of dietetic treatment in keeping the blood phenylalanine at a satisfactory low level. So far as the records examined show, however, there was no evidence of this.

3. *Dietetic Difficulties.*—Difficulties with the diet were not infrequently present, often requiring admission to hospital for further stabilization, but, unless breaks in diet lasted more than a week or so, no obvious unsatisfactory results were observed. Infants and young children alleged to refuse the special diet took it in hospital, and intensive instruction of the mothers was necessary. Children of school age presented some difficulties over the midday meal at school, but the education authorities and teachers were always most helpful. Occasional raiding of the larders at home probably does no permanent harm. It is interesting to note that in two affected young children there was a clear history of a severe dislike for ordinary milk from an early age, and later for all protein-containing foods, including eggs. A few parents either refused to co-operate or claimed that it was impossible to get the children to take the special diet. This was the case in certain older children rather than in babies. In one instance the reason given was that a child was no more backward than an elder sister. Investigations showed that the latter child was also affected and untreated. They were members of a migrant gipsy family and were best left alone.

Physical Progress

The records examined have not always shown details of height and weight. When available, heights and weights were converted into percentile groups (Tanner and Whitehouse, 1959). The results are shown in Table V. In general there is no evidence that phenylalanine-restricted diet resulted in poor physical development. In the case of twins, one of whom was affected and treated from the age of 17 days (the other twin being normal), the treated child at the age of 9 was actually 1 in. (2.5 cm.) taller than her sister.

TABLE V.—*Height and Weight of Treated Patients*

Percentile Status	No. of Patients	
	Height	Weight
Not recorded ..	15	3
below the 3rd ..	3	3
3–9	4	7
10–24	11	13
25–49	12	11
50–74	9	14
75–89	2	1
90–96	—	3
97 and over ..	1	2
Total ..	57	57

Criteria for Treatment

In the early days of the treatment of phenylketonuria patients, most of the children found with this abnormality were past the age of infancy, and some " rule of thumb " had to be devised. As experience developed it seemed likely in most instances that a rise of about 20 points in the intelligence level might be achieved by treatment, and even if this did not raise the child into the educational level (educationally subnormal or fit for ordinary school) it seemed worth while even to raise the child from the severe to the moderately subnormal level. In the report of Woolf *et al.* (1958) a rough guide was set out as follows: " We consider treatment worth initiating if the child is 2 years old or under and the G.Q. not less than 20, or 3 years old with a G.Q. of 30 or over, or 4 years old with a G.Q. of 40 or over. In any border-line cases it is probably wise to try six months' treatment with careful psychological testing at the beginning, at 3 months and at the end of this period."

The paper went on to state that it was important to rule out any other form of brain disease such as that due to birth trauma in the widest sense. In the light of further experience it is probably wise to add that the presence of " fits " would make a favourable outcome unlikely. With this reservation, however, it would be fair to state that the policy set out in 1958 is still valid. In addition, all young babies detected by routine screening should certainly be treated.

When to Stop Treatment

This question is of increasing importance as the number of children under treatment grows and the children get older. We have not felt that ethically we could yet stop treatment in any of the patients here reported as doing well. Theoretically it is possible that there is a point in maturation of the brain when a raised phenylalanine level in the blood ceases to cause damage or, to put it another way round, the brain cells develop some degree of tolerance. An attempt to test this by a consideration of the immediate effects of a dose of phenylalanine on the electroencephalogram has been made in the department of electroencephalography at the Hospital for Sick Children (Clayton, Moncrieff, Pampiglione, and Shepherd, 1966). Twelve children received dietetic treatment for phenylketonuria were selected and in seven a considerable increase in the abnormality of the electroencephalogram occurred after a phenylalanine load. It would seem unwise to relax dietetic restrictions in these children. Five children showed only mild or negligible changes during the phenylalanine-tolerance test. These were all children whose intelligence quotients at the time of the test were around normal. Three had started treatment in the first two months of life, and in the other two, though starting treatment at nearly 2 and 3 years old respectively, a remarkable improvement had occurred in their measured intelligence levels. Even in these children we are still hesitant to increase their phenylalanine intake at present.

Summary

From 1955 to the end of 1965 57 children with phenylketonuria, who were treated or at least given a trial of treatment, were studied.

Only 10 of the patients were detected in infant welfare centres, and only two of these were under 6 weeks of age. Seven were detected because a previous sibling had the condition. Unfortunately, the majority were discovered after mental subnormality had become apparent.

The best results were obtained when treatment was started in early infancy.

Sometimes surprisingly good results occurred in older children, with a rise in intelligence level which enabled them to go to a school for the educationally subnormal or to a normal school.

All but three of the 18 children with epilepsy responded badly to dietary treatment.

There was no evidence that dietary treatment resulted in poor physical development.

Thanks are due to the physicians at the hospital for permission to study their patients; to Mr. H. Goldstein for help with the statistical analysis; to the staff of the Department of Psychological Medicine for their interest in the psychometric testing; and to the dietitians and ward staff for their co-operation in the treatment of the patients. We are grateful to the Nuffield Foundation for financial assistance.

REFERENCES

Coates, S., Norman, A. P., and Woolf, L. I. (1957). Ibid., 32, 313.
Clayton, B., Francis, D., and Moncrieff, A. (1965). *Brit. med. J.*, 1, 54.
—— Moncrieff, A. A., Pampiglione, G., and Shepherd, J. (1966). *Arch. Dis. Childh.*, 41, 267.
Moncrieff, A., and Wilkinson, R. H. (1961). Ibid., 1, 763.
Medical Research Council (1963). *Brit. med. J.*, 1, 1691.
Tanner, J. M., and Whitehouse, R. H. (1959). *Growth and Development Record.* London.
Woolf, L. I., Griffiths, R., and Moncrieff, A. (1955). *Brit. med. J.*, 1, 57.
—— —— —— Coates, S., and Dillistone, F. (1958). *Arch. Dis. Childh.*, 33, 31.

Studies in the Epidemiology of Tinea Pedis. VIII: Fungal Infection in a Long-stay Hospital

MARY P. ENGLISH,* M.SC.; R. R. WETHERED,† B.A., B.M., B.CH.; ETHEL H. L. DUNCAN,‡ M.A., B.SC.

Brit. med. J., 1967, 3, 136–139

Tinea pedis has been studied in many different types of community, each yielding different but complementary information about the epidemiology of the disease. It now seems certain that the most common means of transmission is the direct contact of healthy feet with small fragments of skin shed by infected persons (Gentles, 1957; English and Gibson, 1959b; Gip, 1966). This may happen in various ways, the relative importance of which will differ in different communities. It is also known that the incidence of infection is higher in persons living a communal life (Marples and di Menna, 1949; English, Gibson, and Warin, 1961; Wrede, 1965) or using communal washing facilities or swimming-baths (Tritsmans and Vanbreuseghem, 1955; Gentles and Holmes, 1957; English, Gibson, and Duncan, 1960) than in those not doing so; and that, in children, incidence rises with age (English and Gibson, 1959a; Munro-Ashman and Clayton, 1962; Polemann, 1955). There is dispute about the extent to which fungi are carried on, and hence dispersed by, lesion-free feet (Rosenthal, Baer, Litt, Rogachefsky, and Furnari, 1956; English, 1962). That many people have a natural resistance to the disease is a constantly observed fact, though the nature of this resistance and the proportion of the population protected by it are unknown.

The two fungi responsible for the overwhelming majority of cases of tinea pedis in this country are *Trichophyton interdigitale* and *T. rubrum*. The incidence of *T. rubrum* is increasing rapidly, and recent figures from dermatological clinics in Bristol show that it now occurs more often in them than *T. interdigitale*. However, English and Gibson (1959a) and English *et al.* (1961) have shown that both in day schools and in boarding-schools *T. interdigitale* was by far the most common fungus, and this has been confirmed in another boarding-school by Munro-Ashman and Clayton (1962). Similar figures for a sample of the adult population not attending skin clinics are not available, but English and Turvey (work to be published) have recently shown that in patients attending a chiropody clinic, almost entirely for complaints other than tinea pedis, 20 of the 33 infections found were attributable to *T. interdigitale* and only five to *T. rubrum*. *T. interdigitale*, therefore, is still the most common cause of tinea pedis in the population at large. *Epidermophyton floccosum*, the third causal organism, is comparatively rare and its incidence seems to be changing little. The clinical manifestations and epidemiology of these three species differ, but only very tentative suggestions regarding the reasons for this have been put forward.

It seemed possible that information on some of the above points might be provided by the study of a large, relatively stable community of adults living communally for most or all of their lives. During 1964 the attention of one of us (R. R. W.) had been attracted by the large number of patients in one section of a long-stay hospital for mentally retarded men who had clinically severe tinea pedis, and it was decided that a detailed epidemiological study of this hospital should be undertaken.

Subjects

The hospital housed some 400 male patients of all degrees of mental subnormality, some of whom also had mild to severe physical handicaps.

Patients were grouped in "lodges," each housed in separate buildings or parts of buildings. Lodge 7, the largest, was also used for the supervision and discipline of difficult patients, and it was therefore likely that patients from most other lodges spent periods there. Other transfers between lodges occurred at intervals, but many patients had been in the same lodge for a very long time. Lodge 9 was reserved for the elderly sick.

Lodges 7 and 8 each had a 60-bed dormitory; other dormitories ranged in size from 6 to 24 beds. Bathrooms were communal and each contained a number of baths. Up to the end of 1964 one bathroom served lodges 1–5, another lodges 6–8, and lodge 9 had its own. In December of that year additional bathrooms were brought into use so that one was shared by lodges 1 and 2, another by lodges 3–5, and lodges 6, 7, and 8 had one each.

Of the 358 patients included in the survey, 7 were under 20 years old and 276 (77%) were over 40; 326 (91%) had lived in the hospital for three years or more and 236 (66%) for 11 years or more.

---

* Mycologist, Bristol Royal Hospital.
† General Practitioner, Bristol.
‡ Senior Lecturer in Medical Statistics, University of Bristol.

Patients were bathed twice weekly, clean socks and towels being issued after each bath. Towels were likely to be shared and used as bath mats; socks (which were all woollen) were not shared between launderings, but patients did not have their own towels or socks, which were laundered centrally and reissued indiscriminately. Each patient had his own slippers or house shoes, but these were not marked, as were other clothes. In fact, patients rarely wore them and often walked about in the dormitories bare-footed.

Clinical, Laboratory, and Statistical Methods

Scrapings were taken from 358 patients during the summer of 1965 by two of us (M. P. E. and R. R. W.) with the assistance of two registrars in dermatology. Patients omitted from the survey were either on licence or on holiday. Clinical details were taken down by nurses from the hospital. The feet and hands of all patients were examined and samples taken from all lesions of skin or nails which might possibly be attributed to fungal infection; if there were no such lesions, or if only nail lesions were found, scrapings were taken from webs between the fourth and fifth toes.

Details of the patient's age, length of residence at the hospital, lodge, physical capability, abnormalities, etc., were collected by the hospital's nurses from the patients' notes.

Laboratory investigations were carried out by M. P. E. Scrapings were cultured the day after they were taken. All were plated on glucose-peptone agar with chloramphenicol and cycloheximide and incubated for at least one week at 29° C.; further fragments of those from which no dermatophytes grew were then examined microscopically in 20% potassium hydroxide. In a number of cases in which a fungus was seen on microscopy but cultures had failed it was possible to obtain fresh scrapings from which the fungus was successfully isolated.

Nails which were positive on microscopy but not in culture were examined for non-dermatophyte fungi by replating them on cycloheximide-free medium, but were regarded as infected by these fungi only if at least 5/20 inocula yielded the same organism.

Cultures from patients' socks were made (1) by shaking or scraping them over plates of glucose-peptone-cyclohexamide-chloramphenicol agar (Broughton, 1955) and (2) by soaking small pieces of the fabric in the cooled molten medium and pouring-plates. Both methods were satisfactory.

The planning of the survey and the analysis of results were the responsibility of the third author (E. H. L. D.). The questionary used for recording patients' histories and laboratory and clinical findings was prepared in such a way that the replies could be used for punched-card analysis without further coding.

Mycological and Clinical Results

Table I shows the number of patients infected with each fungus or pair of fungi, and also the number of isolations of each organism. *T. interdigitale* was the dominant species, but a high percentage of *T. rubrum* was also recorded; *E. floccosum* was comparatively rare. Isolates of *T. interdigitale* varied considerably in appearance, but the variations were not constant on subculturing. *T. rubrum* isolates, on the other hand, were almost all of the same distinctive type, which remained constant over many subcultures. The strain was very strongly pigmented and was unusual in being intermediate between the "granular" and "downy" types (English, 1964). All non-dermatophytes were found in toe-nails; that there were no *Aspergillus* spp. is unexpected (Walshe and English, 1966). The culture failure rate of 7.5% was well within normal limits.

TABLE I.—*Incidence of Infections and Number of Isolations Among* 358 *Patients Examined*

Fungus	Persons Infected		Isolations	
	No.	% of Total Persons Infected	No.	% of Total Isolations
T. interdigitale	73	50·0	89	54·6
T. rubrum	38	26·0	51	31·3
E. floccosum	1	0·7	4	2·5
Non-dermatophytes* ..	6	4·1	7	4·3
T. interdigitale + *T. rubrum*	12	8·2	—	—
T. interdigitale + *E. floccosum*	2	1·4	—	—
T. interdigitale + non-dermatophytes* ..	1 }17	0·7 }11·7	—	—
T. rubrum + *E. floccosum* ..	1	0·7	—	—
T. interdigitale + microscopically positive only	1	0·7	—	—
Microscopically positive only	11	7·5	12	7·4
Total	146	40·8	163	

*All from toe-nails. *Scopulariopsis brevicaulis*, 2 isolates; *Fusarium* sp., 1 isolate; *Cephalosporium* sp., 1 isolate; *Penicillium* sp., 1 isolate; cultures failed, 2.

Double infections, either concurrent or combined (Partridge, 1952), were found in 17 (11.7%) of infected patients, and their occurrence was not related to the length of the patient's stay in hospital, his age, or the incidence of fungi in his lodge, all factors affecting opportunity for cross-infection. This contrasts with the observations of Gentles and Holmes (1957) in coal miners, and suggests that lack of resistance in the patient may also be a factor in the occurrence of double infections.

Table II shows the sites infected by dermatophytes only. The hands were involved in 6 out of 140 patients with tinea pedis; in addition, one patient had also had a widespread infection with *T. rubrum* the previous year, which had responded to treatment. Nurses reported that groin infections, which they would probably notice while bathing patients, were not very common; if this was so it was unexpected in view of the high incidence of *T. rubrum* in the feet (English and La Touche, 1957) and the common occurrence of tinea cruris in all-male communities.

TABLE II.—*Sites of Infection (excluding non-dermatophytes) Among* 358 *Patients Examined*

Site	Patients Infected	
	No.	% of Total Patients
Feet only	91	25·4
Feet and toe-nails	34	9·5
Toe-nails only	9	2·5
Feet and hands (including finger-nails)	1	0·3
Feet, toe-nails, and hands (including finger-nails) ..	5	1·4

The clinical behaviour of *T. interdigitale* and *T. rubrum* is compared in Table III. The results confirm the observations of others that *T. rubrum* tends to cause extensive infections while those of *T. interdigitale* are more restricted. Toe-nails were involved in 19 out of 89 (21%) *T. interdigitale* infections and 21 out of 51 (41%) *T. rubrum* infections: in 3 out of 19 cases of *T. interdigitale* infections of this site the skin of the feet was not affected, but all *T. rubrum* infections of the toe-

TABLE III.—*Comparison of Extent of Infection by T. interdigitale and T. rubrum (double infections counted twice)*

Site	*T. interdigitale*			*T. rubrum*			Total Infections of Site
	No. of Cases	% Total Cases	% Total Infections of Site	No. of Cases	% Total Cases	% Total Infections of Site	
Skin of feet only ..	70	78·7	71·4	29	56·8	28·6	99
Toe-nails only ..	3	3·4	100·0	—	—	—	3
Skin of feet and toe-nails	16	18·0	48·5	17	33·3	51·5	33
Skin of feet, toe-nails, and hands	—	—	—	4	7·8	100·0	4
Hands only	—	—	—	1	2·0	100·0	1
Total No. of cases	89			51			

nails were part of a more widespread condition. All hand infections were attributable to *T. rubrum*.

Dermatophytes were present in the lesion-free toe-webs of 19 patients; 17 of these had *T. interdigitale*, one *T. rubrum*, and one a fungus found on microscopy only. Three of the *T. interdigitale* infections were associated with clinical onychomycosis caused by the same fungus, and here the nails were obviously the source of contamination. The great preponderance of *T. interdigitale* over *T. rubrum* (Götz, Sturde, and Hantschke, 1965) probably reflects the comparatively mild nature of infections due to the former fungus and perhaps a tendency to spontaneous resolution. The occurrence of lesion-free infections was unrelated to the age of the patient, the length of his stay in hospital, or the incidence of infections in his lodge.

In view of the differences of opinion on the importance of lesion-free carriers in the epidemiology of tinea pedis, 17 of the above patients were re-examined after one year: 10 were found to be still infected, but to have developed lesions; six were no longer infected; and one (*T. interdigitale*) remained infected without lesions. Most cases of apparent toe-web "carriers," therefore, were probably simply stages in the onset or regression (Svendsen, 1961) of an infection, or contamination from a clinical infection of the nail; only one patient out of 358 could be regarded as a carrier in the usual sense. This is a lower rate than that found by Götz and Hantschke (1965) in a similar investigation on coal miners. These workers reported that 41 out of 1,240 (3%) carried dermatophytes asymptomatically over a period of a year; they do not, however, state whether any of these men had toe-nail infections.

Epidemiological Results

Table IV shows that the incidence of infection varied very appreciably from lodge to lodge. However, probability tests showed that for *T. interdigitale* all such interlodge variation could have occurred by chance; for *T. rubrum* only, the incidence in lodge 7 was significantly different from that in other lodges ($P<0.05$), and, for the total fungi, the incidence in lodge 1 was significantly higher than in other lodges ($P<0.01$). The ratio % *T. rubrum*/% *T. interdigitale* for lodge 7 was 1/0.95; that for all other lodges combined was 1/1.91—that is, the proportion of *T. rubrum* infections in lodge 7 was significantly higher than that in other lodges ($P<0.05$). There was no significant difference in average incidence in patients using different bathrooms, either when grouped according to bathrooms in use up to and during 1964 (Table IV) or when the new bathrooms in use after this date were considered.

TABLE IV.—*Incidence of Infection in Lodges (excluding non-dermatophytes). Double Infection with T. interdigitale and T. rubrum Recorded in Both Columns A and B; Column C Shows Total Number of Infected Patients*

Lodge		A *T. interdigitale* Infections		B *T. rubrum* Infections		*T. rubrum*/*T. interdigitale* Ratio	C All dermatophyte Infections		Total Patients in Lodge
		No.	%	No.	%		No.	%	
1	Bathroom shared till Dec. 1964	9	37·5	5	20·8	1/1·8	16	*66·6*	24
2		9	20·5	4	9·1	1/2·3	12	27·3	44
3		11	39·4	4	14·3	1/2·8	13	46·4	28
4		9	23·1	6	15·4	1/1·5	14	35·6	39
5		3	11·5	2	7·7	1/1·5	5	19·2	26
Total		41	25·5	21	13·0		60	37·3	161
6	Bathroom shared till Dec. 1964	7	26·0	2	7·4	1/3·5	9	33·3	27
7		18	22·2	19	*23·4*	*1/0·9*	35	43·2	81
8		15	25·4	6	10·2	1/2·5	22	37·3	59
Total		40	24·0	27	16·2		66	39·5	167
9		8	26·7	3	10·0	1/2·7	14	46·7	30
Grand total ..		89	24·9	51	14·2	1/55	140	39·0	358

Figures in italics are statistically significant (see text).

Other factors investigated and found to be unrelated to the incidence of infection were size of dormitory, patient's age, mongolism, deformities of the feet (Svendsen, 1961), and mobility. With regard to mobility, it was found that of nine patients who had been unable to walk from birth, four had tinea pedis.

A long stay in hospital was found to increase significantly the likelihood of infection. Of 31 patients who had been in residence for under three years, 6 (19%) were infected; while of 327 who had been in residence for a longer period 134 (41%) were infected ($P=0.02$).

Hyperhidrosis appeared to inhibit fungal infection, for none of the 12 hyperhidrotic patients had the disease ($P=0.00164$ by Fisher's exact probability test).

TABLE V.—*Effect of Age on Incidence of Toe-nail Infections*

Age in Years	*T. interdigitale* Infections		*T. rubrum* Infections		All Fungal Infections Including Non-dermatophytes		No. of Patients Examined
	No.	%	No.	%	No.	%	
Under 50 ..	5	3·0	4	2·4	18	10·9	165
50 and over	14	7·3	17	8·8	37	19·3	193
Significance	Not significant		$P<0{\cdot}02$		$P<0{\cdot}05$		

Toe-nail infections were found to be unrelated to the length of the patient's stay in hospital, but those due to *T. rubrum* and total fungi (including non-dermatophytes) were significantly related to the patient's age (Table V) (Rosman, 1966; Walshe and English, 1966). The incidence of onychomycosis due to *T. rubrum* was significantly higher in lodge 7 than in all other lodges, but that of *T. interdigitale* onychomycosis was not (Table VI).

TABLE VI.—*Incidence of Toe-nail Infections in Lodges*

Lodge	*T. interdigitale* Infections		*T. rubrum* Infections		No. of Patients
	No.	%	No.	%	
7	5	6·2	9	11·1	81
All others ..	14	5·1	12	4·3	277
Significance ..	Not significant		$P<0{\cdot}05$		

Cultures were made (1) from one pair of socks from each of three patients with *T. interdigitale* infection and one pair from a patient with *T. rubrum* infection after they had been worn for four days and (2) from another pair of socks from each of the same patients after these had been worn for four days and washed in the hospital laundry. The appropriate fungus was recovered from all the unlaundered socks, and a few colonies of *T. interdigitale* were also obtained from those of the *T. rubrum* patient in addition to his own fungus, presumably a legacy from the previous wearer. After laundering, a few colonies of *T. interdigitale* were isolated from the socks of one of the *T. interdigitale* patients, but cultures from the other socks were negative. Thus laundering considerably reduces the quantity of potential inoculum in socks but does not eliminate it.

Discussion

When this survey was undertaken it was supposed that all the conditions making for the highest possible incidence of tinea pedis would be present. In fact, the average incidence of all dermatophytes, 39%, was lower than that in miners in one of the pits investigated by Gentles and Holmes (1957) (57%) and also than that in pits in the Ruhr (69%) (calculated from Götz *et al.*, 1965). However, the incidence in lodge 1 of the hospital (66.6%) was significantly higher than that in other lodges and of the same order as that in miners. It may be, therefore, that conditions in lodge 1 were such that a near maximum level of infection had been reached and that, left unchecked, the same level would eventually be attained throughout the hospital. In view of the coincidence of the figures for patients in lodge 1 and of those for miners it is possible that the number of persons remaining uninfected, 30–40%, represents the proportion of persons in the adult male population who are resistant to tinea pedis. The nature of this resistance is a matter of speculation (Munro-Ashman and Clayton, 1962), on which this survey throws no light; but so high a figure would explain the great difficulty found by workers who have tried to establish experimental infections in human feet (Baer, Rosenthal, Rogachefsky, and Litt, 1955; Strauss and Kligman, 1957).

Some interesting aspects of the epidemiology of the two dominant fungal species are brought out by this survey. That there was no statistically significant difference in the incidence of *T. interdigitale* in the different lodges suggests that the fungus had been present for a long period, probably with repeated introductions, leading to an even spread throughout the community. The instability of the *T. interdigitale* isolates in culture prevented any speculation over the introduction of different strains of that fungus. The *T. rubrum* isolates, however, were not only stable on subculture but were almost all of the same distinctive type, intermediate between the well-recognized "granular" and "downy" forms, a type rarely found in diagnostic practice in the district (English, 1964). This suggests a single introduction at some time in the past which spread through the community, possibly followed by more recent introductions of other forms which have not yet had time to spread. The idea of early, multiple introductions of *T. interdigitale* but a single, more recent introduction of *T. rubrum* is compatible with knowledge of the relative incidences of the two species in the population at large (see introduction) and with the fact that *T. rubrum* has only recently reached even its present incidence in this country.

Patients in the closest contact with the original case of *T. rubrum* infection would be likely to become infected before those less close, and, once infected, their condition would not regress spontaneously. Therefore, supposing that there had not yet been time for all susceptible patients to have contracted the disease, the original introduction would have occurred in the lodge with the highest infection rate. This is lodge 7, the only one in which both the *T. rubrum* infection rate and the *T. rubrum/T. interdigitale* ratio were significantly higher than in all other lodges. *T. rubrum* infections in lodge 7 were also clinically more extensive and conspicuous than elsewhere (this being the lodge that originally drew the attention of R. R. W. to the problem of tinea pedis in the hospital), and were therefore likely to have been established longer, as was confirmed by the abnormally high incidence of *T. rubrum* onychomycosis in this lodge compared with an average incidence of *T. interdigitale* nail infections.

Cross-infection in the hospital must obviously have occurred by a number of routes. Within lodges it would have taken place in the dormitories, where the patients were often barefooted. Scissors used for cutting the patients' nails might also be implicated, though these were not examined. But if the bulk of the *T. rubrum* infections were indeed the result of a single introduction, these must also have been spread between lodges. This could partly be accounted for by the transfer of patients from lodge to lodge and also, between groups of lodges, by the sharing of bathrooms up to 1964, though the latter effect must have been comparatively slight as no statistical significance could be shown. As well as being probably of minor importance generally, neither of these two routes accounts for the fact that, out of nine crippled patients who had never walked, four had tinea pedis. Broughton (1955) has shown that dermatophyte fungi can be isolated from the socks of infected persons both before and after laundering, and we have confirmed this. It seems probable that the custom in this hospital of the communal ownership of socks and towels must have been an important factor in the spread of tinea pedis: in fact, if the high incidence of infection in crippled patients is any guide, it was probably the most important route between lodges. Though Broughton (1955) and Sanderson and Sloper (1953) suggest that socks are a likely means of cross-infection, our observations are probably the first to offer strong evidence that this was so in a particular community.

Summary

The incidence of tinea pedis, including tinea unguium, in a long-stay hospital for mentally retarded men was 40.8% of 358 men examined. Of the infections, 50% were attributable to *Trichophyton interdigitale*, 26% to *T. rubrum*, 0.7% to *Epidermophyton floccosum*, 4.1% (nails only) to non-dermatophytes, 11.7% to mixed infections, and 7.5% were microscopically positive but cultures failed.

The incidence of *T. rubrum* was significantly higher in patients in one of the "lodges" into which the hospital was divided than in the others, but there was no significant difference in the incidence of *T. interdigitale* infections in lodges. Infection was related to the length of the patient's stay in hospital but not to his age, the communal bathroom used by him, or other factors examined. Four out of nine crippled patients who had never walked had tinea pedis. The appropriate fungus was isolated before laundering from the worn socks of three patients with *T. interdigitale* infection and of one patient with *T. rubrum* infection; after laundering the fungus was recovered from the socks of one of the patients with *T. interdigitale* infection.

In view of the failure of laundering to eliminate the fungus from worn socks, of the fact that socks were not the property of patients but were reissued indiscriminately after laundering, and of the high infection rate in patients who had never been able to walk, it is suggested that infected socks were a more important route of cross-infection in this community than contaminated floors.

We are indebted to Dr. R. P. Warin, Bristol General Hospital, for initiating this survey and for his suggestions and encouragement throughout. Our thanks are due to Dr. T. C. Leahy for allowing us access to the hospital and for putting every facility for the investigation at our disposal; to the nursing staff of the hospital for their invaluable co-operation and interest; to Mr. T. G. Morgan, who carried out a great deal of the laboratory work; and to Dr. M. M. Walshe and Dr. R. Heeler for assistance in taking the scrapings.

REFERENCES

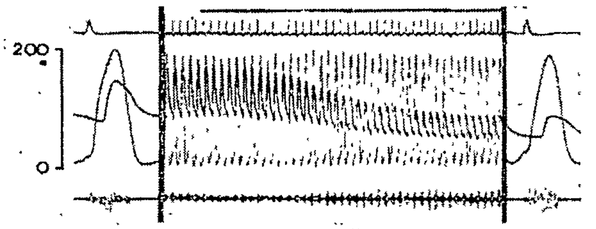
Baer, R. L., Rosenthal, S. A., Rogachefsky, H., and Litt, J. Z. (1955). *Amer. J. publ. Hlth*, **45**, 784.
Broughton, R. H. (1955). *Brit. J. Derm.*, **67**, 249.
English, M. P. (1962). Ibid., **74**, 50.
—— (1964). *Sabouraudia*, **3**, 205.
—— and Gibson, M. D. (1959a). *Brit. med. J.*, **1**, 1442.
—— —— (1959b). Ibid., **1**, 1446.
—— —— and Duncan, E. H. L. (1960). Ibid., **2**, 573.
—— —— and Warin, R. P. (1961). Ibid., **1**, 1083.
—— and La Touche, C. J. (1957). *Brit. J. Derm.*, **69**, 311.
Gentles, J. C. (1957). *Brit. med. J.*, **1**, 746.
—— and Holmes, J. G. (1957). *Brit. J. industr. Med.*, **14**, 22.
Gip, L. (1966). *Acta derm.-venereol. (Stockh.)*, **46**, Suppl. No. 58.
Götz, H., and Hantschke, D. (1965). *Hautarzt*, **16**, 543.
—— Sturde, H.-C., and Hantschke, D. (1965). *Dermatologica (Basel)*, **130**, 130.
Marples, M. J., and di Menna, M. E. (1949). *Med. J. Aust.*, **2**, 156.
Munro-Ashman, D., and Clayton, Y. (1962). *Proc. roy. Soc. Med.*, **55**, 551.
Partridge, B. M. (1952). *Trans. St. John's Hosp. derm. Soc. (Lond.)*, **31**, 34.
Polemann, G. (1955). *Arch. klin. exp. Derm.*, **201**, 24.
Rosenthal, S. A., Baer, R. L., Litt, J. Z., Rogachefsky, H., and Furnari, D. (1956). *J. invest. Derm.*, **26**, 41.
Rosman, N. (1966). *Brit. J. Derm.*, **78**, 208.
Sanderson, P. H., and Sloper, J. C. (1953). Ibid., **65**, 252.
Strauss, J. S., and Kligman, A. M. (1957). *Arch. Derm.*, **76**, 70.
Svendsen, I. B. (1961). *Acta derm.-venereol. (Stockh.)*, **41**, 150.
Tritsmans, E., and Vanbreuseghem, R. (1955). *Belg. Geneesk.*, **11**, 625.
Walshe, M. M., and English, M. P. (1966). *Brit. J. Derm.*, **78**, 198.
Wrede, E. (1965). *Mykosen*, **8**, 66.

Effects of Prompt Squatting on the Systolic Murmur in Idiopathic Hypertrophic Obstructive Cardiomyopathy*

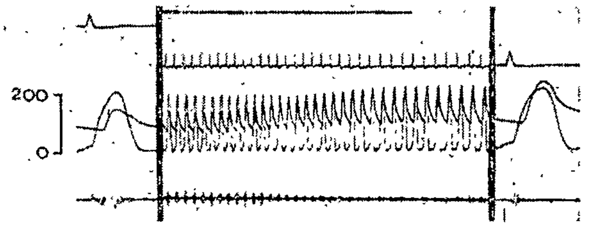
M. NELLEN, M.D., F.R.C.P., F.R.C.P.ED., F.A.C.C.; M. S. GOTSMAN, M.D., M.R.C.P., M.R.C.P.GLASG.
L. VOGELPOEL, M.D., M.R.C.P.; W. BECK, M.SC., M.MED., M.R.C.P.
V. SCHRIRE, M.SC., PH.D., M.D., F.R.C.P., F.R.C.P.ED., F.A.C.C.

Brit. med. J., 1967, 3, 140–143

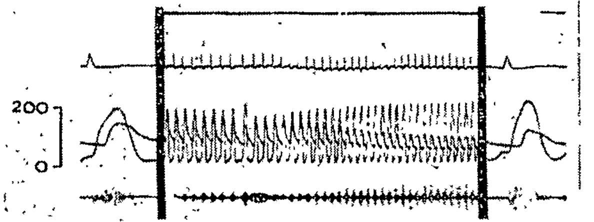
In patients with hypertrophic obstructive cardiomyopathy obstruction to left ventricular ejection varies from moment to moment. The pressure gradient can be increased by amyl nitrite, which lowers peripheral resistance (Braunwald and Ebert, 1962; Wigle *et al.*, 1965; Hancock and Fowkes, 1966), or can be reduced or abolished by systemic vasoconstriction with phenylephrine, methoxamine, or angiotensin (Braunwald and Ebert, 1962; Braunwald *et al.*, 1964a; Wigle *et al.*, 1965) or by aortic constriction (Pierce *et al.*, 1964). Inotropic agents—digitalis and isoprenaline—increase the obstruction by increasing the vigour of ventricular contraction; this effect can be prevented by drugs which block the sympathetic beta-receptors (Braunwald and Ebert, 1962; Braunwald *et al.*, 1962; Harrison *et al.*, 1964). Reduction in circulating blood volume and the Valsalva manœuvre reduce ventricular volume, increase contractility, and increase the obstruction (Braunwald *et al.*, 1964b; Marcus *et al.*, 1964; Shah *et al.*, 1965a, 1965b). During these manipulations of the circulation the murmur varies in intensity, becoming louder with more severe obstruction, and can be virtually abolished when the gradient disappears (Goodwin, 1964; Nellen *et al.*, 1965) (Fig. 1), thus reflecting the haemodynamic situation.



AMYL NITRITE



PHENYLEPHRINE



ISOPRENALINE

FIG. 1.—Hypertrophic obstructive cardiomyopathy. The systolic murmur reflects the haemodynamic situation with amyl nitrite, phenylephrine, and isoprenaline. Pressure measurements in left ventricle and femoral artery. Simultaneous external phonocardiogram shown in lower channel.

Squatting provides a simple bedside method of acutely increasing venous return, effective filling pressure of the heart, stroke output, and systemic arterial pressure (Sharpey-Schafer, 1956). We have therefore studied the effect of this manoeuvre on the systolic murmur in 11 patients with hypertrophic obstructive cardiomyopathy, and report the results in this paper. This effect has been compared with that from eight patients who have fixed valvar aortic stenosis and five patients with mitral incompetence, as the murmur in these cases may resemble that of hypertrophic obstructive cardiomyopathy. In addition, to help us in assessment of the mechanism of squatting we studied the effect of this procedure on the murmur of pulmonary stenosis.

Patients and Methods

In 11 patients the clinical diagnosis of hypertrophic obstructive cardiomyopathy was confirmed by cardiac catheterization cineangiocardiography, and the dynamic response to manipulation of the circulation by drugs affecting the severity of the left ventricular obstruction (Braunwald *et al.*, 1964a). The peak systolic pressure gradient between the inflow and outflow tracts of the right ventricle (intraventricular gradient) was measured. Mitral incompetence was assessed on cineangiocardiography. The clinical and haemodynamic features in each patient are given in Table I. In one patient (Case 10) the diagnosis was made on clinical grounds and by the typical response of the murmur to vasoactive drugs (Nellen *et al.*, 1965). Auscultation and phonocardiography were performed with the patient in the standing and squatting position, and the intensity and length of the systolic murmur was noted. Phonocardiograms were recorded on an Elema Mingograph 4 channel recorder (moving magnet ink jet galvanometers). Systemic arterial pressure was measured simultaneously with a cuff sphygmomanometer in both positions.

Squatting had to be prompt to achieve the optimum results. The patient was told to hold the edge of the examining couch while squatting. The stethoscope or phonocardiograph microphone was applied to the chest at the site of maximum intensity of the murmur, and the investigator then squatted rapidly and promptly with the patient, listening to the intensity of the murmur during held expiration. Prolonged breath-holding was avoided.

Eight patients with discrete valvar aortic stenosis and without mitral valve disease were studied for comparison of the effect of squatting on the systolic murmur. The clinical details of these cases and the results of cardiac catheterization and cineangiocardiography are given in Table II. The diagnosis has been confirmed at operation. Five cases with rheumatic mitral incompetence were diagnosed clinically by accepted criteria and the effect of squatting on the systolic murmur was also studied. Three cases of moderate pulmonary stenosis proved by catheterization were also investigated.

---

* From the Cardiac Clinic, Department of Medicine, University of Cape Town, and the Cardiovascular-Pulmonary Research Group, supported in the Department of Medicine by the Council for Scientific and Industrial Research.

Results

There was a rise in arterial and pulse pressure on squatting in each patient with hypertrophic obstructive cardiomyopathy. After 5–10 beats bradycardia occurred. The systolic murmur was promptly abolished in two and shortened and softened markedly in intensity in seven of the patients (Table I, Fig 2). In Case 10 the systolic murmur softened slightly—this patient was on a full dose of propranolol. In Case 11 the response was variable. The first heart sound usually softened and broadened. The second heart sound was unaltered or increased slightly in intensity. A fourth heart sound was recorded in five patients while standing. In three it moved towards the first sound, while in the other two there was little change in relation to the first sound on squatting. In no case did the murmur intensify.

In our studies of valvar aortic stenosis we found a similar increase in blood pressure and bradycardia, but the systolic murmur increased in intensity and length in six of the eight patients (Table II, Fig. 3). In the other two the change was insignificant. These two latter patients had poor left ventricular function as assessed by an elevated end-diastolic pressure in the left ventricle, left ventricular pulsus alternans, and an enlarged ventricle contracting poorly at cineangiocardiography.

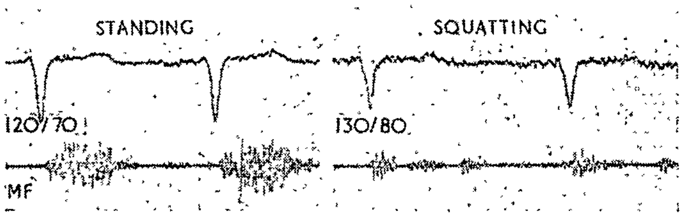


Fig. 2.—Case 3. Hypertrophic obstructive cardiomyopathy. Phonocardiogram (M.F.=medium frequency) taken medial to the apex. The systolic murmur is virtually abolished on squatting. (Lead V, of the electrocardiogram is indicated in the top tracing. Each large square on the record indicates 0.05 second.)

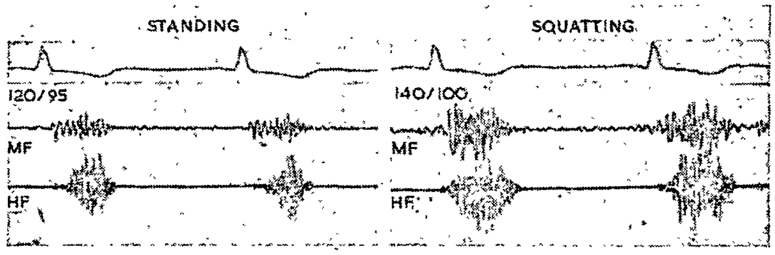


Fig. 3.—Case V. Valvar aortic stenosis. Phonocardiogram taken at the aortic area. The systolic murmur increases in intensity on squatting. (Upper tracing shows lead I of the electrocardiogram. M.F.=medium frequency; H.F.=high-frequency phonocardiogram.)

In five patients with rheumatic mitral incompetence the systolic murmur increased definitely but slightly on squatting. The third heart sound and mid-diastolic flow murmur also increased in intensity (Fig. 4). In three cases the systolic murmur of pulmonary stenosis intensified appreciably on squatting (Fig. 5).

Discussion

It has been shown (Sharpey-Schafer, 1956) that when normal subjects squat arterial mean pressure increases. The increase is greatest after a few seconds; thereafter mean pressure falls and eventually stabilizes at a level higher than the standing or sitting level. This we have confirmed (Fig. 6). The immediate rise in arterial pressure is believed to have two causes, the major factor being an increase in stroke output due to an increase in effective cardiac filling pressure, which in turn is due to squeezing blood out of the veins of the legs. The second factor, a minor one, is a small increase in peripheral arterial resistance due to the hydrostatic effect of the posture change and kinking of the femoral arteries. After a few seconds mean arterial pressure falls slightly owing to peripheral dilatation and stabilizes at a new level which is still higher than the control value. Bradycardia also occurs. This is a delayed baroceptor response. The slowing of the heart rate occurs at the highest blood pressure levels, but the changes in mean pressure and pulse pressure are still present if no rate changes occur, as in thyrotoxicosis or after atropine (Sharpey-Schafer, 1956). Squatting is thus an excellent procedure for increasing the effective filling pressure of the heart acutely; it is the converse of the Valsalva manœuvre (Sharpey-Schafer, 1955, 1956). This has been confirmed by Brotmacher (1957a, 1957b), who also demonstrated an increase in right atrial and pulmonary capillary wedge pressure when patients squat in the lying position. However, simultaneous oesophageal pressure was not measured in his cases.

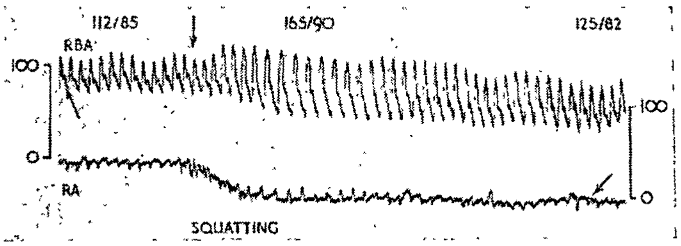


Fig. 6.—Effect of squatting on the arterial and right atrial pressure of a subject with mild pulmonary stenosis. Right atrial pressure increases very slightly on squatting. Mean arterial and pulse pressure increase, but there is a later fall and bradycardia from the baroceptor response; pulse and mean pressure are still greater than control values. (Zero level taken at the sternal angle in each position. Left-hand scale shows pressures in mm.Hg while standing and right-hand scale shows pressures on squatting.)

Similar studies by O'Donnell and McIlroy (1959) confirm Sharpey-Schafer's findings. They also showed that when subjects squat in a swimming-pool, so that the effect of gravity is removed, the haemodynamic response does not occur. A sudden increase in venous return and effective cardiac filling pressure would appear to be the cause of the increase in intensity of the systolic murmur in our cases of pulmonary stenosis. Increased peripheral resistance would not be a factor here. Our findings

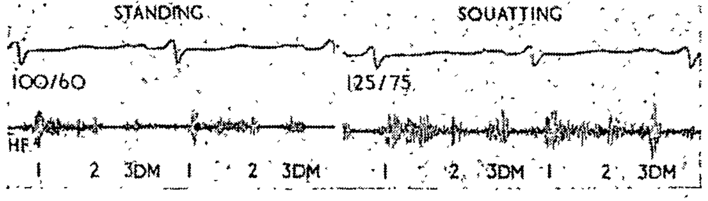


Fig. 4

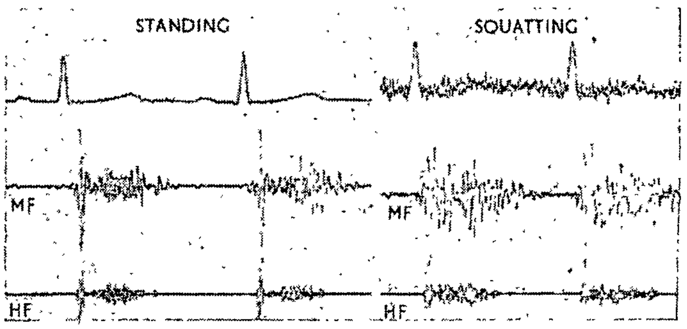


Fig. 5

Fig. 4.—Rheumatic mitral incompetence in coloured girl aged 16. Phonocardiogram taken at the mitral area. The systolic murmur, third heart sound (3), and mid-diastolic murmur (D.M.) intensify on squatting. (1=first heart sound; 2=second heart sound. Upper tracing shows standard lead I of the electrocardiogram.) Fig. 5.—Moderate pulmonary stenosis in European boy aged 9. Phonocardiogram taken at second left intercostal space. The systolic murmur intensifies on squatting. (Standard lead II of the electrocardiogram shown in upper tracing.)

TABLE I.—*Clinical and Haemodynamic Data on 11 Cases of Hypertrophic Obstructive Cardiomyopathy with the Effect of Squatting on the Blood Pressure and Systolic Murmur*

Case No.	Age and Sex	Race	Peak Systolic Pressure Gradient between L.V. and F.A. (mm. Hg)				Intra-ventricular Gradient in R.V. (mm. Hg)	M.I. (Cine)	Blood Pressure (mm. Hg)		Effect of Squatting on Intensity of Murmur
			Rest	AN	PE	ISOP			Standing	Squatting	
1	57 M	E	20	92	0	82	3	±	130/90	140/95	Abolished
2	66 F	E	5	—	—	115	0	0	140/80	160/90	,,
3	59 F	E	110	130	0	175	7	±	110/65	195/100	Softens markedly
4	48 F	C	5	22	—	33	0	±	110/65	125/70	,, ,,
5	35 M	E	15	62	—	105	4	+	110/80	130/100	,, ,,
6	44 M	E	0	20	—	—	0	—	130/90	150/100	.. ..
7	54 M	E	42	104	0	120	10	0	80/60	130/60	.. ..
8	51 F	E	18	40	10	—	7	±	125/70	150/75	,, ,,
9	41 F	E	10	40	5	55	0	0	80/60	100/60	,, ,,
10	25 F	E	0	—	—	—	—	—	110/60	120/70	Softens slightly (on propranolol)
11	26 M	C	70	110	55	—	0	+	90/70	110/60	Variable

AN = Amyl nitrite. ISOP = Isoprenaline. F.A. = Femoral artery. M.I. = Mitral incompetence. C = Coloured. PE = Phenylephrine. L.V. = Left ventricle. R.V = Right ventricle. E = European.

TABLE II.—*Clinical and Haemodynamic Information in Eight Cases of Aortic Stenosis, and Effect of Squatting on Blood Pressure and Systolic Murmur. (Poor Left Ventricular Function was Indicated by Left Ventricular Pulsus Alternans, an Elevated End-diastolic Pressure in the Ventricle, or Impaired Ventricular Contractility Assessed by Cineangiocardiography)*

Case No.	Age and Sex	Race	Pressure Gradient Across AO. Valve (mm. Hg)	Cardiac Index (L./min./M.²)	AO Valve Area (sq. cm.)	L.V. Function	Blood Pressure (mm. Hg)		Effect of Squatting on Intensity of Murmur
							Standing	Squatting	
I	63 M	E	115	1·8	0·4	Normal	100/75	120/100	Increases
II	26 F	C	117	2·8	0·5	,,	120/70	130/80	,,
III	8 M	E	45	4·2	0·7	,,	90/60	110/60	,,
IV	61 M	E	115	3·3	0·5	Poor	160/100	180/110	,,
V	61 M	E	—	3·9	—	Normal	120/95	140/100	,,
VI	17 M	E	94	5·1	0·4	,,	90/60	110/70	,,
VII	43 M	E	120	3·4	0·5	Poor	115/85	120/80	Little change
VIII	63 M	E	80	1·3	0·7	,,	145/95	150/100	Little change, alternans abolished

in hypertrophic obstructive cardiomyopathy can similarly be explained by an increase in venous return which increases left ventricular filling and end-diastolic volume—an effect similar to a rapid infusion of blood or fluid or tilting the patient into a head-down position (Braunwald *et al.*, 1964a ; Shah *et al.*, 1965a ; Mason *et al.*, 1966).

With a larger intraventricular volume, the gradient lessens so that the stroke volume and mean arterial pressure increase. Though " contractility " may be enhanced initially, this is overcome by the increase in ventricular dimensions which reduces the degree of obstruction. An additional factor could be the baroceptor response to the raised arterial pressure and peripheral resistance leading to bradycardia and reduction of left ventricular contractility—a negative inotropic effect. A similar response to induced hypertension occurs during phenylephrine infusion, which diminishes the murmur of hypertrophic obstructive cardiomyopathy (Harrison *et al.*, 1964 ; Nellen *et al.*, 1965 ; Lewis *et al.*, 1965). These three factors—increased end-diastolic volume bradycardia, and reduced contractility—reduce the abnormal dynamic obstruction in the left ventricle. The systolic murmur, reflecting the intraventricular gradient, softens.

The murmur in hypertrophic obstructive cardiomyopathy can possibly be attributed to two other factors, obstruction to right ventricular outflow and mitral incompetence. In the present group of patients systolic pressure gradients within the cavity of the right ventricle were too small to account for the significant murmurs. Criley *et al.* (1965) suggested that the murmur is due to mitral incompetence from abnormally aligned papillary muscles in the small end-systolic cavity. We have assessed the degree of mitral incompetence from the cineangiocardiograms of our patients. In each patient reflux of dye into the left atrium was present, but this was often observed during diastole or during ventricular premature systoles, so that the degree of true incompetence was difficult to estimate. Our studies, in patients with hypertrophic obstructive cardiomyopathy, of the simultaneous response of the murmur and the pressure gradient within the left ventricle, recorded during manipulation of the circulation, indicate that the intensity of the murmur is related to the pressure gradient recorded (Nellen *et al.*, 1965). This suggests that the intraventricular obstruction is the most likely cause of the murmur, though mitral incompetence from abnormally aligned papillary muscles cannot be excluded.

The hypothesis of increased venous return can also explain the effect of squatting on the systolic murmur of aortic and pulmonary stenosis. This increases the stroke output of the left ventricle, more blood is ejected through a constant orifice per unit time, the velocity of flow is increased, and the murmur becomes louder and longer. If ventricular function is compromised, however, the stroke output increase does not occur (Thomas and Shillingford, 1965). A similar mechanism may apply to rheumatic mitral incompetence. The augmented venous return increases forward flow across the mitral valve, and hence the mid-diastolic flow murmur and third heart sound increase in intensity. The systolic murmur also increases slightly in loudness.

The softening of the murmur in squatting is thus a useful bedside test for recognizing hypertrophic obstructive cardiomyopathy. It increases significantly in intensity in the majority of patients with valvar aortic stenosis and slightly in mitral incompetence.

Summary

In 8 out of 11 patients with hypertrophic obstructive cardiomyopathy the systolic murmur softened and shortened in length with prompt squatting, while in two it was abolished.

In six out of eight patients with discrete valvar aortic stenosis there was an increase in intensity and duration of the systolic murmur on squatting. A similar but much less striking increase was observed in five subjects with mitral incompetence.

The response of the systolic murmur in hypertrophic obstructive cardiomyopathy to prompt squatting is a useful aid to bedside clinical diagnosis.

We wish to thank Dr. W. Beck, our colleagues in the cardiac clinic, and our laboratory staff for assistance with the catheterization procedures, and Dr. J. G. Burger, Superintendent of Groote

Schuur Hospital, for permission to publish. We acknowledge with thanks the continued financial support of the Council for Scientific and Industrial Research and the City Council of Cape Town.

REFERENCES

Braunwald, E., Brockenbrough, E. C., and Frye, R. L. (1962). *Circulation*, **26**, 166.
—— and Ebert, P. A. (1962). *Amer. J. Cardiol.*, **10**, 489.
—— Lambrew, C. T., Rockoff, S. D., Ross, J., and Morrow, A. G. (1964a). *Circulation*, **30**, Suppl. No. 4, p. 3.
—— Oldham, H. N., jun., Ross, J., jun., Linhart, J. W., Mason, D. T., and Fort, L., III (1964b). Ibid., **29**, 422.
Brotmacher, L. (1957a). *Brit. heart J.*, **19**, 559.
—— (1957b). Ibid., **19**, 567.
Criley, J. M., Lewis, K. B., White, R. I., and Ross, R. S. (1965). *Circulation*, **32**, 881.
Goodwin, J. F. (1964). *Brit. med. J.*, **1**, 1527.
Hancock, E. W., and Fowkes, W. C. (1966). *Circulation*, **33**, 383.
Harrison, D. C., Braunwald, E., Glick, G., Mason, D.T., Chidsey, C. A., and Ross, J., jun. (1964). Ibid., **29**, 84.
Lewis, R. P., Bristow, J. D., Farrehi, C., Kloster, F. E., and Griswold, H. E. (1965). *Amer. J. Med.*, **38**, 842.
Marcus, F. I., Westura, E. E., and Summa, J. (1964). *Amer. Heart J.*, **67**, 324.
Mason, D. T., Braunwald, E., and Ross, J., jun. (1966). *Circulation*, **33**, 374.
Nellen, M., Beck, W., Vogelpoel, L., Swanepoel, A., and Schrire, V. (1965). *S. Afr. med. J.*, **39**, 304.
O'Donnell, T. V., and McIlroy, M. B. (1962). *Amer. Heart J.*, **64**, 347.
Pierce, G. S., Morrow, A. G., and Braunwald, E. (1964). *Circulation*, **30**, Suppl. No. 4, p. 152.
Shah, P. M., Amarasingham, R., and Oakley, C. M. (1965a). *Brit. Heart J.*, **27**, 83.
—— Yipintsoi, T., Amarasingham, R., and Oakley, C. M. (1965b). *Amer. J. Cardiol.*, **15**, 793.
Sharpey-Schafer, E. P. (1955). *Brit. med. J.*, **1**, 693.
—— (1956). Ibid., **1**, 1072.
Thomas, M., and Shillingford, J. (1965). *Brit. Heart J.*, **27**, 17.
Wigle, E. D., David, P. R., Labrosse, C. J., and McMeekan, J. (1965). *Amer. J. Cardiol.*, **15**, 761.

Reduction of Clotting in Scribner Shunts by Long-term Anticoagulation

A. J. WING,* M.A., B.M., M.R.C.P. ; J. R. CURTIS,† M.B., B.S., M.R.C.P.
H. E. DE WARDENER,‡ M.B.E., M.D., F.R.C.P.

Brit. med. J., 1967, **3**, 143–145

Drukker *et al.* (1966) reported that 612 patients had been placed on regular dialysis treatment programmes in Europe by May 1966. For all these patients the Achilles heel of the treatment remains the arteriovenous shunt. The "life" of the shunts varies from centre to centre. Mean survival rates of between 2 and 14 months have been reported (Ramirez *et al.*, 1966 ; Pendras and Smith, 1966).

Shunt life is influenced by infection and clotting. There have been six infections in 16¼ patient-years' experience in this unit. The frequency of clotting incidents is much higher ; 59 during the same period (cf. Erickson *et al.*, 1966). This represents one clotting incident every 3.3 patient-months. At this rate, in a 10-bedded unit treating 30 patients 109 such incidents could be expected in the course of one year's operation.

When a shunt has clotted, declotting is necessary. Both events must be assumed to cause damage to the cannulated vessels. The clot causes anoxia to the intima, and the declotting procedure may traumatize the vessels. In addition it exposes the cannula site to the risks of infection. The risk of serious complications due to embolism appears to be slight. Clots are often released into the circulation at this procedure, and, despite the frequency with which it is carried out, there have been only isolated reports of collapse (Sokol, 1964) and of infected pulmonary emboli (Pendras and Erickson, 1965). Death has occurred on three occasions, each in a different unit, after declotting of arterial cannulae. Each patient became deeply unconscious after the procedure and some cerebral incident seems to have occurred. In our unit declotting is not carried out by the patients themselves and therefore they must come to the unit when they find that their shunt has clotted. A clotted shunt induces anxiety in the patient, for it is often the first of a series of clotting episodes and may be the signal that the cannula is coming to the end of its life. The significance of the loss of a cannula does not escape these patients. Clotting episodes place demands on the staff "on call," and the incidence of such episodes dictates in part the staff requirements for these units.

Long-term oral anticoagulation with warfarin sodium has been given to some of our patients. This communication reports the results so far.

Methods

Anticoagulants are not given to any patient until a clotting episode has occurred. Therefore, after their original cannulation the patients are included in the untreated group. When a clot occurs oral anticoagulants are begun. Warfarin sodium is used and the prothrombin time is kept at 1.5 times the control time. Prothrombin times are estimated by Quick's one-stage method with the use of lung thromboplastin (Geigy). A loading dose of 30 mg. is given and 48 hours later a maintenance dose is prescribed. The maintenance dose required by our patients is in the range of 3–12 mg. a day. During the first 48-hour period 5,000 units (50 mg.) of heparin is injected six-hourly by the patient himself into the shunt through a medicated sleeve described elsewhere (Evans, 1966). If further clotting occurs despite adequate anticoagulation, a venogram is obtained. If there is reason to suspect that the arterial cannula is at fault—that is, poor flows during dialysis without high pressure in the "venous" line—an arteriogram is also obtained. If angiography shows an obvious cause for clotting or poor flows, then surgical correction is necessary.

Because of this method of selection the treated group is made up of patients who have shown themselves to be at risk, and therefore includes patients whose cannulae have already been damaged by at least one clotting episode. The untreated group is made up of patients whose shunts have never clotted, and also includes those patients whose anticoagulants have been discontinued.

---

* Senior Registrar.
† Lecturer in Medicine.
‡ Professor of Medicine.
Department of Medicine, Charing Cross Hospital Medical School, Fulham Hospital, London W.6.

Results

Anticoagulation has reduced the frequency of clotting in the treated group.

Our total experience is now 195 patient-months. For 135 of these months anticoagulants have not been given, and during this time 52 clotting episodes have occurred. This represents a frequency of 4.6 clotting episodes per patient-year, or one every 2.6 patient-months. In the remaining 60 patient-months anticoagulants have been given and seven clotting episodes have occurred, a frequency of 1.4 clotting episodes per patient-year, or one every 8.6 patient-months.

Fig. 1 shows the difference between the incidence of clotting episodes in the treated and untreated groups.

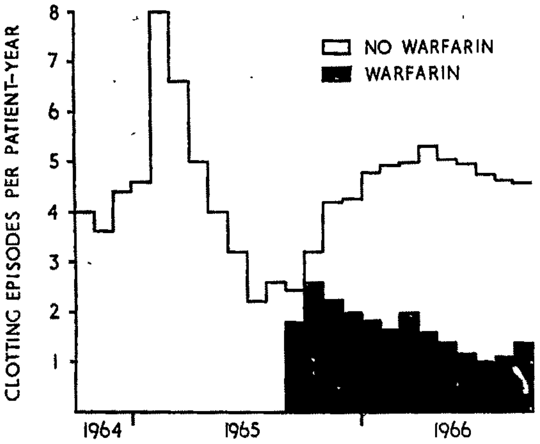


FIG. 1.—Number of clotting episodes that have occurred per patient-year is shown. The incidence of these episodes has been calculated month by month on a cumulative basis. Thus the incidence at any one month represents total experience up to that date. Open area=Number of episodes per patient-year in patients not receiving oral anticoagulation. Blackened area=Number of episodes per patient-year in patients treated with warfarin.

Case Histories

The following case histories illustrate the use and effect of anticoagulants in three patients (see Fig. 2).

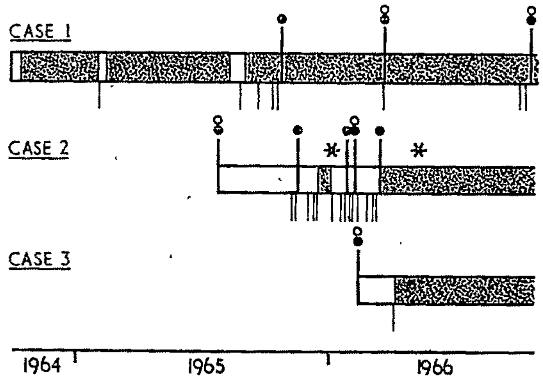


FIG. 2.—Each block represents the cannula history of individual patients, Cases 1, 2, and 3. For descriptions see text. Stippled area=Period for which warfarin was given. Each vertical bar below each block represents a clotting incident. Thick vertical bars extending above the blocks represent cannulation operations. Closed circle=New venous cannula. Open circle=New arterial cannula. Asterisks=Haemorrhagic complications occurring in Case 2.

Case 1.—A woman aged 24 with terminal renal failure due to chronic pyelonephritis had been on intermittent haemodialysis since 12 August 1964. Because of recurrent septicaemia, bilateral nephrectomy was carried out on 2 October 1964. Splenectomy was also done at this time in case it should later be possible to offer the patient renal transplantation. After operation clotting of the shunt occurred and the platelet count was raised for three months (375,000 to 850,000/cu. mm.). Warfarin was given. On two occasions, in February and August 1965, attempts were made to tail off the warfarin, but each time rebound clotting occurred. This patient is now on permanent anticoagulation. Recent clotting while adequately anticoagulated was associated with marked angiographic abnormalities.

Case 2.—A man aged 44 with terminal renal failure due to chronic pyelonephritis and gouty nephropathy had been on intermittent haemodialysis since 16 July 1965. After three months' good cannula function he damaged his shunt and eventually recannulation was necessary. There followed a rapid succession of clotting episodes, and four recannulations were carried out in three months. A first attempt at treatment with warfarin when the prothrombin time was kept at 2.0 times the control time resulted in a haematoma ; the drug was stopped and his shunt clotted. Anticoagulants were reintroduced in February 1966 and no further clotting has occurred. He developed a haemarthrosis in a previously gouty joint in April 1966 but there have been no further complications.

Case 3.—A woman aged 23 with terminal renal failure due to chronic pyelonephritis had been on intermittent haemodialysis since 15 January 1966. Previous transfusions, infusions, and cutdowns at another hospital had severely reduced the number of veins suitable for cannulation, and her first successful cannulation was in the left brachial artery and basilic vein. Clotting of the shunt occurred after six weeks. Fortunately, anticoagulation has so far prevented any further clotting. Considerable fibrin formation during dialysis has been noted in this patient.

Complications

There have been four haemorrhagic complications. Two spontaneous haematomas occurred in the treated group, and on both occasions the prothrombin time was 2.0 times the control time. One, in the neck, threatened respiratory obstruction. The haemarthrosis in one of Case 2's gouty joints required aspiration. One treated patient developed a haematoma in a cannulation wound.

Discussion

The risks of the use of anticoagulants are well documented (Hudson, 1965). They are those due to haemorrhage and those due to hypersensitivity. Of the four haemorrhagic complications in this unit two occurred when the prothrombin time was prolonged well above the 1.5 times the control which is now regarded as optimal. Should hepatitis develop, dosage requirements may change rapidly, and frequent estimations of the prothrombin time are indicated. Gastrointestinal haemorrhage and pericarditis are contraindications to the use of anticoagulants. Dangerous hypersensitivity reactions can be avoided by using warfarin as opposed to phenindione (Hollman and Wong, 1964).

Patients who clot their shunts repeatedly have, on average, a shorter shunt "life" (cf. Pendras and Smith, 1966). The use of warfarin in such patients has reduced the frequency of clotting and has prolonged the life of their shunts. We believe that the added risks are worth taking in those patients who are known to be at risk of clotting their shunts. Some patients do not have clotting problems. In our untreated group we have three patients totalling 2 years 10 months' experience who have never clotted their shunts. Erickson *et al.* (1966) have reported that cannulated haemodialysed patients have a higher level of blood-clotting factors than a random non-uraemic control group. They have also found that the level of clotting factors is higher in "clotters" than in "non-clotters." This work suggests that it may eventually be possible to predict which patients should receive anticoagulants.

There is a further difficulty in handling anticoagulants in these patients: once begun, they are difficult to withdraw. This has been attempted on six occasions in five patients, and on four of these occasions due care was taken to "tail off" the dosage. The other two occasions were regarded as serious haemorrhagic emergencies requiring abrupt cessation of anticoagulants. Four out of the six attempts to withdraw anticoagulants resulted in clotting of the shunts, and in three of these the site was lost within a fortnight. A further patient who discontinued his warfarin because of a misunderstanding promptly clotted his shunt.

Clotting in the shunts is due in part to blood-clotting factors, and because of this warfarin has reduced their frequency. Clotting may also be initiated if the patient is made hypotensive owing to excessive ultrafiltration during dialysis. There remain mechanical defects in the components of the shunt and structural defects in the cannulated vessels which may precipitate clotting. When repeated clotting of the shunt has occurred without hypotensive episodes and despite adequate anticoagulation, then a venogram and, if indicated, an arteriogram are obtained. Under these circumstances a structural defect in one or both vessels has always been demonstrable. Such abnormalities have included stenosis of the vessel near the cannula tip, malalignment, and aneurysmal dilatation (see Figs. 3–6). These radiographic appearances only serve to emphasize the extreme importance of careful surgery and expert cannula care. Attention to heparinization during dialysis is necessary to minimize fibrin formation, which may lead to deposition in the cannulated vein. Erickson *et al.* (1966) have observed one patient in whom such fibrin formation was a problem and who also suffered repeated clotting episodes. Warfarin abolished both.

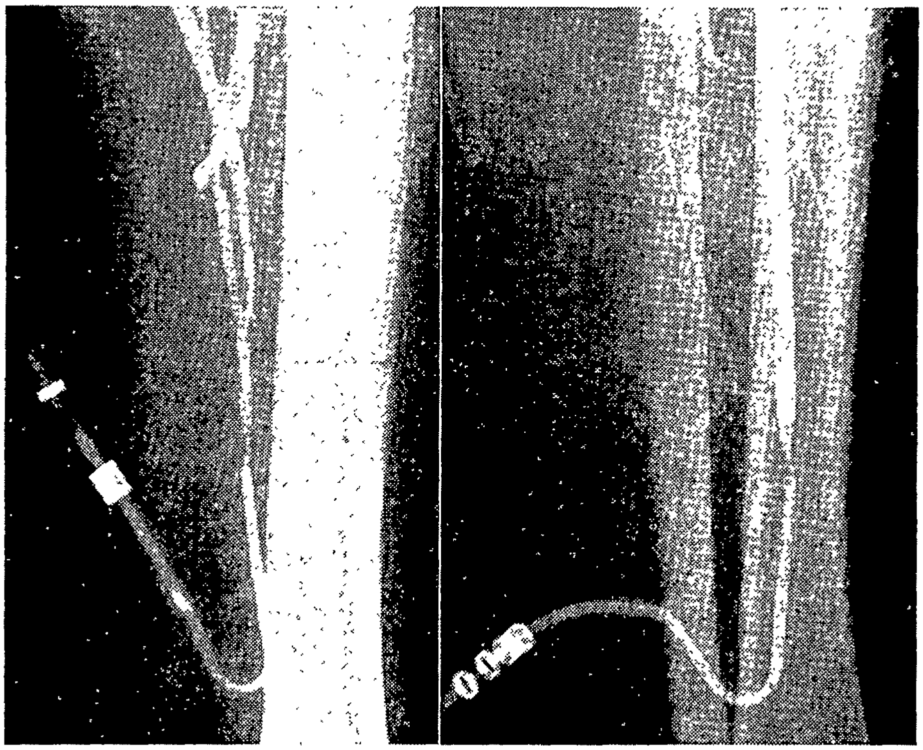


FIG. 3 FIG. 4

FIGS. 3 and 4.—Venograms showing stenotic lesions at cannulae tips. These are very commonly found. In both patients the cannula was successfully placed a little higher up the same vessel.

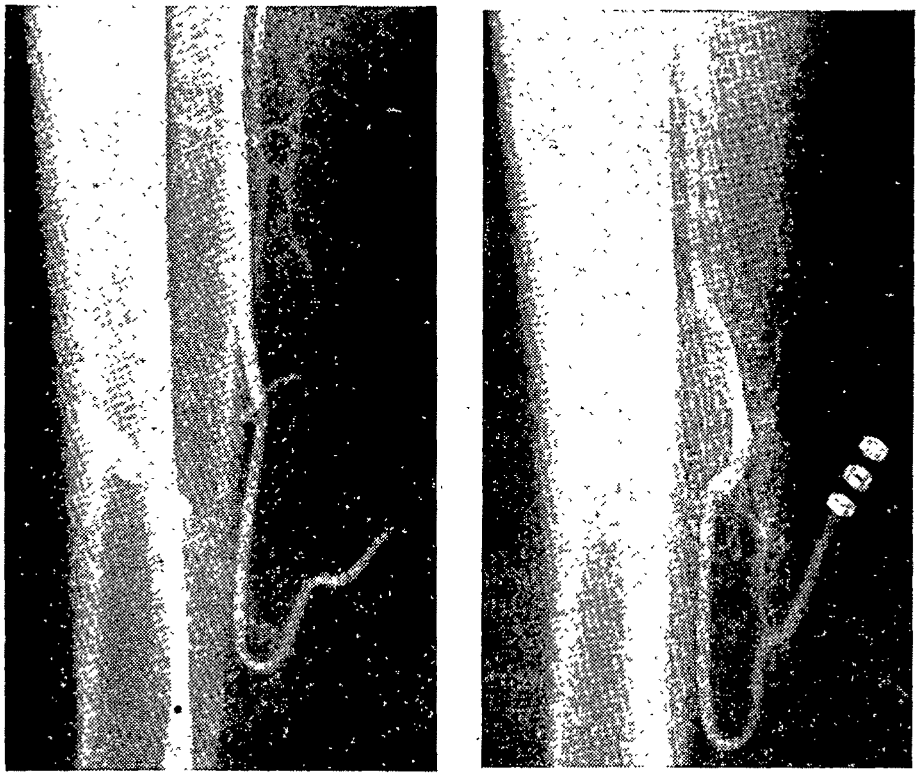


FIG. 5 FIG. 6

FIG. 5.—Arteriogram showing angulation at junction of Teflon tip and vessel. This gave rise to poor flows during dialysis, and eventually clotting occurred. FIG. 6.—Arteriogram showing an S-bend deformity of the artery. The cannula had been inserted incorrectly in relation to the tendon of flexor digitorum longus. Intermittent cessation of flow during dialysis occurred, and eventually the shunt clotted. Note the leash of small vessels. This shunt had previously been infected.

Summary

Oral anticoagulation with warfarin has been given to a selected group of patients being treated by intermittent haemodialysis. The group was composed of patients whose shunts were known to be at risk because of previous clotting episodes. Treatment has decreased the frequency of clotting episodes and has prolonged the "life" of the shunts in this group of patients. Any success with the use of anticoagulants should not be allowed to detract from emphasis on accurate cannula placement and good cannula care, and on avoidance of hypotensive episodes.

REFERENCES

Drukker, W., Alberts, C., Ode, A., Roozendaak, K. J., and Wilmink, J. (1966). *Proceedings European Dialysis Transplant Association*, vol. 3, 90.

Erickson, R. V., Williman, M., and Pendras, J. P. (1966). *Trans. Amer. Soc. artif. intern. Org.*, **12**, 205.

Evans, D. B. (1966). *Brit. med. J.*, **2**, 883.

Hollman, A., and Wong, H. O. (1964). Ibid., **2**, 730.

Hudson, R. E. B. (1965). *Cardiovascular Pathology*, vol. 1, p. 197. London.

Pendras, J. P., and Erickson, R. V. (1965). *Trans. Amer. Soc. artif. intern. Org.*, **11**, 238.

—— and Smith, M. P. (1966). Ibid., **12**, 222.

Ramirez, O., Swartz, C., Onesti, G., Mailloux, L., and Brest, A. N. (1966). Ibid., **12**, 220.

Sokol, A. (1964). In *Proceedings of the Working Conference on Chronic Dialysis, Washington, 1964*, p. 27.

Diagnostic Paracentesis in the Acute Abdomen

W. N. W. BAKER,* M.B., B.S., F.R.C.S.; D. B. MACKIE,* M.B., M.CHIR., F.R.C.S.
J. F. NEWCOMBE,† M.CHIR., F.R.C.S.

Brit. med. J., 1967, 3, 146–149

Diagnostic paracentesis of the peritoneal cavity in abdominal emergencies has been practised in the United States for many years, but has never become popular in this country (Morris, 1966).

The first comprehensive study of the technique was carried out by Neuhof and Cohen (1926), who reported enthusiastically on its use as a diagnostic aid in the evaluation of closed abdominal injuries, acute pancreatitis, and primary pneumococcal or streptococcal peritonitis. Though no cases were reported in their paper, they also predicted a wider use for the test in the diagnosis of ruptured hollow viscera and bleeding ectopic pregnancies.

Later studies have confirmed these observations, especially in relation to blunt abdominal trauma (Thompson and Brown, 1954; Economy *et al.*, 1960). Williams and Zollinger (1959) reviewed 273 abdominal injuries, 80% of which were non-penetrating, and reported that needle paracentesis had proved accurate in 79% of these cases. They compared the relative diagnostic values of paracentesis and *x*-ray findings in the same series, and found that radiology was more valuable in injuries to kidney and bladder (where paracentesis is usually negative), but that paracentesis was far superior as a diagnostic aid in lacerations of liver, spleen, or pancreas.

Keith *et al.* (1950) stated that it is often a useful investigation in acute pancreatitis. They obtained fluid in 12 out of 15 consecutive cases, and in all of these the amylase levels were higher than those found in the serum. Moreover, the peritoneal fluid amylase remained high for two to three days after the serum levels had returned to normal. However, Moretz and Erickson (1954) warn that peritoneal fluid amylase is also raised in perforated peptic ulcer and intestinal strangulation, and care must be taken in interpreting this finding.

The accuracy of the procedure was investigated experimentally by Giacobine and Siler (1960). Their observations on dogs showed that there was a linear relation between the amount of fluid in the peritoneal cavity and the probability of obtaining a sample by needle paracentesis. The low rate of positive results with small amounts of fluid was shown radiologically to be due to pooling in the pelvis, paravertebral gutters, and subphrenic spaces.

Material and Methods

The cases were an unselected series of 101 patients admitted as acute abdominal emergencies to a general hospital. There were 50 males and 51 females in the series, with an age range from 6 to 89 years.

Technique

The standard procedure throughout this investigation was the four-quadrant tap advocated by Byrne (1956). Though most authors advocate the use of a spinal puncture needle, entirely satisfactory results were obtained with a 2-ml. or 5-ml. disposable syringe and No. 12 needle. Local anaesthetic was not routinely employed and asepsis was confined to socially clean hands and a spirit skin preparation.

The needle was inserted at the sites shown in the Diagram. Light intermittent suction was applied as the needle tip was moved about within the peritoneal cavity, seeking pockets of free fluid. This is necessary to obtain a sample when only a small quantity of fluid is present as a thin film beneath the parietal peritoneum.

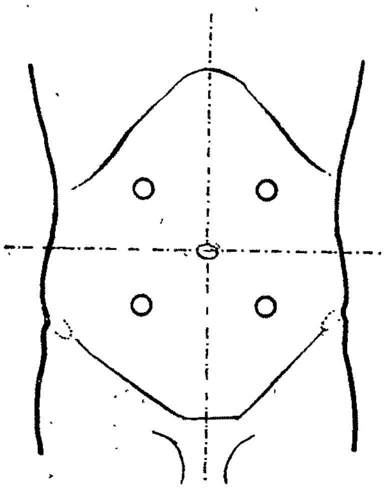


Diagram showing sites of puncture in the standard four-quadrant paracentesis

Occasionally a very small quantity (less than 0.5 ml.) of clear peritoneal fluid is obtained in the absence of intra-abdominal morbidity. When a larger quantity than this is obtained there is nearly always an underlying cause. For this reason we have regarded a paracentesis as "positive" if clear fluid in excess of 0.5 ml. has been obtained. If the fluid is obviously pathological—for example, pus—then the paracentesis is "positive" regardless of its volume.

The necessity of carrying out a full four-quadrant technique before pronouncing a paracentesis to be negative was demonstrated on several occasions in this series. In one case pus was obtained only from the *right upper* quadrant though the lesion was a perforated diverticulum of the sigmoid colon in the *left lower* quadrant. This also shows that the method gives no indication of the probable site of the primary lesion.

Safety of the Technique

The objection to the technique most often raised has been on the grounds of safety. This point has been investigated experimentally in dogs by Moretz and Erickson (1954). When isolated segments of intestine were deliberately punctured and subsequently inflated no leakage occurred until a pressure of 260 mm. Hg was reached. Even in complete intestinal obstruction the intraluminal pressure seldom rises above 15 mm. Hg in the small bowel and 20 mm. Hg in the large bowel

---

* Surgical Registrar, Central Middlesex Hospital, London. Present address: Middlesex Hospital, London W.1.

† Consultant Surgeon, Central Middlesex Hospital, London.

(Wangensteen, 1942). Leakage from accidental puncture is therefore a very small hazard. Nevertheless, in the presence of distended bowel the risk must be increased, and we believe that paracentesis should not be done in these circumstances.

No complication was recorded in any of the 101 cases reported, though visceral puncture did occur. The gall-bladder, the stomach, and the colon were each penetrated at some time. In those cases undergoing subsequent laparotomy no evidence of haemorrhage or peritoneal soiling was found. This confirms the findings of all previous authors. Indeed, the only complication recorded in the literature is of a haematoma of the rectus sheath after a paramedian tap (Drapanas and McDonald, 1961).

Interpretation of a Positive Paracentesis

Frank Blood.—The withdrawal of pure blood that fails to clot on standing can only mean that a significant intraperitoneal haemorrhage has occurred. Accidental puncture of a blood vessel does occur but can readily be distinguished by the fact that blood from this source clots within a few minutes.

Serosanguineous Fluid.—This type of exudate has been reported in a number of situations, including strangulated hernia (Hill *et al.*, 1942) and acute pancreatitis (Keith *et al.*, 1950). In the present series it was found in only two cases. One was a traumatic rupture of the kidney with a retroperitoneal haematoma, in which the paracentesis did not contribute towards the diagnosis. The other was a case of acute cholecystitis, described in detail below (Case 1).

Purulent Fluid.—This may vary from the offensive frank pus obtained from a perforated appendix or diverticulum of the colon to the thin turbid fluid associated with localized inflammatory disease. The latter contains numerous polymorphs on smearing the centrifuged deposit (see Case 1 below).

Bile-stained Fluid.—This type of fluid is characteristic of a perforated ulcer, and in the present series was the most common finding on paracentesis. Usually the fluid is turbid and contains food particles. A most important observation in our series was that the fluid was *never* acid when tested with ordinary litmus paper. Even when the sample was obtained very soon after the onset of acute symptoms the fluid was either neutral or alkaline. On one occasion the gall bladder was accidentally punctured in the right hypochondrium, yielding pure bile. This was correctly interpreted and no harm resulted.

Faecal.—When the intestine is accidentally punctured it is usually easy to recognize this by naked-eye inspection of the material aspirated. In cases of doubt, microscopy reveals a mixture of intestinal bacteria and debris with no evidence of polymorphs. No complications have resulted from this accident and there is no reason why the paracentesis should not be attempted with a fresh needle and syringe at a different site in the same quadrant.

Misinterpretation of a Positive Paracentesis

On two occasions a positive paracentesis was misinterpreted, and since each case illustrates a useful point they are described in detail.

Case 1.—An 87-year-old woman was admitted to hospital as an emergency with a history of severe upper abdominal pain of sudden onset. Examination revealed tenderness and guarding in the upper abdomen. A plain *x*-ray film showed no gas under the diaphragm. The serum amylase was less than 500 Somogyi units. On abdominal paracentesis a small quantity of serosanguineous fluid was obtained from the right hypochondrium. Microscopy of the centrifuged deposit showed numerous polymorphs, indicating the presence of an inflammatory lesion. Despite the nature of this fluid a clinical diagnosis of perforated peptic ulcer was made. At laparotomy the gall bladder was found to be acutely inflamed, and immediately surrounding it was a collection of free fluid identical to the aspirated sample. The stomach and duodenum were entirely normal.

Comment.—This is one of the two cases in which a positive paracentesis was obtained in the presence of local inflammatory disease. The point demonstrated is that where pathological fluid is obtained the diagnosis must be consistent with its type. Here the fluid was quite uncharacteristic of a perforated peptic ulcer, and this diagnosis should not have been made.

Case 2.—A man aged 62 was admitted to hospital with a history of upper abdominal pain for the preceding three days which had become much more severe that day. On admission there was clinical and radiographic evidence of bronchopneumonia. He was a known chronic bronchitic and was under treatment for recurrent episodes of congestive cardiac failure. However, there was also evidence of a perforated viscus, with marked tenderness over the whole abdomen and guarding in the epigastrium. Bowel sounds were absent. This diagnosis seemed confirmed when, on abdominal paracentesis, bile-stained fluid with food particles was obtained from the *left iliac fossa.* The *p*H of the fluid was not tested. All attempts to pass a Ryle tube failed. Since his condition was rapidly deteriorating it was decided to proceed with laparotomy. At operation no free fluid was found in the peritoneal cavity. The stomach was full of fluid and extended right down to the left iliac fossa. On its anterior surface was a puncture mark indicating that the attempted paracentesis had in fact withdrawn gastric contents. The patient died shortly after operation. At necropsy no cause was found for his abdominal symptoms. The only positive finding was an organizing bronchopneumonia, and it must be presumed that this was responsible for his entire clinical picture.

Comment.—This case has revealed a possible source of error that has not hitherto been reported. Two omissions probably account for the misinterpretation of the paracentesis. Firstly, if the *p*H of the fluid had been tested it would very probably have been acid. As stated above, fluid from a perforated peptic ulcer appears invariably to be either neutral or alkaline. Secondly, it proved impossible to pass a Ryle tube preoperatively. Had this been achieved, the large aspirate would have been noted and a repeat paracentesis would have proved negative. It therefore seems desirable always to test the *p*H of the fluid obtained from cases of suspected perforation. It would also seem more reliable to perform the paracentesis *after* gastric aspiration. However, this must be a very uncommon source of error.

Interpretation of a Negative Paracentesis

It cannot be too strongly emphasized that *a negative paracentesis has no positive significance.* If operation is indicated on clinical grounds, then, whatever the diagnosis may be, the fact that no fluid has been obtained from the peritoneal cavity must be completely disregarded.

If there is no clear indication for immediate surgery on clinical grounds, a negative paracentesis may help to justify continuation of conservative treatment, but it should be given no significance in arriving at a diagnosis.

Results

Of the 101 cases in which diagnostic paracentesis was performed, an acute abdominal condition was demonstrated at laparotomy or necropsy in 64. Of four further cases presenting with severe abdominal pain, two were subsequently shown to have malignant disease, one had a coronary thrombosis, and one had tuberculosis of the urinary tract. Ascitic fluid was obtained from the former two cases; in the latter two the paracentesis was negative.

There was therefore a total of 68 cases in which a firm diagnosis was made. In this group a positive paracentesis was obtained in 33 and a negative result in 35. In Table I these results are analysed according to final diagnosis.

From these data a clear pattern emerges. Diagnostic paracentesis was found to yield accurate positive information in 22 out of 28 cases of visceral perforation. No attempt was made to compare the relative accuracy of this technique with that of diagnostic radiography, but it is unlikely that the latter method would have proved significantly better.

TABLE I.—*Abdominal Emergencies With Known Diagnosis*

	Paracenteses		
	No.	Positive	Negative
Group I. Visceral Perforations			
Stomach and duodenum	19	14	5
Small bowel	2	2	0
Colon and appendix	7	6	1
Total	28	22 (79%)	6
Group II. Intraperitoneal Haemorrhage			
Ectopic	2	2	0
Leaking arterial anastomosis	2	2	0
Ruptured spleen	3	2	1
Total	7	6 (86%)	1
Group III. Localized Intra-abdominal Inflammatory Disease			
Acute appendicitis	11	0	11
Cholecystitis	5	1	4
Salpingitis	3	0	3
Pancreatitis	2	0	2
Diverticulitis	1	0	1
Acute duodenal ulcer	1	0	1
Primary peritonitis	1	1	0
Liver abscess	1	0	1
Total	25	2 (8%)	23
Group IV. Miscellaneous			
Intestinal obstruction	4	1	3
Malignant disease	2	2	0
Urinary tract tuberculosis	1	0	1
Coronary thrombosis	1	0	1
Total	8	3	5
Grand total	68	33	35

In cases of intraperitoneal haemorrhage blood was obtained in six out of seven paracenteses, a comparable degree of accuracy with the large series of such cases reported by Williams and Zollinger (1959).

In direct contrast to these findings are the results for localized inflammatory disease. Here it is quite clear that diagnostic paracentesis is most unlikely to give useful information. In only two cases out of 25 was a positive paracentesis obtained. One was the case of acute cholecystitis described above (Case 1). The other was a case of peritonitis, for which no cause was found at laparotomy and which was therefore classified as a primary peritonitis.

Only two cases of acute pancreatitis were encountered in this series, and no fluid was obtained from either of them.

Of the four patients with intestinal obstruction only one yielded a positive result. As stated above, the technique is not recommended for florid cases of obstruction, and in this series it was used only when the diagnosis was not clear. It may have a place in the diagnosis of intestinal strangulation (Hill *et al.*, 1942), but the one such case in this series produced a negative result. At laparotomy there was a small amount of faeculent blood-stained fluid in the peritoneal cavity, but paracentesis had failed to detect it.

A recurrent problem in which the test may prove an outstanding aid to diagnosis is that of the postoperative patient who develops intra-abdominal complications. A recent anaesthetic, followed by the customary analgesia, makes the interpretation of physical signs notoriously difficult in these cases. Brief summaries of two such cases are given.

Case 3.—A 57-year-old man presented with an 18-month history of severe intermittent claudication of his left buttock and thigh after walking 25 yards (23 metres). An aortogram revealed atherosclerotic occlusion at the aortic bifurcation. He underwent an aorto-iliac thrombendarterectomy on 21 February 1966. Two hours after the end of the operation he had a cardiac arrest in the ward. He was resuscitated from this successfully, but 15 minutes later his blood pressure again fell rapidly. At the time it was not clear whether this was due to myocardial damage or to bleeding from the aortic suture line. A diagnostic paracentesis was performed and non-clotting blood obtained from the right lower quadrant. On this evidence he was immediately returned to the theatre and the wound reopened. The diagnosis of leaking aortic suture line was confirmed (the peritoneal cavity containing some 2 litres of blood). Unfortunately the heart arrested again on the table before the bleeding could be properly controlled, and though it was restarted by open cardiac massage the patient did not survive.

Case 4.—A 52-year-old woman was admitted to hospital with a diagnosis of coronary thrombosis, and while on treatment suddenly developed the signs of an embolus at the aortic bifurcation. On 1 June 1966 an emergency aorto-iliac and bilateral femoral thrombectomy was performed. Her immediate postoperative condition was satisfactory, with a rapid return of the peripheral pulses in both legs. However, 12 hours later she began to deteriorate rapidly with signs of peripheral circulatory failure. It was thought likely that leakage had occurred from her arterial suture line, so a diagnostic paracentesis was performed. This produced heavily bloodstained fluid with a faecal odour from the right lower quadrant. She was taken back to the theatre and re-explored. At operation there was approximately 1 litre of blood in the peritoneal cavity, presumed to be due to a leak from the aortic suture line, though this was dry when exposed. However, the most significant finding was infarction of the colon, which accounted for the faeculent odour of the aspirate and which was undoubtedly the cause of the rapid deterioration in her condition. The inferior mesenteric artery was pulseless. An emergency colectomy was performed but the patient died a few hours later.

Comment.—Though unfortunately both these patients died, they do nevertheless illustrate that valuable information can be obtained from a diagnostic paracentesis in the early postoperative period when the critical decision has to be made whether or not to reoperate. Almost certainly in both these cases the correct decision would have been made eventually, but where speed of decision was essential no other single clinical investigation could have supplied the information so swiftly or so accurately.

Undiagnosed Abdominal Pain

There remains to be considered the group of 33 patients who were admitted with acute abdominal pain for which no cause was firmly established. They are analysed in Table II, and, broadly speaking, fall into two categories: (A) those with suspected acute intra-abdominal inflammatory disease; and (B) those with suspected intra-abdominal bleeding or a perforated viscus following blunt abdominal trauma.

TABLE II.—*Undiagnosed Abdominal Conditions*

	Paracenteses		
	No.	Pos.	Neg.
Group A, suspected inflammatory disease	23	1	22
„ B, suspected bleeding or ruptured viscus (a) Spleen	8	0	8
(b) Bladder	2	0	2
Total	33	1	32

Of the 23 cases in group A the one positive paracentesis was obtained in a woman of 83 admitted with a clinical diagnosis of acute cholecystitis. Turbid fluid containing polymorphs was obtained from the right hypochondrium, which supported this diagnosis. Though the patient recovered on conservative treatment she was not regarded as a candidate for subsequent surgery, and the diagnosis was not confirmed radiologically.

Negative paracenteses were obtained in all 10 cases in group B. Only one of these underwent operation. This was for a suspected traumatic rupture of the bladder, but laparotomy revealed only a retroperitoneal haematoma. The remaining nine cases all recovered on conservative treatment.

Discussion

This investigation has served to clarify the place of paracentesis in a variety of acute abdominal conditions.

In the first place the findings confirm the opinion of previous authors that the test is both simple and completely safe. We have also confirmed that a full four-quadrant technique is essential before a paracentesis can be regarded as negative.

Though the number of cases is small, the most accurate results have been obtained in suspected intraperitoneal haemorrhage. Since there is experimental evidence (Giacobine and Siler, 1960) that a volume of 500 ml. of free fluid in the peritoneal cavity will give a 78% positive paracentesis rate, the method is likely to be more sensitive and accurate than any other single diagnostic aid. We strongly recommend its use in all cases of blunt abdominal trauma, and particularly when the clinical picture is confused by the presence of other injuries.

In visceral perforations again a high yield of positive results was obtained, but in evaluating the method in this situation there are other factors to consider. Firstly, the clinical picture is usually much clearer than in intra-abdominal haemorrhage, so that in many cases ancillary aids to diagnosis are not required. Secondly, another simple diagnostic method—the plain erect and supine abdominal *x*-ray films—is available and also gives a high yield of positive results.

In cases where the clinician is in no doubt about the diagnosis, neither method is necessary and laparotomy need not be delayed. There are, however, many situations in which varying degrees of doubt exist regarding whether or not perforation has taken place. In these cases has paracentesis any advantage over *x*-ray examination as a method of diagnosis ?

In favour of paracentesis we can say: (*a*) it is a test that can be performed immediately by the clinician at the bedside ; (*b*) it disturbs the patient far less than the manipulations required to obtain a satisfactory view of the erect abdomen ; (*c*) it is an extremely useful test for hospitals lacking a 24-hour radiological service ; and (*d*) it gives a yield of positive information which is at least comparable to that of *x*-ray techniques.

By contrast, in localized inflammatory disease the yield of positive information is so low that abdominal paracentesis cannot be recommended as a useful diagnostic aid. The only exception to this may be in helping to differentiate between a localized inflammation and a perforated viscus, where the history and examination are equivocal.

Finally, we must repeat the warning, as have many previous authors, that a *negative paracentesis has no significance.* Serious underlying conditions may be present despite a negative tap. Our figures demonstrate that this is especially likely in localized inflammatory disease, but it is true also in intraperitoneal haemorrhage and visceral perforations.

In conclusion, therefore, we believe that diagnostic paracentesis is a useful procedure in the evaluation of patients with suspected intraperitoneal haemorrhage and visceral perforation, but has little place in the diagnosis of localized intra-abdominal inflammatory disease.

Summary

The value of diagnostic paracentesis has been studied in 101 patients admitted as cases of acute abdominal emergency.

The technique has been shown to be both simple and safe. Though visceral puncture may occasionally occur, no complications have resulted.

Analysis of the results shows that a high yield (approximately 80%) of positive paracenteses can be expected in cases of intraperitoneal haemorrhage and perforated viscus. Conversely, a very low yield (less than 10%) was obtained in localized inflammatory disease.

The test is strongly recommended as routine in all cases of blunt abdominal trauma. It is also extremely useful in the early diagnosis of complications after abdominal surgery.

In visceral perforation the method offers a useful alternative to radiological diagnosis, and in certain respects is to be preferred.

Our thanks are due to Mr. J. W. P. Gummer for permitting us to include his patients in this study.

REFERENCES

Byrne, R. V. (1956). *West. J. Surg.*, **64**, 369.
Drapanas, T., and McDonald, J. (1961). *Surgery*, **50**, 742.
Economy, D., Koucky, C., and Novack, R. L. (1960). *Amer. J. Surg.*, **99**, 647.
Giacobine, J. W., and Siler, V. E. (1960). *Surg. Gynec. Obstet.*, **110**, 676.
Hill, F. C., O'Loughlin, B. J., and Stoner, M. (1942). Ibid., **74**, 121.
Keith, L. M., Zollinger, R. M., and McCleery, R. S. (1950). *Arch. Surg.*, **61**, 930.
Moretz, W. H., and Erickson, W. G. (1954). *Amer. Surgn*, **20**, 363.
Morris, P. J. (1966). *Brit. J. Surg.*, **53**, 707.
Neuhof, H., and Cohen, I. (1926). *Ann. Surg.*, **83**, 454.
Thompson, C. T., and Brown, D. R. (1954). *Surgery*, **35**, 916.
Wangensteen, O. H. (1942). *Intestinal Obstructions*, 2nd ed. Springfield, Illinois.
Williams, R. D., and Zollinger, R. M. (1959). *Amer. J. Surg.*, **97**, 575.

Treatment of Stress Incontinence by Maximum Perineal Electrical Stimulation

THOMAS MOORE,* M.D., M.S., F.R.C.S. ; PHILIP F. SCHOFIELD,† M.D., F.R.C.S.

Brit. med. J., 1967, 3, 150–151

Stress incontinence is one of the commonest symptoms to occur in the female. It has been estimated that more than 50% of nulliparous women have incontinence when severe stress is placed on the bladder (Nemir and Middleton, 1954). However, it is only when incontinence occurs on minor stress such as coughing or walking that the patient presents for advice.

Jeffcoate (1961) suggests that the main factor is the loss of the normal urethrovesical angle. Lapides *et al.* (1960a, 1960b) felt that the principal defect was shortening of the urethra due to absence of the lengthening effect of the pelvic floor muscles. These views are probably not divergent, as descent of the bladder base can produce both the alteration in the angle and urethral shortening. Vincent (1959, 1966) has shown how mechanical raising of the perineum by an external appliance can tighten the pelvic floor muscles and the urethra and abolish incontinence.

On theoretical grounds incontinence occurs from either the uncontrolled action of the bladder muscle or some defect in the normal resistance of the bladder-neck and urethra. Beck, Hsu, and Maughan (1965) showed low urethral pressures due to general laxity of the urethral musculature in stress incontinence.

Perineal muscle exercises and faradism are known to bring improvement in this type of case (Jones, 1963). Some years ago one of us (T. M.) carried out studies of the electrical activity of the urethral muscles in all types of incontinent females by placing needle electrodes along the urethral wall. In one patient, in whom the anaesthesia was not deep enough, reflex contraction of the whole pelvic floor muscles followed introduction of the electrodes. Afterwards the patient's incontinence was mysteriously much improved.

Because of this observation it was decided to treat incontinent females empirically by causing maximal contractions of the pelvic floor muscles by electrical stimulation, under anaesthesia.

Method

Ten patients, who had only cystoscopy and measurement of urethral length, were used as a control group. Eighteen patients with marked stress incontinence had cystoscopy, measurement of urethral length, and maximal perineal faradism (see Table). Ten patients with other types of incontinence, four cases of enuresis, three cases of urge incontinence, and three cases with gross structural changes in the urethra had the same examination and treatment.

The faradism was given by electrodes—a mobile one placed over the perineal body and a stationary one under the sacrum—by a selective treatment unit (Stanley Cox Ltd.). The faradic surge consisted of pulses of one millisecond and the whole surge lasted for two to three seconds. There was then a pause of two to three seconds before a further faradic surge. The intensity of the stimulation was increased until all the voluntary musculature gave a maximal contraction. From four to six maximal tetanic contractions were produced in each patient.

Classification of the results is difficult, but these have all been assessed after treatment by one of us (P. F. S.) and the patients who have no further stress incontinence in the first three months after treatment are placed in the "cured" category. It was accepted that patients may be classified as improved if they stated that the treatment was worth while, that the amount of protective pads worn per day was fewer than three, and if the assessor was convinced from the history and examination of the urethra when the patient was straining that there was improvement. All other patients were classified in the failure group.

Results

No other type of incontinence showed any improvement. One of the group of 10 patients who had only cystoscopy showed improvement but relapsed at four months. Ten out of 18 patients with stress incontinence were either considerably or completely relieved of their symptoms (see Table).

Investigation and Results of Treatment of Stress Incontinence

Age	Cystoscopy	Urethral Length in cm.	Neurological Signs	Result
41	Cystitis cystica	2·1	—	Failure
46	None	2·7	—	Cured
46	,,	2·0	—	Improved
50	,,	1·8	—	Failure
31	,,	2·3	—	,,
43	Trabeculation	2·2	—	Cured
55	None	—	—	Failure
52	Trabeculation	2·3	—	Improved
38	None	2·0	—	Cured
27	,,	3·5	—	,,
32	,,	1·9	—	,,
21	,,	2·5	—	Failure
26	,,	2·4	—	,,
38	,,	1·9	—	Improved
37	,,	1·6	—	Failure
26	,,	—	—	Improved
47	,,	2·5	—	Failure
44	,,	2·1	—	Cured

Four patients relapsed partially by six months, but two of them responded to further faradism under general anaesthesia and the other two did not feel their symptoms were severe enough to require treatment. Six patients have remained much relieved for one year.

Six of the eight patients who failed to respond were treated by Lapides's (1961) operation ; five of these were relieved of all symptoms, but one still had stress incontinence.

Discussion

Urinary control is a learned function, and, as with any learned lesson, there are various degrees of success. Urinary control in the normal female is often not perfect ; in fact, more than 50% of normal nulliparous females have slight incontinence on occasions of severe and sudden stress (Nemir and Middleton, 1954). More gross degrees of loss of control are only too distressingly common.

In the past, treatment has taken two main lines: (1) operation to alter the orientation of the bladder-neck and urethra or to

---

* Consultant Surgeon, Department of Urology, Manchester Royal Infirmary.
† Senior Surgical Registrar, Department of Urology, Manchester Royal Infirmary. Present address: Cleveland Clinic, Ohio, U.S.A.

elongate the urethra ; and (2) physical treatment by exercises and electrical stimulation to improve the perineal musculature.

Electrical stimulation to the perineum has been carried out for many years in the treatment of minor stress incontinence, and electrical devices have recently been used to treat incontinence of both urine and faeces (Caldwell, 1963 ; Hopkinson and Lightwood, 1966 ; Caldwell, Flack, and Broad, 1965). Caldwell *et al.* (1965) delivered a square wave pulse to the urinary sphincter in a patient with urinary incontinence after spinal injury, with gratifying results. It is interesting to note that some patients recover sufficient sphincter power to discard the electrical apparatus in time.

The cause of stress incontinence is an imbalance between the pressure in the bladder and the resistance in the urethra. Normally all conditions of stress causing an increase of intravesical pressure are accompanied by a corresponding increase in the urethral resistance. The mechanism of this reaction is that increase of abdominal muscle tone is always accompanied by an increase in the tone of the pelvic floor muscles and a consequent elongation of the urethra by the contraction of the pubococcygeus muscle. Lapides *et al.* (1960a, 1960b) and Lapides (1961) stated that in the female a urethral length of 3 cm. was necessary for continence. Personal observations have confirmed that in most cases of stress incontinence the urethra is less than 3 cm. long and have also shown that in cases of stress incontinence standing causes a shortening of the urethra. This is due to loss of tone of the pelvic floor muscles, which do not contract in response to the increased intra-abdominal pressure and elongate the urethra. In normal females without stress incontinence standing causes an increase in the length of the urethra by 1 cm. or more. We have also shown that during maximal stimulation under general anaesthesia the urethra lengthens by 1 cm. or more, to return to its original length when the electrical stimulation is stopped.

We presume that when the anaesthetic has worn off the tone of the perineal floor muscles returns and is greater than before treatment. The change in the length of the urethra and possibly some narrowing of the urethral lumen associated with the return of tone of the perineal muscles increases the urethral resistance, in accordance with Laplace's law.

In successful cases we have not remeasured the urethra to confirm its elongation because of a fear of causing further symptoms. The success of the treatment we presume is because maximum perineal contraction of the perineal muscles causes a maximum physiological rehabilitative response and is better than long-continued intermittent faradism or voluntary exercises. The improvement that follows the stress incontinence occurring directly after childbirth by pelvic floor muscle exercises is well known. In our view it is likely that such patients would recover more quickly if treated with maximal perineal electrical stimulation.

It will be noted from the Table that improvement in stress incontinence occurred in some cases in which the urethra was much shorter than 3 cm., though it was more likely to occur in those cases in which the urethra was more than 2 cm. long. The fact that such results can be obtained with very short urethrae shows how effective the method can be.

The encouraging results in which 6 (33%) out of 18 patients with stress incontinence have been completely relieved of symptoms and a further 4 (22%) considerably improved merit further studies. We are so convinced of the efficiency of the method and by its safety and simplicity that we now tend to try it in any case of urinary incontinence. In some cases of neurogenic bladder it might well have a most beneficial effect in restoring better power to muscles not completely paralysed by the nervous disease. It should, however, be tried in all cases of true stress incontinence before operation is advised, particularly in those patients with a short history and a urethra shorter than normal in the standing position only by 1 cm. or less.

Summary

Stress incontinence of urine in the female is usually due to loss of tone of the pelvic floor muscles with consequent shortening of the urethra. In the erect posture the urethra must be at least 3 cm. long.

Cases were treated by causing maximal contraction of these muscles by electrical stimulation under general anaesthesia. Of 18 cases so treated 33% were completely relieved and 22% much improved.

During contraction of the pelvic floor muscles the urethra lengthens by 1 cm. or more, to return to its previous length when the contraction ceases.

It is suggested that in the successful cases the maximal perineal muscle electrical stimulation has restored the postural tone of the pelvic floor, so that all increases of intra-abdominal pressure are again accompanied by the normal pelvic floor contraction and lengthening of the urethra. Possibly one maximum contraction of a muscle restores power better than repeated submaximal contractions, the more usual method.

This treatment should always be tried before operative measures are advised, particularly when investigation has shown that in the erect posture the urethra is only 1 cm. or less short of the critical length (3 cm.).

We wish to thank the staff of the Department of Physical Medicine, Manchester Royal Infirmary, for administering the electrical stimulation to these patients.

REFERENCES

Beck, R. P., Hsu, N., and Maughan, G. B. (1965). *Amer. J. Obstet. Gynec.*, **91**, 314.
Caldwell, K. P. S. (1963). *Lancet*, **2**, 174.
—— Flack, F. C., and Broad, A. F. (1965). Ibid., **1**, 847.
Hopkinson, B. R., and Lightwood, R. (1966). Ibid., **1**, 297.
Jeffcoate, T. N. A. (1961). *J. roy. Coll. Surg. Edinb.*, **7**, 28.
Jones, E. G. (1963). *Clin. Obstet. Gynec.*, **6**, 220.
Lapides, J. (1961). *Brit. J. Urol.*, **33**, 284.
——Ajemian, E. P., Stewart, B. H., Breakey, B. A., and Lichtwardt, J. R. (1960a). *J. Urol.*, **84**, 86.
—— —— —— Lichtwardt, J. R., and Breakey, B. A. (1960b). *Surg. Gynec. Obstet.*, **111**, 224.
Nemir, A., and Middleton, R. P. (1954). *Amer. J. Obstet. Gynec.*, **68**, 1166.
Vincent, S. A. (1959). *Ulster med. J.*, **28**, 176.
—— (1966). *Bio-Med. Engng*, **1**, 438

Hepatocellular Damage with Ethacrynic Acid

K. K. DATEY,* M.D., F.R.C.P.ED., M.R.C.P., F.A.C.C., F.C.C.P.; S. N. DESHMUKH,† M.D.;
C. P. DALVI,‡ M.D., B.SC., F.I.C.A., F.C.C.P.; N. M. PURANDARE,§ M.D.

Brit. med. J., 1967, 3, 152–153

Ethacrynic acid is a potent diuretic agent and has been particularly useful in cases of fluid retention refractory to other diuretic agents (Datey *et al.*, 1967). This is a new drug, and all its toxic effects are still not known. Some side-effects and toxic effects have been well documented. Toxic effects such as cholestatic jaundice, agranulocytosis, and thrombocytopenia have been reported in one patient each (Merck Sharp and Dohme, 1964). A toxic effect not reported so far is presented in this communication.

Case Report

A man aged 25 with rheumatic heart disease (mitral stenosis and aortic stenosis with incompetence), subacute bacterial endocarditis, and gross congestive cardiac failure was admitted to the K.E.M. Hospital, Bombay, on 24 August 1966. He was given the appropriate antibiotic therapy, a low-salt diet, digitalis, and ethacrynic acid. In the first eight days the diuretic response was good and he lost 8 lb. (3.6 kg.) (with 50 mg. of ethacrynic acid daily). However, his urinary output subsequently decreased and an additional dose of 50 mg. of ethacrynic acid was given on alternate days. Various tests, including serum electrolytes, liver function, blood urea nitrogen, etc., were carried out periodically to detect the toxic effects of this drug. Two weeks after starting the therapy mild jaundice was noticed (Fig. 1), and, as we were not certain of its aetiology, the drug was continued and the tests were repeated every four days. When two consecutive tests showed deterioration (Fig. 1), ethacrynic acid was omitted and all other treatment was continued. Though the drug was omitted, the jaundice increased for about a week and then began to recede. It cleared in another two weeks. During this period, when ethacrynic acid was omitted, other diuretics were used. However, they were relatively ineffective. As the condition of the patient deteriorated, ethacrynic acid had to be restarted in a dose of 50 mg. daily. Subsequently the dose had to be increased to 200 mg. daily to get the desired diuretic response. During the next seven weeks hypokalaemia and hypochloraemia often appeared but were corrected by appropriate measures. Seven weeks after restarting this drug mild jaundice developed and the serum transaminase levels were high (Fig. 1). Hence the drug was again discontinued. The jaundice regressed, and six days later, though the serum bilirubin was 1.5 mg./100 ml., the serum transaminase levels had become normal.

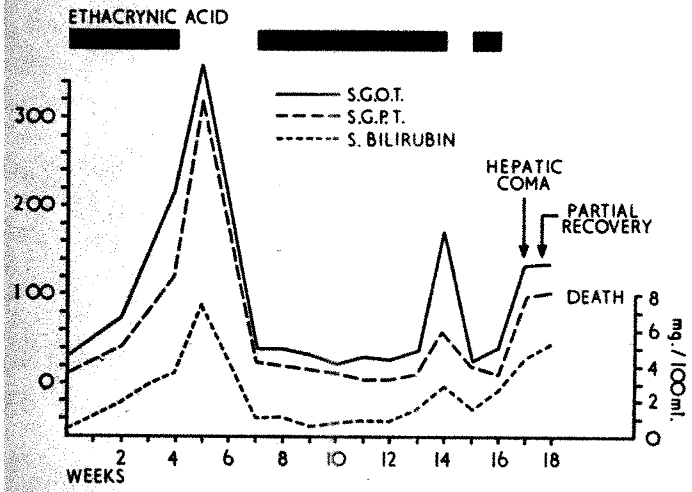


FIG. 1.—Changes in S.G.O.T., S.G.P.T., and serum bilirubin during the course of therapy with ethacrynic acid.

As the cardiac status of the patient deteriorated and there was fluid retention (the weight gain was 2 kg.) during this period, and as other diuretics proved ineffective, ethacrynic acid was restarted, 50 mg. initially. In the next seven days he was given 50 to 150 mg. of ethacrynic acid daily. Jaundice again developed and this time mental changes were also present. The drug was immediately discontinued. Both jaundice and mental changes progressed gradually. In the beginning there was hypersomnia, reduction of spontaneous movements, a fixed stare, and apathy. Intermittent changes included childishness, irritability, and loss of concern for his disease. Speech became slow and slurred, the voice monotonous and often faint. The characteristic "flapping tremors" were observed for a short time, a few hours before coma supervened. He was treated appropriately for hepatic coma, and after three days he came out of coma but still had mental confusion and hypersomnia. No further improvement occurred for the next four days, the serum bilirubin remaining at 4.25 mg./100 ml. and serum aspartate aminotransferase (S.G.O.T.) and serum alanine aminotransferase (S.G.P.T.) 108 and 94 units respectively (Fig. 1). The patient died the next day in congestive cardiac failure.

Post Mortem Examination

The body was emaciated and poorly built. There was an icteric tinge on the skin and in the conjunctiva. The heart was enlarged and showed changes of rheumatic mitral and aortic valve stenosis, with evidence of healed bacterial endocarditis. There was a small healed infarct in the cortex of the left kidney in addition to chronic venous congestion. The lungs and the spleen showed chronic venous congestion. The cut surface of the liver had the typical

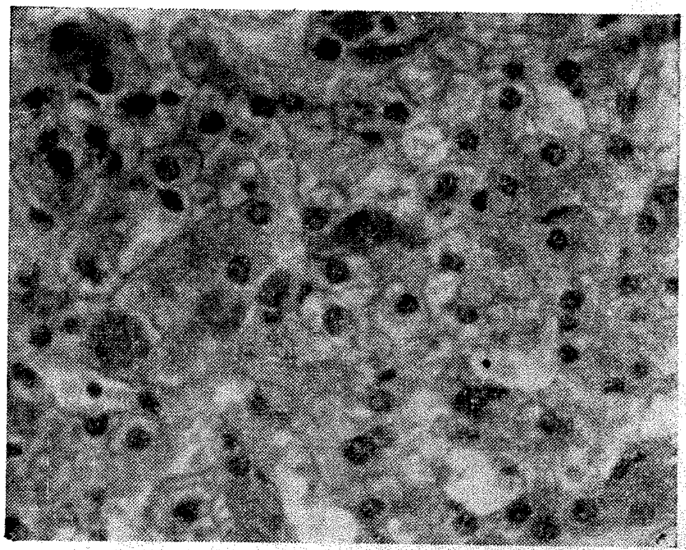


FIG. 2.—Photomicrograph showing area of focal necrosis. (×400.)

---

* Honorary Professor of Medicine, G.S. Medical College, Bombay; Director, Department of Cardiology, K.E.M. Hospital, Bombay; Honorary Physician and Cardiologist, Bombay Hospital, Bombay; Consultant in Cardiology, St. George's Hospital, Bombay.

† Assistant Cardiologist, V.R.A. Research Project, K.E.M. Hospital, Bombay.

‡ Honorary Assistant Physician, K.E.M. Hospital, Bombay; Assistant Professor of Medicine, G.S. Medical College, Bombay.

§ Professor of Pathology, G.S. Medical College, Bombay.

nutmeg appearance of chronic passive congestion. There was a small patch of necrosis, yellowish in colour, in the right lobe. This was rather friable. The gall bladder and biliary tract were normal.

Histology.—The liver showed changes of chronic venous congestion in most of the liver lobules and consisted of dilated central veins and dilated and congested sinusoids. A few cells around the dilated central veins showed changes of necrosis. The periportal connective tissue was slightly increased. In addition to this, in many areas the parenchymatous cells showed evidence of focal necrosis irregular in distribution (Fig. 2), and quite different from that seen in chronic venous congestion. These areas of necrosis morphologically resembled those produced by carbon tetrachloride injury in experimental animals. The necrosed cells showed pyknotic nuclei and indistinct cell walls. The cytoplasm showed hydropic degeneration and in places the presence of amorphous eosinophilic material. A few vacuoles could be seen in some cells. Kupffer cells were prominent and contained increased pigment. The bile ducts showed a moderate degree of proliferation. However, no stagnation of bile could be seen.

Discussion

Jaundice due to drugs is usually hepatocellular or cholestatic and rarely haemolytic. The clinical and biochemical differentiation of the various types is well known.

Ethacrynic acid has been reported to produce cholestatic jaundice in one patient (Merck Sharp and Dohme, 1964); however, to the best of our knowledge there are no reports of hepatocellular damage due to it. Experimentally, it has been proved that this drug is stored in the liver and secreted in the bile (Beyer *et al.*, 1965). The highest concentration of ^{14}C ethacrynic acid, after one week of its intravenous administration, was found in the liver, though this was only 2% of the dose, less than 3% being present in all the other organs (Merck Sharp and Dohme, 1964). We feel that in our patient this may account for the increase in jaundice for some days, even after the drug was withdrawn.

In our case the rise in S.G.O.T., S.G.P.T., and serum bilirubin and positive flocculation tests clearly indicates that the jaundice was hepatocellular in nature. The hepatocellular damage was probably due to ethacrynic acid, because on the first two occasions the jaundice developed when the drug was administered and regressed when it was discontinued. On the third occasion, however, after restarting the drug the patient developed hepatic coma and increasing jaundice. He recovered from the coma with appropriate measures, though the jaundice persisted. The irregular distribution of focal necrosis in the liver, quite different from that seen in chronic venous congestion, which shows centrilobular focal necrosis and resembling morphologically that produced by carbon tetrachloride in experimental animals, is in favour of its being due to the drug and not to acute or chronic heart failure. This correlates well with the clinical observations. As the drug is stored in the liver it is not surprising that hepatocellular damage was produced. Hence caution is required in the administration of this potent drug.

Summary

Ethacrynic acid is a new diuretic agent. Some of its side-effects and toxic effects are well documented, while others have been reported but rarely. A new toxic effect, hepatocellular damage, is reported in this communication.

The drug was supplied by the courtesy of Merck Sharp and Dohme Ltd.

REFERENCES

Beyer, K. H., Baer, J. E., Michaelson, Joan K., and Russo, H. F. (1965). *J. Pharmacol. exp. Ther.*, **147**, 1.

Datey, K. K., Shah, R. M., Deshmukh, S. N., and Dalvi, C. P. (1967). *J. postgrad. Med.*, **13**, 63.

Merck Sharp and Dohme (1964). Synopsis of Clinical Experience with Ethacrynic Acid.

Preliminary Communications

Sugar Consumption in Acne Vulgaris and Seborrhoeic Dermatitis

Brit. med. J., 1967, **3**, 153–155

There is little concrete evidence that diet plays a part in the aetiology of disorders of the skin, except in nutritional deficiency diseases such as pellagra and kwashiorkor. Nevertheless, many authorities implicate diet—dietary excess rather than dietary deficiency—as an aetiological agent, notably in acne vulgaris and, to a less extent, in seborrhoeic dermatitis. Consequently, changes in diet are frequently recommended as part of the treatment of these diseases. Of 10 recent textbooks, diet is mentioned in 9 in connexion with the cause or treatment of acne, and in 6 in connexion with seborrhoeic dermatitis. In neither disease are the authors unanimous; most frequently mentioned, however, is an excessive intake of fat or of carbohydrate, or of both. In addition chocolate is several times specifically mentioned in connexion with acne.

There are three criteria by which one tests the hypothesis that a dietary component is implicated in the causation of a disease (Yudkin, 1953). Firstly, there should be evidence that the diet of persons with the disease differs significantly from that of persons without the disease. Secondly, the symptoms and signs should be those that are known to be, or at least are plausibly suspected of being, caused by dietary imbalance. Thirdly, correction of the dietary imbalance should result in correction of the signs and symptoms.

In this paper we bring evidence of the first sort: that patients with seborrhoeic dermatitis consume significantly more sugar (sucrose) than persons without the disease. We believe that this is the first demonstration of a dietary difference in such patients. We have also shown that there is no such difference in patients with acne.

If the excessive amounts of a dietary constituent are thought to be a possible cause of disease, there are several reasons—evolutionary, historical, and metabolic—why sugar should be regarded as a likely candidate (Yudkin, 1963). It happens, too, than in practice it is more feasible to assess sugar intake than the intake of any other dietary constituent (Yudkin and Roddy, 1966). For these reasons, we measured the sugar intake of patients and control subjects with a short questionary that could be completed in 10–15 minutes by each of the subjects (see Appendix by J. Yudkin below).

The patients were referred to one of us at the skin clinics held at two hospitals. Seborrhoeic dermatitis was diagnosed when the patient presented with severe scaling of the scalp, together either with itchy scaly patches of the sternal or interscapular region or about the eyelids or nasolabial folds, or with intertrigo of the axillae, groins, or retroauricular areas, or with both types of lesions. All the patients had had previous attacks, and the current attack had lasted at least one month. All except one of the 16 patients were males; the ages ranged from 14 to 68.

Acne was diagnosed on the basis of comedones on the face, back, or chest, together with papules, pustules, or cystic lesions. There were nine male and seven female patients, aged between 15 and 27.

The patients with acne and dermatitis were all those who were seen during the period of study, except that, as usual, we did not include in our final assessment those whose sugar consumption, by admission or by implication, had changed.

As control subjects we used two different groups of people. The first were patients suffering from warts and attending the same skin clinics. Again, they were selected only on the basis of their diagnosis and on the apparent constancy of their sugar consumption. They were listed in the order in which we saw them, and from the list we then selected those who matched, as well as possible, the age and sex of the patients with acne or the patients with dermatitis. This was important, because we have found a difference in sugar intake between men and women and at different ages (Salter and Yudkin, to be published). It was, however, possible to find only 13 control patients of appropriate age for the 16 patients with seborrhoeic dermatitis. Moreover, it was not possible to match the distribution of male and female control patients with the distribution of the nine male and seven female patients with acne. For these reasons we used a second group of controls for each disease. These were apparently healthy men and women, either from a London factory or from a large London office. Their sugar intake had been measured during a large-scale survey that was being carried out for other purposes. This second group of controls was also selected from the list of subjects, made in the order in which they were seen, by choosing the first subject in the list that matched in age and sex the first patient with acne or dermatitis, then the first subject that matched the second patient, and continuing until all the patients were matched with apparently healthy control subjects.

RESULTS

The intake of sugar by the patients with acne was not significantly different from that of either group of control patients (Table I). On the other hand, the intake of sugar by the patients with seborrhoeic dermatitis was significantly higher than that of either group of control patients (Table II). This was true both for total sugar and for the sugar taken in tea and coffee ("beverage sugar"). Statistical analysis was carried out with the Mann–Whitney test for Control group 1, and with the Wilcoxon Matched-Pairs Signed-Ranks Test for Control group 2 (Siegel, 1956).

TABLE I.—*Sugar Intake of Subjects With Acne and of Control Subjects (Control 1: Patients With Warts; Control 2: Healthy Factory and Office Workers)*

Group	No.	Age (Mean, Years)	Sugar Intake (g./day)			
			Total		Beverage	
			Mean	Median	Mean	Median
Acne . .	16	19·5	121	103	65	70
Control 1	16	20·0	111	97	47	48
„ 2	16	19·7	120	118	63	55

No significant differences in sugar intake between groups (P > 0·05).

TABLE II.—*Sugar Intake of Subjects With Seborrhoeic Dermatitis and of Control Subjects (Control 1: Patients With Warts; Control 2: Healthy Factory and Office Workers)*

Group	No.	Age (Mean, Years)	Sugar Intake (g./day)			
			Total		Beverage	
			Mean	Median	Mean	Median
Dermatitis	16	38·2	170	185	104	109
Control 1	13	36·5	108	109	65	56
„ 2	16	38·1	110	110	61	57

Significant differences.—Total sugar intake: dermatitis and control 1—P < 0·01. Dermatitis and control 2—P < 0·02. Beverage sugar.—Dermatitis and control 1—P < 0·02. Dermatitis and control 2—P < 0·05.

DISCUSSION

The numbers of patients with either skin disease was small, chiefly because we made every effort to choose those in whom the diagnosis was not in doubt. Apart from this, there was no selection either of the patients with skin disease or of those acting as controls. The selection of the second group of control subjects from the factory and the office was only on the basis of age and sex. The lists of the patients and of the healthy control subjects had been drawn up in the order in which they were seen. This latter list was scanned from the beginning until a subject was found that matched in age and sex the first patient. This procedure was repeated with the next patient, and continued until all the patients had been matched.

In spite of the small number of subjects, we found a significantly higher intake of sugar in patients with seborrhoeic dermatitis than in control subjects. We believe, therefore, that this represents a real difference. We cannot of course say whether or not this relation between disease and sugar intake is a causal one. The findings, however, do suggest that it would be worth while to determine in a controlled experiment the effect of a reduction of dietary sugar on the course of the disease.

Our findings indicate that patients with acne have an intake of sugar no different from that of control subjects. This does not of course mean that diet is not involved in the causation of the disease or that changes in diet would not affect its progress. But further and more elaborate investigation would be required to test this possibility.

SUMMARY

The consumption of sugar (sucrose) by patients with seborrhoeic dermatitis was found to be significantly higher than that of two groups of control subjects. On the other hand, the consumption of sugar by patients with acne vulgaris was found to be no different from that of control subjects.

Mrs. Jill Morland was in receipt of a personal grant from the Medical Research Council while this work was being carried out.

D. G. G. BETT, B.M., M.R.C.P.,
Consultant Dermatologist, Farnborough Hospital, Kent.
JILL MORLAND, B.SC.,
Research Assistant, Queen Elizabeth College, University of London.
JOHN YUDKIN, M.A., M.D., PH.D., F.R.I.C.,
Professor of Nutrition and Dietetics, Queen Elizabeth College, University of London.

REFERENCES

Siegel, S. (1956). *Non-Parametric Statistics.* New York.
Yudkin, J. (1953). *Lectures on the Scientific Basis of Medicine*, vol. 1, p. 364. London.
—— (1963). *Lancet*, **1**, 1335.
—— and Roddy, J. (1966). *Brit. J. Nutr.*, **20**, 807.

Appendix: Measurement of Sugar Consumption by Questionary

We have reported several studies in which we have measured the consumption of sugar (sucrose) by a method based on a simple questionary. The original method involved the completion of the form by an interviewer (Yudkin and Roddy, 1964). More recently, the questionary has been simplified further so that it can be completed by the subject himself (Yudkin and Morland, 1967). We have given reasons for our belief that the method is reliable (Yudkin, 1964) and we have more recently tested its reliability against the method that involves the subject recording in a diary all the food and drink consumed over a period of seven days (Yudkin and Roddy, 1966).

The simplified questionary is set out below. In all of our studies we have attempted to consider only those persons who, so far as we can ascertain, have had a constant sugar consumption for many years. For this reason we include questions relating to "special" diets, and we eliminate from our final assessments those subjects who we have reason to believe have changed their sugar consumption.

The calculation of the amount of sugar in prepared foods and drinks is made from analyses published in food tables or from figures supplied by manufacturers. As for sugar itself, we take a heaped teaspoon as containing 6 g., a level teaspoon 4 g., a heaped dessertspoon 15 g., and a level dessertspoon 10 g.

I am grateful to Janet Roddy and Jill Morland, who helped to devise and test this questionary, and to the Medical Research Council, who supported the work.

JOHN YUDKIN, M.A., M.D., PH.D., F.R.I.C.,
Professor of Nutrition and Dietetics, Queen Elizabeth College, University of London.

DIETARY QUESTIONARY

NAME .... AGE ....

N.B.—IF THERE IS AN ALTERNATIVE MARKED* PLEASE CROSS OUT THE ONE WHICH DOES NOT APPLY

If your weight has increased in the last few years, are you making a serious effort to check or decrease it ? Yes/No*

If "Yes," are you restricting sweet or sugary foods, or sugar ? ....
....
....
....

If you are on a special diet *now* why are you on this diet ? ....
....

How long have you been on this diet ? ....

Have you *ever* been on any other special diet ? Yes/No*

If "Yes"
Why were you on this diet ? ....
Approximately when did you start this diet ? ....
How long did it last ? ....

If your eating habits have permanently changed as a result of being on the diet, in what way ? ....
....

Go through an average day in your mind, and write down how many cups of tea and coffee you consume:

	Tea	Coffee	Other hot beverages (Cocoa, chocolate, etc.)
Before breakfast	.... cups	.... cups	.... cups
At breakfast	.... cups	.... cups	.... cups
Mid-morning break	.... cups	.... cups	.... cups
Midday meal	.... cups	.... cups	.... cups
Teatime	.... cups	.... cups	.... cups
Evening meal	.... cups	.... cups	.... cups
Bedtime	.... cups	.... cups	.... cups
Other	.... cups	.... cups	.... cups

How much sugar do you take in tea ? ....teaspoons
Are the spoons level or heaped ? ....
How much sugar do you take in coffee ? ....teaspoons
Are the spoons level or heaped ? ....
Have you always taken the same amount of sugar in these beverages ? Yes/No*
If "No," how much did you take before ? ....
When did you change ? ....
Do you *regularly* use artificial sweeteners, e.g. saccharine, saxine, etc. Yes/No*
How long have you used them ? ....
How much of the following do you eat or drink *per week* ?
Sweets, toffees, and fancy chocolates ....lbs. ....oz.
No. of 2-oz. chocolate bars ....
Fizzy drinks, non-alcoholic ....glasses
(inc. tonic water, ginger-beer, etc.) ....small bottles
Fruit squash ....glasses
Fruit juice (tinned or bottled) ....glasses
How many a *week* do you have of the following:
Porridge ....portions
Plain breakfast cereals ....portions
Sugar-coated breakfast cereals ....portions
Jam or marmalade ....teaspoons
Sweet biscuits ....number
Pudding or sweet at midday (including tinned fruit) ....portions
Pudding or sweet for tea or evening meal (including tinned fruit) ....portions
Individual cakes and/or slices of cake ....number
How many spoons of sugar do you take on breakfast cereals ? ....
Are they teaspoons or dessertspoons ? ....
Are they level or heaped ? ....
How many spoons of sugar do you take on porridge ? ....
Are they teaspoons or dessertspoons ? ....
Are they level or heaped ? ....

REFERENCES

Yudkin, J. (1964). *Lancet*, **2**, 478.
—— and Morland, J. (1967). *Amer. J. clin. Nutr.*, **20**, 503.
—— and Roddy, J., (1964). *Lancet*, **2**, 6.
—— —— (1966). *Brit. J. Nutr.*, **20**, 807.

Medical Memoranda

Hepatitis with Biliverdinaemia in Association with Indomethacin Therapy

Biliverdin is the first bile pigment formed in the catabolism of the haem portion of haemoglobin. In man biliverdin is almost entirely reduced to bilirubin, which is excreted in the bile. The development of biliverdinaemia and biliverdinuria in association with disease, or as an iatrogenic effect, has not been reported. We here present a case of biliverdinaemia and biliverdinuria which developed after the administration of indomethacin (1-*p*-chlorobenzoyl-5-methoxy-2-methylindol-3-acetic acid).

CASE REPORT

A man aged 46 was employed as an unskilled labourer not at risk of exposure to toxic materials or gases. He was admitted to hospital on 14 May 1966 with a four-year history of intermittent joint pains which had been treated with salicylates and phenylbutazone outside hospital. For three weeks before admission he was having indomethacin 75 mg. daily.

On 7 May he had noticed that his urine was green, and soon was off his food and complaining of occasional abdominal pains. The only relevant feature in his past history was that he had suffered from brucellosis in 1957.

On physical examination the skin of the whole body presented a greenish hue, most evident on the trunk, while the conjunctivae were of normal colour. The temperature was 100° F. (37.8° C.); pulse 76/min. and regular; respiratory rate 20/min.; weight 62.6 kg.; and height 160 cm. The liver was palpable 7.5 cm. below the right costal margin. It was firm but not tender. The spleen was not palpable, and there were no intra-abdominal masses. Both hands showed early changes of rheumatoid arthritis. No physical abnormalities were detected elsewhere.

LABORATORY FINDINGS

Hb 13.9 g./100 ml.; P.C.V. 47%; R.B.C. 4,800,000/cu. mm.; reticulocytes 1.8%; leucocytes 7,200/cu. mm., with a normal differential count; blood film—slight anisocytosis, some spherocytic forms, and very occasional poikilocytes, no basophilic, polychromatic, or nucleated erythrocytes; osmotic fragility of erythrocytes—initial lysis at 0.48% NaCl (control at 0.46% NaCl), complete lysis at 0.28% NaCl (control at 0.30% NaCl); E.S.R. 15 mm. in first hour (Westergren); one-stage prothrombin time 17 sec. (control 15 sec.); bone-marrow smear—normoblastic erythropoiesis, normal myeloid series.

The serum was of a definite green colour. The van den Bergh reaction was delayed direct and the total serum bilirubin 3.3 mg./100 ml. Serum aspartate aminotransferase, 55 i.u./l.; alanine aminotransferase 94 i.u./l.; alkaline phosphatase 55 K.–A. units/

100 ml. Blood urea 30 mg./100 ml. and total plasma cholesterol 630 mg./100 ml. Total serum protein concentration 6.0 g./100 ml., with albumin 3.0 g./100 ml. Filter paper electrophoresis showed a slight reduction in serum albumin, with some increase in alpha$_1$- and alpha$_2$-globulins, a significant reduction in betaglobulin, and some increase in gammaglobulins. Serum uric acid 6.2 mg./100 ml. and serum pseudocholinesterase 160 units/100 ml. (range of normal sera 130–310 units/100 ml.). The latex fixation tests for C-reactive protein and the R.A. factor were positive.

The urine was a dark green. It had a *p*H of 5.8 and contained a trace of protein but no glucose or reducing substances. No urobilinogen or urobilin was detected. Fouchet's test gave a strong green spot indicative of biliverdin. The diazo reaction was negative even on the addition of ethyl alcohol. The sediment contained only an occasional crystal of calcium oxalate. *Pseudomonas pyocyanea* was not cultivated from the urine. The faeces were green in colour and also gave a strong green spot with Fouchet's reagent.

The pigment in the urine was isolated in large quantities and identified as biliverdin by the absorption spectrum of its solution in 5% methanolic hydrochloric acid and that of its zinc complex after oxidation with iodine. The spectra observed agreed with those reported by Gray *et al.* (1961a ; 1961b) for biliverdin.

Histological sections (Fig. 1) of liver tissue obtained by percutaneous puncture on 23 May showed centrilobular degeneration, swelling and some fatty change of parenchymal cells, and regeneration of hepatic cells. Both the parenchyma and portal zones contained many neutrophils and mononuclear cells, including plasma cells. Bile stasis, mostly within Kupffer cells, adjacent to the foci of necrosis was evident. van Gieson staining showed increased collagen deposition around the central veins but no increase in the portal tracts. There was some bile-duct proliferation, but the ducts were not obstructed. The overall picture was that of an acute hepatitis.

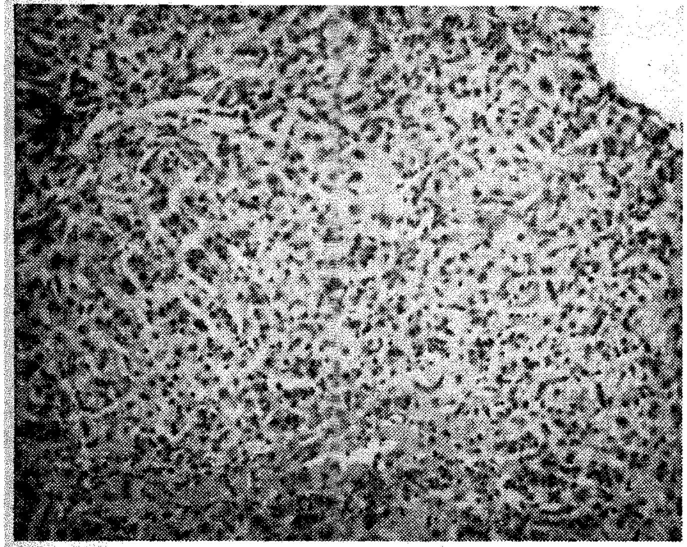


FIG. 1.—Section of liver tissue. Centrilobular degeneration, swelling and some fatty change of parenchymal cells, and regeneration of hepatic cells. There is infiltration of both the parenchyma and portal zone by many neutrophils and mononuclear cells, including plasma cells. (Haematoxylin and eosin. ×165.)

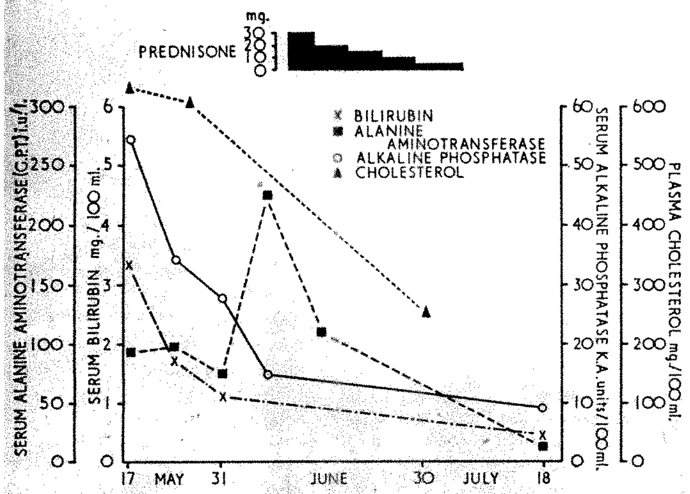


FIG. 2.—Main biochemical changes during the period of observation.

Indomethacin therapy was stopped, and conservative treatment was instituted, with bed rest, a high protein and carbohydrate diet with elimination of fats, and parenteral vitamin supplements for the first three weeks.

The main biochemical changes during the period of observation are shown in Fig. 2. As the serum alanine aminotransferase rose considerably above the level on admission, prednisone was prescribed at an initial dose of 30 mg. daily. This was followed by sustained progress. Within six weeks of the start of prednisone therapy the liver was no longer palpable, the urine and faeces had regained their normal colour, and the serum chemistry became normal.

The patient was discharged from hospital on 5 August 1966 and has remained well.

COMMENT

Temporary mental or neurological symptoms, haemorrhages, haemocytopenias, and even fulminating infections have been reported in the course of indomethacin therapy (W.H.O., 1966). Bruckner and Randle (1965) reported hepatotoxicity associated with indomethacin, but the evidence they produced is very tenuous. In a personal communication the manufacturers claim that there has been no proved case of hepatotoxicity produced by indomethacin. However, Kelsey and Scharyj (1967) have reported a case of fatal hepatitis which was probably due to indomethacin.

The tests of liver function employed and the histological changes in the liver seen in the case presented here are consistent with the diagnosis of cholestatic hepatitis similar to that produced by drugs such as chlorpromazine. In the present case salicylates and phenylbutazone had been taken several months before the illness, while indomethacin had been taken for three weeks before admission to hospital.

Biliverdinaemia presumably results from blockage of the reduction of biliverdin to bilirubin. Singleton and Laster (1965) have demonstrated the existence of high biliverdin reductase activity in guinea-pig liver and spleen. They also demonstrated biliverdin reductase activity in human liver. The development of biliverdinaemia and biliverdinuria has not yet been recorded. Two explanations for its occurrence may be suggested. It is possible that in producing hepatitis indomethacin severely inhibited the activity of biliverdin reductase in the patient's liver, and probably also in the spleen. It is also possible that the patient has a congenital partial deficiency of biliverdin reductase, which came to light as a result of the hepatitis.

We wish to express our thanks to Professor G. P. Xuereb, the Royal University of Malta Medical School, and to Dr. P. J. Scheuer, the Royal Free Hospital, London, for their helpful opinions on the histological sections, and to Dr. Barbara H. Billing, the Royal Free Hospital, London, for advice.

FREDERICK F. FENECH, M.D., M.R.C.P., M.R.C.P.ED., D.C.H.,
Physician and Part-time Lecturer in Medicine.
WILLIAM H. BANNISTER, M.A., M.D., D.PHIL.,
Professor of Physiology.
J. L. GRECH, M.D., D.C.P., D.M.J., M.C.PATH.,
Pathologist and Lecturer in Forensic Medicine.
St. Luke's Hospital and Royal University
of Malta Medical School,
Malta.

REFERENCES

Bruckner, F. E., and Randle, A. P. H. (1965). *Ann. phys. Med.*, **8**, 100.
Gray, C. H., Kulczycka, A., and Nicholson, D. C. (1961a). *J. chem. Soc.*, p. 2268.
—— Lichtarowicz-Kulczycka, A., Nicholson, D. C., and Petryka, Z. (1961b). Ibid., p. 2264.
Kelsey, W. M., and Scharyj, M. (1967). *J. Amer. med. Ass.*, **199**, 586.
Singleton, J. W., and Laster, L. (1965). *J. biol. Chem.*, **240**, 4780.
World Health Organization (1966). Clinical and Pharmacological Evaluation of Drugs. Drug Information Sheet No. 57.

Mycobacterium Battey Infection Resembling Tuberculosis

Brit. med. J., 1967, **3**, 157–158

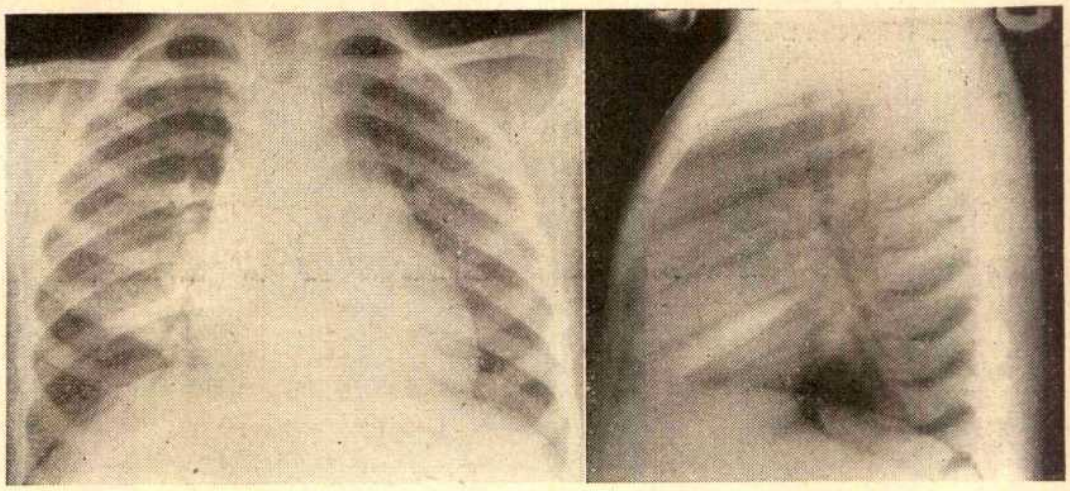
Anonymous (atypical or unclassified) mycobacteria are well established as pathogens for man (Chapman, 1960). They are able to mimic the clinical and pathological manifestations formerly attributed only to *Mycobacterium tuberculosis*. Recent Australian and American experience suggests that there is significant morbidity resulting from infection by anonymous myobacteria. Further, the amount of anonymous mycobacterial infection prevalent sometimes exceeds that of *Myco. tuberculosis* (Smyth *et al.*, 1964 ; Walker and Patron, 1964 ; Carruthers and Edwards, 1965 ; Curry, 1965). The British literature does not reflect a similar experience (Lefford *et al.*, 1966).

One of the anonymous mycobacteria, the Battey bacillus, is recognized as an important and common aetiological agent of pulmonary disease in adults and cervical lymph node disease in children (Smyth *et al.*, 1964). No documented cases of pulmonary disease in children caused by *Mycobacterium Battey* could be found. Neither were any reports found of a child with both pulmonary and lymph node disease occurring together except rare cases of disseminated fatal infection (Volini *et al.*, 1965).

This report describes the case of a child with a pulmonary lesion and cervical adenitis. The hospital admission diagnosis was tuberculosis, but comparative skin testing predicted *Myco. Battey* infection, and this organism was recovered from the lymph node.

CASE REPORT

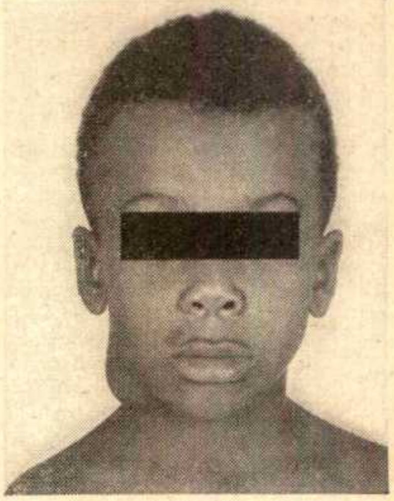
A boy aged 3 years 9 months presented with a six-weeks history of a lump in the right side of his neck which had been increasing in size. At the onset of his illness there were a few days when he felt feverish, but his temperature was not recorded. Before admission he had been treated with antibiotics. No other symptomatology was elicited except for some occasional tenderness of the lump in his neck. One week before admission he had been seen at another hospital where a Heaf test was found to be strongly positive.



FIGS. 2 and 3.—*X*-ray films showing opacity in right middle lobe.

The child had been admitted to our hospital two years previously for investigation of idiopathic convulsions. At that time a Heaf test was recorded as negative. In the year before admission he had had no further convulsions and had been on no anticonvulsant therapy. There was no family history of tuberculosis or any known tuberculous contacts. The family was of West Indian extraction, but had been in Britain for nine years and the patient was born at a local hospital. He had not been given B.C.G. vaccine.

Physical examination showed him to be an apparently fit and alert negro boy at the 50th percentile by height and the 30th percentile by weight for age. A mass protruding from the right side of his neck seemed to involve the submandibular as well as the upper anterior cervical lymph nodes (Fig. 1). The mass was hard, with slight tenderness, and was not fluctuant or warm. It measured 1 by 1½ in. (2.5 by 3.8 cm.) and we could not be sure whether it was a single node or a bunch of smaller nodes matted together. The presence of a 4+ Heaf test on his arm was confirmed. The rest of the physical examination was within normal limits. Temperature on admission was 98.6° F. (37° C.).



[redacted]

FIG. 1.—Photograph of patient, showing mass in neck.

Chest *x*-ray examination showed an opacity in the medial segment of the right middle lobe (Figs. 2 and 3). The sedimentation rate was 37 mm. in the first hour (Westergren) ; haemoglobin 11.9 g./100 ml. ; white blood cell count 10,600/cu. mm., with a differential count of 44% neutrophils, 8% eosinophils, 42% lymphocytes, and 6% monocytes. Sickling test and Paul–Bunnell screening test were negative. Urine analysis was normal. Serum Na, K, Cl, urea, Ca, and P were normal. Cultures of nose, throat, and rectum showed normal flora.

At admission a presumptive diagnosis of tuberculosis was made on the basis of a strongly positive Heaf test in a child under 4 years of age, a recent skin-test conversion, a lesion in the chest, an enlarged "cold" cervical node, and a raised sedimentation rate. Comparative skin testing by the Mantoux technique was performed with purified protein derivative (P.P.D.)-tuberculosis (human), P.P.D.-avian, and P.P.D.-Battey. Three gastric washings were done and the child was given penicillin as a therapeutic trial.

After two weeks of penicillin therapy he remained asymptomatic but had occasional episodes of low-grade fever with no change in his chest lesion or sedimentation rate. His node became fluctuant, and incision with drainage, under cover of isoniazid (20 mg./kg./day) and P.A.S. (300 mg./kg./day), was performed. His tonsils and adenoids were removed simultaneously in order to search for a possible focus of infection.

After surgery, treatment was continued with isoniazid and P.A.S. His node decreased markedly in size with no further drainage after the first month. By the end of three months his sedimentation rate had returned to normal and his chest *x*-ray film had cleared. Six months after onset of therapy he remained well with no evidence of persistence or recurrence.

Bacteriology and Pathology

The skin test antigens (P.P.D.) used for all the Mantoux testing were supplied by the Central Veterinary Laboratory, Weybridge. The human antigen was prepared from strains C, D.T., and P.N. obtained from children with *Myco. tuberculosis* infections. The Battey antigen was prepared from an American strain 100616. The avian antigen was prepared from strain D4 isolated from infected domesticated poultry. All three strains were supplied as containing 2 mg. (100,000 units) per ml. Previous to skin testing the material was freshly diluted to deliver 0.00001 mg. (0.5 unit) per dose. Comparative Mantoux skin testing was done on two separate occasions. The first test compared the avian with the human antigen. Both were positive (greater than 5 mm. induration), but the avian reaction was twice as large as the human. The second test compared Battey, avian, and human antigens placed simultaneously. The Battey showed 15 mm., the avian 12 mm., and the human 5 mm. of induration.

Pus from the node was sent to three separate laboratories. Identiication of the organism was arrived at independently by two of hese laboratories. The other could not distinguish it from *Myco. uberculosis.* The pus was negative by Gram and P.A.S. stains but showed acid-fast organisms by Ziehl–Neelsen stain. Bacterial nd fungal cultures were sterile, but acid- and alcohol-fast bacilli were grown on Löwenstein–Jensen slope after six weeks' incubation. These were subsequently identified as non-photochromogens of the Battey type belonging to Runyon group III. Sensitivities were done with the use of standard strains as comparison and resistance ratios were obtained. These showed the organism to be sensitive to cycloerine but resistant to streptomycin, viomycin, P.A.S., isoniazid, thionamide, and thiosemicarbazone. (We can only note that the linical response as reported was at variance with these in vitro ensitivity tests.)

Histology of tonsils and granulation tissue from the node showed miliary "tubercles" with macrophages, lymphocytes, and multiucleate giant cells with early caseation.

Gastric washings were negative for acid-fast organisms and showed o growth on culture.

Discussion

The role of *Myco. Battey* infection among children in Great Britain is not clear. Marks (1964) mentions four cases of ervical adenitis in children caused by *Myco. avium.* This organism, in his classification, is probably closely related to or synonymous with *Myco. Battey* (*Lancet*, 1962). Marsden and Hyde (1962), in their review of cervical adenitis among children caused by anonymous mycobacteria, did not identify the Battey bacillus in any of their cases.

Skin testing has been done only on a limited scale and generally by the Heaf technique, which provides a poor guide to the degree of tuberculin sensitivity (Griffith *et al.*, 1963). Yet the Battey purified protein derivative has been shown to be an excellent case-finding tool and diagnostic adjunct (Palmer *et al.*, 1959). In addition, it has been suggested that it can be utilized as a screening tool for all anonymous mycobacterial infections as it shows extensive cross-reactions to other mycobacteria (Walker and Patron, 1964).

The issue is further clouded by gross variation in standards of tuberculosis bacteriology. Laboratories very often fail to distinguish between tubercle bacilli and anonymous mycobacteria (Marks, 1965). Yet the therapeutic problem created by these organisms is as great as that due to primary resistance of tubercle bacilli because of their generally poor response to chemotherapy (Lefford *et al.*, 1966).

As a result, we find it difficult to accept that *Myco. Battey* infection, especially among children, is virtually absent from Great Britain. To do so might lead to diagnostic, epidemiological, and therapeutic error (Smith *et al.*, 1965).

ADDENDUM.—We refer readers to two articles which appeared after submission of this paper and which present evidence for differential Mantoux-testing in children (Keay and Edmond, 1966; Mackellar *et al.*, 1967).

We thank Mr. I. W. Lesslie, of the Central Veterinary Laboratory, for supplying the mycobacterial P.P.D. antigens and for his aid in identifying the organism.

B. R. ADELS, M.D.
P. J. N. COX, M.A., B.M., M.R.C.P., D.C.H.

Paediatric Unit,
St. Mary's Hospital Medical School,
London W.2.

References

Carruthers, K. J. M., and Edwards, F. G. B. (1965). *Amer. Rev. resp. Dis.*, **91**, 887.
Chapman, J. S. (1960). *The Anonymous Mycobacteria in Human Disease*, p. 3. Illinois.
Curry, F. J. (1965). *New Engl. J. Med.*, **272**, 415.
Griffith, A. H., Marks, J., and Richards, M. (1963). *Tubercle (Lond.)*, **44**, 135.
Keay, A. J., and Edmond, E. (1966). *Lancet*, **2**, 1425.
Lancet, 1962, **2**, 1153.
Lefford, M. J., Mitchison, D. A., and Tall, R. (1966). *Tubercle (Lond.)*, **47**, 109.
Mackellar, A., Hilton, H. B., and Masters, P. L. (1967). *Arch. Dis. Childh.*, **42**, 70.
Marks, J. (1964). *Proc. roy. Soc. Med.*, **57**, 479.
—— (1965). *Mth. Bull. Minist. Hlth Lab. Serv.*, **24**, 2.
Marsden, H. B., and Hyde, W. A. (1962). *Lancet*, **1**, 249.
Palmer, C. E., Edwards, L. B., Hopwood, L., and Edwards, P. Q. (1959). *J. Pediat.*, **55**, 413.
Smith, D. H., Doherty, R. A., and de Lemos, R. A. (1965). Ibid., **67**, 759.
Smyth, J. T., Kovacs, N., and Harris, W. P. (1964). *Tubercle (Lond.)*, **45**, 223.
Volini, F., Colton, R., and Lester, W. (1965). *Amer. J. clin. Path.*, **43**, 39.
Walker, S. H., and Patron, L. R. (1964). *Amer. J. Dis. Child.*, **108**, 460.

Current Practice

TODAY'S DRUGS

Fenfluramine

With the help of expert contributors we publish below notes on a selection of drugs in current use.

Fenfluramine is an appetite depressant recently marketed in this country by Selpharm Laboratories Ltd. under the name Ponderax. It is not subject to the Drugs (Prevention of Misuse) Act, 1964.

Chemistry and Pharmacology

Fenfluramine (trifluoromethyl-3 phenyl-1 ethylamino-2-propane hydrochloride) has been shown in animal studies effectively to reduce food intake.[1] Fenfluramine is not metabolized to amphetamine by animals or man but is present in the blood and urine partly unchanged and as nor-fenfluramine.[2] It is excreted slowly, which may account for its prolonged anorectic effect,[3] and there is accumulating evidence of its fixation in fatty tissues.[4] Like amphetamine and other amphetamine derivatives[5] it may have a direct effect in accelerating lipolysis.[4] It is a sympathomimetic amine which, when given to animals in doses sufficient to cause marked appetite suppression, does not cause overt stimulation of the central nervous system, although both mild stimulating and sedative effects have been demonstrated.[1, 6] Although qualitatively the effect of fenfluramine on the cardiovascular system resembles that of amphetamine, in quantitative terms this effect is much less marked,[6–8] and in both animals and man occasional reduction of the blood pressure has been noted.[9, 10]

Toxic and Side-effects

When given in therapeutic doses the drug may have a sedative effect.[9–13] Diarrhoea has also been reported[10, 14] and may prove troublesome.[14] A few patients experience a symptom complex comprising light-headedness, abdominal discomfort, dry mouth, and generalized tiredness and muscle ache. Hypersensitivity reactions, habituation, and addiction have not yet been reported.

Self-poisoning with fenfluramine has been followed by spontaneous recovery.[2] In the case reported in detail overdosage caused an unusual clinical state of drowsiness with dilated unreactive pupils and sluggish reflexes.

Clinical Use

Clinical experience with fenfluramine in Britain is limited and it is still too early to form a definite opinion of its relative therapeutic value. A number of clinical trials have suggested that it is an effective anorectic agent[9–14] and that it may have several advantages over amphetamine and the amphetamine derivatives in the treatment of simple obesity. Thus, because of the clinical absence of stimulation of the central nervous system, it seems likely that habituation and addiction will not occur; this feature may be of particular value in the treatment of adolescent obesity. In some patients fenfluramine has a sedative effect, even when given in small doses,[9–13] and may be useful in treating those patients with co-existing anxiety states or those who have been disturbed by symptoms of anxiety while taking an amphetamine derivative. Its sedative effect also permits it to be taken in the evenings to try to control late evening or nocturnal hunger. The reported absence of cardiovascular effects allows its use in hypertensive patients[9, 10] when other anorectic drugs are contraindicated. The anorectic effect of fenfluramine may outlast that of other drugs,[14] but this possibility requires to be put to the test. Pending further clinical evaluation it is probably advisable to prescribe only short courses of fenfluramine, which can be repeated if necessary. There is no conclusive evidence that it is substantially more effective than other anorectic agents; it is relatively expensive and like all appetite depressants should not be prescribed indiscriminately. As is the case with all anorexigenic drugs some obese patients do not lose weight appreciably when given fenfluramine.

Dosage

Fenfluramine is available as Ponderax. Each tablet contains 20 mg. of the active ingredient. The recommended adult dose is 2 to 4 tablets daily, though exceptionally up to six tablets daily may be prescribed. Side-effects can be minimized by introducing the drug in a stepwise manner. In children under the age of 12 the recommended dose is 1 tablet daily.

The basic N.H.S. cost of 100 tablets is 38s.

REFERENCES

[1] Alphin, R. S., Fundezburk, W. H., and Ward, J. W., *Toxicol. appl. Pharmacol.*, 1964, **6**, 340.
[2] White, A. G., Beckett, A. H., and Brookes, L. G., *Brit. med. J.*, 1967, **1**, 740.
[3] Duhault, J., and Fenard, S., *Arch. int. Pharmacodyn.*, 1965, **158**, 251.
[4] —— and Boulanger, M., *Journées Ann. Diabét.*, Hôtel Dieu, 1966, 67.
[5] Santi, R., and Fassina, G., *J. Pharm. Pharmacol.*, 1964, **16**, 130.
[6] Le Douarec, J. C., Schmitt, H., and Laubie, M., *Arch. int. Pharmacodyn.*, 1966, **161**, 206.
[7] Le Douarec, J. C., and Schmitt, H., *Thérapie*, 1964, **19**, 831.
[8] Franko, B. V., Honkomp, L. J., and Ward, J. W., *J. Pharm. Pharmacol.*, 1965, **17**, 222.
[9] Lambusier, P., *Vie méd.*, 1965, **46**, 679.
[10] Brodbin, P., and O'Connor, C. A., *Practitioner*, in press.
[11] Duncan, E. H., Regan, N. A., Hyde, C. A., and Sweetman, B., *Brit. J. clin. Pract.*, 1965, **19**, 451.
[12] Traherne, J. B., *Practitioner*, 1965, **195**, 677.
[13] Spence, A. W., and Medvei, V. C., *Brit. J. clin. Pract.*, 1966, **20**, 643.
[14] Munro, J. F., Seaton, D. A., and Duncan, L. J. P., *Brit. med. J.*, 1966, **2**, 624.

PREPARATIONS AND APPLIANCES

Apparatus for Automatic Preparation and Scanning in Cervical Cytology

Mr. M. M. BODDINGTON and Dr. R. A. DIAMOND, of the Clinical Cytology Laboratory, Churchill Hospital, Oxford, write: Population screening for carcinoma of the cervix has been limited by the lack of trained technicians as well as by inadequate laboratory facilities. This problem could largely be solved by automation by means of a mechanized system with a computer capable of analysing cells and arriving at a decision at high speed.

The apparatus described here is an aid to visual scanning of cervical smears by a cytologist, but is also applicable to automatic scanning by a computer technique. To enable a computer to scan cells rapidly an automated strip method with an even cell distribution is essential (A. Ward, personal communication, 1966).

The Vickers Cytology Screening Apparatus is divided into three parts: the first is the *graphing machine,* which places a line of cells on to a clear transparent strip. This is then transferred to the second part, which is a continuous *staining apparatus* that also automatically covers the cells with a clear Scotch tape. The final machine is the *viewing apparatus.*

Collection of Specimen.—The specimen is presented to the graphing machine as a cell suspension. To do this the cervical smear is collected in the usual way and then the spatula is placed into a solution of 1% Carbowax in 40% ethyl alcohol and transferred to the laboratory. By using a narrow container with a conical bottom containing a measured amount of fixative, the container can be placed direct into the centrifuge after removing the spatula. Suspending cells in a Carbowax alcohol solution allows them to be dried on the film strip previous to staining without spoiling the specimen.

GRAPHING MACHINE

The graphing machine has three functions: (1) aspirating excess fluid from concentrated cells; (2) pretreating a transparent film strip (Melinex I.C.I.) with celloidin (Necoloidine B.D.H.); and (3) drawing along the centre of the Melinex a linear film of cells.

A spool of Melinex 250 metres long is mounted on to the machine and laced under the Necoloidine writer through a guide over which the cell writing pen is located. After the cell writer the film is passed through the numbering mechanism, thence through the specimen dryer, and on to the take-up spool (Fig. 1).

The Necoloidine is applied to the Melinex by what might be described as an outsize ball pen. It is hoped that when in production the film will be supplied already coated with Necoloidine. Because the cells are fixed in solution Necoloidine-treated film must be used to prevent the cells from being washed off the film.

The cell writing pen is a linear reciprocating peristaltic pump. It differs from the normal peristaltic pump in that it draws fluid into its pliable plastic tubing and exhausts it out of the input. The unique feature of the pen is that the contaminated tubing is withdrawn, cut, and discarded. The plastic tubing is fed through the top of the pen from a reel, so that on drawing the contaminated tubing out it is automatically replaced by fresh tubing.

After centrifuging the tube is placed under a pipette and the excess fluid aspirated through a pump. The amount of fluid withdrawn is controlled by the attendant and the cell deposit thoroughly resuspended.

The pen is loaded by sucking up the concentrated cells; it is then placed over the centre of the Melinex strip with the protruding plastic tubing, which acts as a nib touching the strip. A motor is started, the tape is drawn beneath the pen, and the peristaltic pump reverses and deposits a line of cells for 61.5 cm., which corresponds to the area scanned on a normal microscope slide when a 5-cm. coverslip is used.

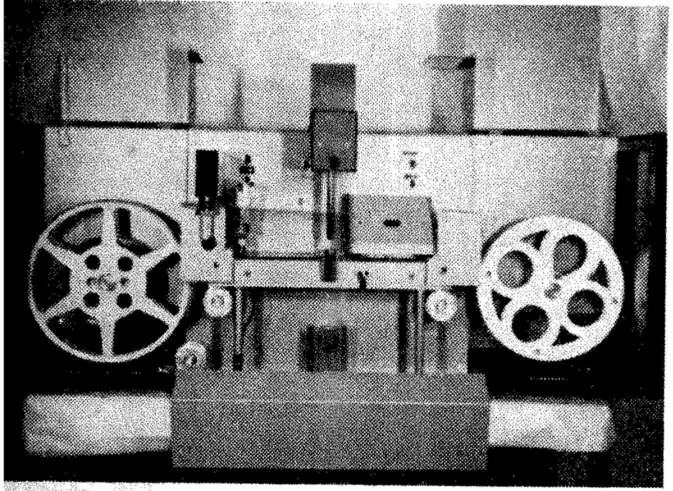


FIG. 1

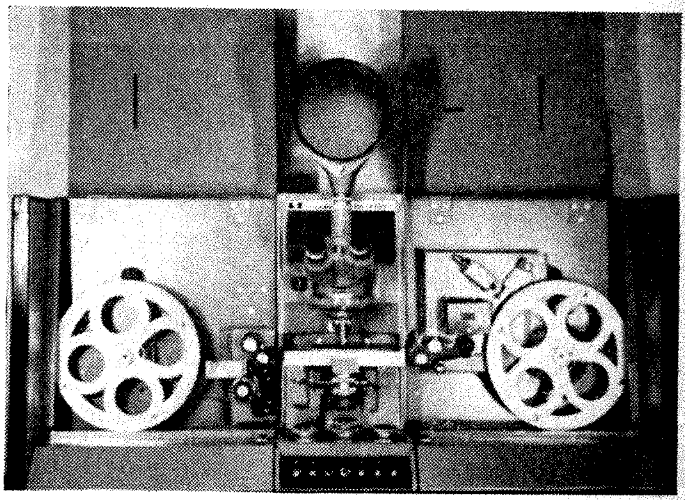


FIG. 3

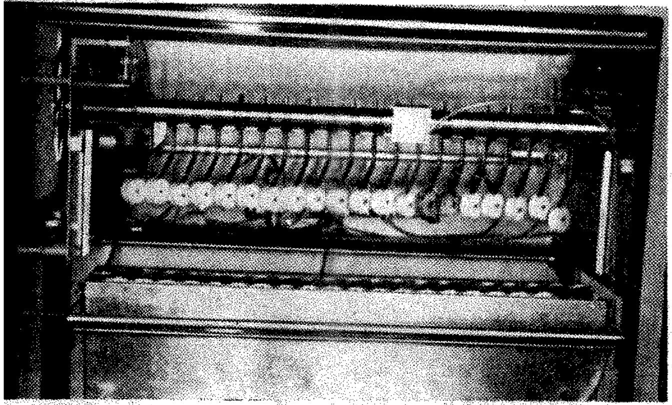


FIG. 2

FIG. 1.—Graphing machine, showing the peristaltic pen (centre) which deposits a line of cells on the transparent film strip as it passes. FIG. 2.—Continuous staining apparatus, showing the series of rollers over which the film strip is looped. Beneath them is the unit containing the individual staining-baths which, when raised, immerses the rollers. FIG. 3.—Viewing apparatus. The prepared film on the left passes under the objective of the microscope (centre) for viewing on the screen or through the binoculars.

Materials.—(*a*) Melinex, 16 mm. wide by 0.075 mm. thick by 250 m. long (I.C.I. product); (*b*) 1% solution of Necoloidine in equal parts of ether/alcohol; (*c*) translucent silicone rubber tubing size 1 by 0.5 mm. Quality P.C. 156.

STAINING APPARATUS

The spool from the graphing machine is loaded on to the continuous staining apparatus and the free end of the prepared film is welded on to a leader strip of Melinex, which is already fed through the apparatus. The prepared film is thus fed backwards through the staining process; the last 9.3 m. must be clean film to act as a leader for the next spool (see Fig. 2).

The staining and clearing process consists of 20 baths, the Papanicolaou technique being used. After the specimen has been cleared in xylene a line of D.P.X. mounting medium is drawn over the line of cells. The film is then covered by Scotch tape, 2 mm. narrower than the film, by passing them together through a roller system so that the tape is pressed evenly over the Melinex. The apparatus is fitted with five safety switches, which stop the machine if any faults develop during the processing.

The prepared specimen is taken up on another spool ready for immediate use on the viewing apparatus, having taken 13.25 minutes for the first specimen to be completed and then 1 minute for each subsequent specimen.

VIEWING APPARATUS

The specimen reading unit is a standard-type microscope, but differing from today's mechanical practice in that the body is focused and the stage remains fixed. The spool of specimens is loaded on the left of the microscope and the strip is located beneath the objective by a simple gate. The strip is drawn past the objective, the operator controlling the scanning speed through a start-stop and variable-speed control (Fig. 3).

The operator can reverse the strip by motor and centre any given field by normal stage control for examination under high power. A precision punch is provided for accurately marking abnormal cells, so that instant review of these can be made when the punched hole passes through a trigger-switched clamp. A similar electromechanical clamp holds each specimen number for reference during the passing of that specimen.

The specimen is viewed through binoculars or on a screen with the normal low- and high-power lens system.

The specimens are conveniently stored on the spools, each 250-m. reel containing up to 200 smears.

DISCUSSION

Initially this apparatus was designed to fit a computerized scanning system, and it is expected that ultimately a pattern recognition computer or similar prescreening device will take over much of the human effort involved in scanning cervical smears (Ward and McMaster, 1966). When this ideal set-up is established the positive material must still be checked by a cytologist, and this continuous-feed mechanism must be readily adaptable for human use.

The first essential is that the cells should be recognizable to the human observer and that the staining technique should therefore be the Papanicolaou method. The technique of suspending the cells in a Carbowax-alcohol solution and allowing them to dry gives a staining reaction almost identical with that by the routine "wet fixation" method used for smears on glass. The suspension gives an even distribution of cells with less clumping, and the gross appearances are somewhat different from those in a direct-smear preparation.

Our experience is similar to that of Davis and Jones (1966) using the cytopipette in that cellular patterns are different and require experience in interpretation. The cytopipette method is readily adaptable to this automated system. Abnormal cells do not appear in natural collections, and, though not so readily picked up by the human eye, the scatter distribution is necessary for a computer "eye."

A method of making and staining strips of cervical smears having been developed, the viewing machine was the next essential. This had to be capable of scanning the film strips without computer aid, and the present model can therefore be used for routine screening identical with the glass-slide method in speed and efficiency.

A detailed time comparison between the routine slide method and the Vickers Cytology Screening Apparatus shows them to be very similar. The staining time is slightly increased; but this is no disadvantage, because it does not involve technician time. Moreover, the "smears" are in numerical order and are ready to scan immediately. The technician time involved in the process is equivalent, apart from 51 seconds required to make each smear on the graphing machine.

The advantages of the system are the uniformity of the preparations, the fixed numerical sequence of forms and smears, and the consequent ease of filing. Staining of large numbers can be carried out overnight, and the automatic selection of previously marked cells for checking is an added refinement.

The main advantage of such a system would be felt in large population surveys. The greater the number of smears to be screened and the larger the laboratory the more efficient will be an automated apparatus of this nature.

Further trials are in progress to substantiate the efficiency of the Vickers Cytology Screening Apparatus in enabling malignant cells to be more readily detected and to shorten the time involved in scanning. Attempts are being made to improve the initial cell suspension and to produce a differential nuclear stain, so that investigations into the effectiveness of a prescreening device attached to this apparatus can be completed.

The application of this system to other pathological services is under investigation.

This work was initiated in the Churchill Hospital Cytology Department by Dr. A. I. Spriggs, who has encouraged and advised us throughout the development of the project. This work was supported by grants to one of us (R. A. D., Research Assistance Area Department of Obstetrics and Gynaecology) from Tenovus and Vickers Instruments, and to Dr. Spriggs by the British Empire Cancer Campaign. The instruments have been designed and constructed by Vickers Ltd., Vickers Instruments, under licence from Mr. P. A. Rock (U.K. Patent No. 1036776 and various overseas patent applications) and under the supervision of Mr. F. H. Smith and Mr. J. F. Taplin (Research Department), and the combination of the complete system was the work of Mr. E. W. Meyer (Forward Development).

REFERENCES

Davis, H. J., and Jones, H. W., jun. (1966). *Amer. J. Obstet. Gynec.*, 96, 605.
Ward, A., and McMaster, G. W. (1966). *Sci. J.*, August.

ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Health in Malawi

Q.—*Are the dangers to health for European children greater in Malawi than at home? Are comparative mortality figures available for children under 5 years of age? What are the main causes of sickness and death in this group?*

A.—Comparative mortality figures for children under the age of 5 years in Malawi are not available. The most recently available data on this subject are those contained in the *Last Report on the Public Health of the Federation of Rhodesia and Nyasaland during the Year 1963 Presented to the Federated Liquidating Agency.*[1] In this report the infantile mortality rate among Europeans in Malawi is given as 3.9 per 1,000, but it is based on only one infantile death. The crude death rate among Europeans in Malawi is reported as 3.3 per 1,000.

In general, those living in this part of Africa would need to take special precautions against malaria and bacillary and amoebic dysentery. The usual precautions against smallpox, yellow fever, and poliomyelitis should also be taken. Though the dangers to health for European children in Malawi are greater than they are in Britain, standard precautions will reduce these dangers to a very low level. Details of such precautions will be found in the publication entitled *Notes on the Preservation of Personal Health in Warm Climates.*[2]

REFERENCES

[1] *Last Report on the Public Health of the Federation of Rhodesia and Nyasaland during the Year 1963 Presented to the Federated Liquidating Agency.* Government Printer, Salisbury.
[2] *The Preservation of Personal Health in Warm Climates*, 1967. Ross Institute, London.

Diet for Alcoholics

Q.—*What diet (and particularly what amount of protein) should be advised for a man who drinks 10 to 20 pints of beer a day?*

A.—The important point is that the heavy drinker should eat a balanced diet containing normal amounts of protein. When alcohol is used as a substitute for food calories and carbohydrate are the main components and liver damage may occur. There is also the observation that if liver damage is already present recovery will follow the giving of an adequate diet, even if drinking continues. A heavy drinker may also need extra vitamins, especially of the B group.

But, despite this, the proper management of such a patient is surely to try to get him to reduce his alcohol intake.

Sterilizing Floors of Swimming-baths

Q.—*What suitable agents are available for sterilizing plimsolls and the floors of swimming-baths to control the spread of warts? Can x-irradiation be used for sterilizing plimsolls?*

A.—There does not appear to be any information on the sensitivity of the wart virus to available methods of disinfection. In structure it is like a polyoma virus, which contains D.N.A., and some D.N.A.-containing viruses have been shown to be readily inactivated by chlorine (e.g., by 10 minutes' contact with the 0.3 to 0.5 parts per million of free residual chlorine commonly present in swimming-bath water).[1] Frequent washing of the floors of swimming-baths and changing-rooms with chlorine solution would be expected to reduce the hazard of wart infection. Almost continuous cleaning and sluicing has been found effective in removing the agents of tinea pedis from the floors of swimming-baths.[2]

If plimsolls are not exchanged there should be little or no risk of acquiring warts from them. X rays and gamma rays inactivate viruses, and could undoubtedly remove the virus of warts from plimsolls, but large doses may be required to inactivate some viruses.[3] Immersion in a hypochlorite solution would probably be effective. Disinfection of footwear, however, is likely to be impracticable.[4]

REFERENCES

[1] Rhodes, A. J., and Van Rooyen, C. E., *Textbook of Virology*, 1962, 4th ed. Baltimore.
[2] English, M. P., and Gibson, M. D., *Brit. med. J.*, 1959, 1, 1446.
[3] Kaplan, C., *J. Hyg. (Lond.)*, 1960, 58, 391.
[4] —— *Chiropodist*, 1957, 12, 269.

Withdrawal of Morphine

Q.—*Is bronchopneumonia a recognized complication of the withdrawal of morphine from patients who have been on regular doses of the drug for some time?*

A.—Among the so-called non-purposive symptoms which may follow the withdrawal of a narcotic drug are insomnia; anorexia; sneezing; lacrimation; coryza, with alternate chills accompanied by gooseflesh; and sweating. In addition the patient often does not eat or drink, and so there may be loss of weight, dehydration, and a disturbance of acid/base and electrolyte balance.

Morphine causes respiratory depression, and it is said that this continues into the withdrawal period.[1] Thus, though one would not claim that bronchopneumonia was a recognized complication of withdrawal, a patient in the withdrawal phase is clearly in a condition in which he is very susceptible to the development of bronchopneumonia.

REFERENCE

[1] Reynolds, A. K., and Randall, L. O., *Morphine and Allied Drugs*, 1957, p. 53. Toronto.

Manual Removal of Placenta

Q.—*Should manual removal of the placenta normally be carried out under anaesthesia?*

A.—Normally general anaesthesia should be used in the operation of manual removal of the placenta. It can be very painful for the woman, and it may cause "shock" when done without anaesthesia. Sometimes it can be very difficult, and it is wise to be prepared for anything that may happen.

With the widespread use of controlled cord traction after the injection of Syntometrine (ergometrine maleate and oxytocin) manual removal is not often needed, and when it is there is no need for undue haste, since bleeding with the placenta still in the uterus is then usually negligible. There is therefore time for proper deliberation in performing the operation.

Despite this, however, it is quite possible manually to remove the placenta after an injection of only an analgesic such as pethidine, and even on occasion with only obstetric gas analgesia if the operator is expert and gentle. Especially is this possible when the placenta has separated and is lying within the lower segment, a fact which can be verified by sterile vaginal examination in the third stage. When the placenta is not definitely separated from the uterine wall general anaesthesia certainly ought to be used.

Oral Contraceptives and Psychosis

Q.—*A woman who had puerperal schizophrenia six years ago has recently had similar symptoms, and these coincided with taking an oral contraceptive for nine months. Is there any evidence that taking oral contraceptives can lead to the puerperal type of schizophrenia in a susceptible individual?*

A.—I know of no published work on this. However, it is not unreasonable to suppose that oral contraception, by inducing a state of pseudopregnancy, has produced in this patient a biochemical milieu similar to that which precipitated her puerperal schizophrenia. In the circumstances I think another method of contraception is indicated.

Tetanus from Water Buffalo

Q.—*Is there evidence that Clostridium tetani is carried by the water buffalo in India, and that their droppings are a source of infection in children who handle dung freely?*

A.—I have been unable to find any positive proof that *Clostridium tetani* has been isolated from the stools of water buffalo in India, but it may be taken that their faeces are a potential source of this organism. All herbivores are likely to swallow spores of *Clostridium tetani* from time to time when they eat grass vegetation contaminated with these organisms. Their droppings should therefore be regarded as a potential source of tetanus.

Notes and Comments

Oral Contraceptives and Epilepsy.—Dr. JEAN MCARTHUR (Family Planning Association, Liverpool 1) writes: I read with interest your expert's reply ("Any Questions?" 17 June, p. 752) to the question on prescribing oral contraceptives for an epileptic woman. The following case suggests that some discrimination should be used when prescribing oral contraceptives in this condition.

A woman aged 23, para 3, who attended a Family Planning Association clinic in January 1965, was being treated with phenobarbitone and Epanutin (phenytoin) for epilepsy, which began in 1962 during her second pregnancy. Lyndiol was prescribed and taken from February to June 1965. During this time the number of convulsions increased, and after six in rapid succession she was admitted to hospital. The Lyndiol was discontinued, because the increasing number of fits was thought to–be due to fluid retention caused by the oral contraceptive.

The patient was anxious to continue on an oral contraceptive, so Gynovlar was prescribed from August to November 1965, and changed to Ovulen after persistent amenorrhoea. From November 1965 until now she has taken Ovulen with satisfactory results. Since discontinuing Lyndiol she has had only occasional convulsions, usually associated with an infection or emotional upset. The anticonvulsant therapy has remained the same throughout.

Lyndiol (usually so free from side-effects in normal patients) together with Lyndiol 2.5, Conovid, and Conovid E belong to the group of oral contraceptives which are predominantly oestrogenic in effect. These should perhaps be avoided in conditions aggravated by fluid retention.

OUR EXPERT replies: The point that needs emphasizing is that the woman about whom the question was asked had not had a fit for 15 years. A woman who has not had any fits for 15 years is not to be regarded as having epilepsy. She should be thought of and treated as a healthy woman.

In considering patients who do have epilepsy, however, we should realize that the biochemical effects of the hormones affecting the menstrual cycle are not yet adequately known. The question of the existence of fluid retention in the body, including the brain, is still being studied, and our knowledge is still inadequate. Any observations on the effects of the different contraceptive pills, including their effects in epileptic patients, should therefore be noted, and when enough interesting data have been collected they should be published.

Book Reviews

Neurological Genetics

The Genetics of Neurological Disorders. By R. T. C. Pratt, M.A.(Oxon.), D.M., F.R.C.P., D.P.M. (Pp. 310+vii. 80s.) London: Oxford University Press. 1967.

This volume, the third in a series on medical genetics, brings together a large amount of scattered information on a wide range of disorders, from the congenital malformations to the presenile and senile dementias, and from the systemic degenerations and leucodystrophies to higher-level disorders, such as dyslexia and stammering. The muscular dystrophies are included, as are migraine and enuresis, but Down's syndrome (mongolism) is not. For genetical principles and for clinical descriptions of the commoner diseases the reader is expected to look elsewhere. Here he will find much concise information on epidemiology, familial risks, twins, parental consanguinity, modes of transmission, metabolic errors, chromosome anomalies, linkage, and biological fitness as measured by fertility.

Neurological diseases are well suited to genetical study because the diagnosis can often be made in secondary cases even when they cannot be examined. Moreover, the nervous system is particularly susceptible to disturbances of metabolism during its development, and later to degeneration of different parts. Even in the infections there may be a genetic factor, as in poliomyelitis and in the parkinsonian phase of encephalitis lethargica. In the idiopathic spinocerebellar ataxias, spinal muscular atrophies and basal ganglia disorders, in the muscular dystrophies, and in some of the epilepsies, evidence for hereditary factors is strong or conclusive, though the mode of transmission varies ; and the same clinical syndrome may include several genetical entities. The risk of epilepsy is highest—about 6%—in close relatives of patients with epilepsy of centrencephalic type beginning early in life. In motor-neurone disease transmission is dominant in some families, but obscure, possibly polygenic, in the majority. In the adult form of myasthenia gravis there is, rather surprisingly, no increase in risk among relatives. In multiple sclerosis there is need for further work by neurologists aware of the requirements of genetical investigations to unravel the environmental and genetical components.

Many inherited disorders affecting the nervous system, like the acquired disorders they may resemble clinically, are due to metabolic faults in the liver or other organs and relatively accessible to study. Much of our knowledge of neuroenzymology is derived from animals, whose brain structure differs from ours, and practically nothing is known of the nature of the enzyme defects in the dementias and systemic degenerations in man. The hopeless prognosis in these disorders and the threat to future generations would seem to justify more histochemical investigation of the human brain, including biopsy.

This book is an admirable work of reference for the medical geneticist, for the paediatrician, neurologist, or psychiatrist, and for the postgraduate student. There are 2,814 references, which in an appendix are conveniently allocated to specific topics and ranked in order of importance. The author's style is lucid and compact, with a pleasing lightness of touch. The standard of production is high. The book epitomizes the new look of modern neurology, now ready to reap the fruits of biochemical discoveries for which clinical and genetical studies have prepared the soil.

D. W. K. KAY.

Story of Charing Cross

The Two Pillars of Charing Cross. The Story of a Famous Hospital. By R. J. Minn. (Pp. 235+xiv ; illustrated. 36s.) London: Cassell. 1967.

This book gives a very readable account of the history of Charing Cross Hospital and Medical School based on the hospital records and on information obtained from recent members of the medical and administrative staff. We found no reference to Dr. William Hunter's *Historical Account of Charing Cross Hospital.*

The book is written in a popular style by a well-known writer and includes brief biographies of many distinguished persons associated with the hospital and school. The pages are enlivened by unusual incidents (as, for example, when Joseph Chamberlain was treated as a "casualty") and by some amusing stories, though we found that related on page 142 scarcely credible.

The hospital was founded by Dr. Benjamin Golding, who in 1818 opened the West London Infirmary and Dispensary in Suffolk Street. In 1821 a move was made to Villiers Street, where 12 beds were provided and students taught. In 1827 the name was changed to Charing Cross Hospital and in 1834 a new hospital of 60 beds was built and opened on the present site. The medical school was lodged in the basement and it was there that David Livingstone and T. H. Huxley were taught medicine. Dr. Golding, who had been for so many years physician to and director of the hospital, died in 1863.

The next 50 years saw great progress. Trained nurses were introduced and a nurse-training school founded, a new medical school was built in Chandos Street, and two extensions of the hospital brought the number of beds to almost 300, but, to our disappointment, we are told relatively little about the moving spirits behind these important developments.

The period before and during the first world war was a difficult time for all voluntary hospitals, but George Verity, who became chairman of the hospital council, worked hard to maintain the efficiency of the hospital, and it was he who in 1921 was the means of bringing in Philip Inman as secretary and superintendent. Inman, possessed of great administrative ability, sound judgement, keen business acumen, and a conciliatory manner, soon made his influence felt, and on the death of Verity in 1936 he was elected chairman of the hospital council. He skilfully guided hospital and school through the troublous times, smoothed the difficulties incidental to the change-over to the National Health Service, and helped to find a suitable site for the future greatly enlarged hospital. His elevation to the peerage and further activities are well known to all.

We hope that in future editions some reference may be made to Dr. Thomas Watts Eden and Sir Thomas Fairbank. On page 176 the account of the accident to Sir Herbert Waterhouse needs modification, for he recovered from the immediate effects of the injury but died suddenly a year later.

ZACHARY COPE.

International Comparisons by Graphical Presentation

Statistical Atlas on Public Health in the Federal Republic of Germany. Vol. 2. 1965 edition. In German, English, and French. (Pp. 228 ; illustrated. DM. 25.) Stuttgart and Mainz: Kohlhammer. 1966.

In addition to the report on Public Health in the Federal Republic of Germany this volume contains international comparisons of medical and vital statistics. A translation of the text is given in English and French.

The book consists of three sections: geography, demography, and medical statistics. The short first section of eight pages gives the distribution of the population density of the world by climate and country. In addition to the tables the data has been displayed in two coloured maps which also give the cities with a population of one million or more inhabitants. In the 36-page section on demography the comparisons are confined to six countries: the Federal Republic of Germany, England and Wales, France, Italy, Sweden, and the United States of America. These countries were selected partly because of the quality and comparability of their statistics.

The data have been displayed in tables and a graph has been drawn for each table. The experience of each country has been shown by a different coloured line. These coloured lines allow a ready and easy comparison to be made of the trends. The section on demography consists of five headings: population, number and changes during the past 60 years; age distribution; births and deaths; life expectancy; infant mortality and stillbirths. The United States had the largest increase in population and the largest proportion of children under 15 years of age, and the smallest proportion of the population aged 65 years and over and the smallest proportion of the population at working ages (59.6%). The Federal Republic of Germany had the largest proportion of persons at working ages—67.1%—and had the second largest increase in population. In the United States the increase was due to an excess of births over deaths, while in the Federal Republic of Germany about half the increase was due to refugees from East Germany. The expectation of life at birth was highest in Sweden, 71.6 years for males and 75.4 years for females, and the lowest expectation of life was in Italy, 65.8 years for males and 70.0 years for females. Sweden had the lowest infant mortality during the past 60 years and Italy the largest during the past 40 years. In recent years Sweden had the lowest stillbirth rate and Italy the largest. The low stillbirth rate in the Federal Republic of Germany is in contrast with the relatively high infant mortality.

The 152-page section on medical and vital statistics starts by considering the incidence of infectious diseases and the incidence of quarantinable diseases throughout the world. Maps are included to illustrate the distribution of leprosy, malaria, plague, relapsing fever, cholera, yellow fever, and smallpox. The remainder of this section gives the crude death rates for each sex and the stardardized death rates for the principal causes of death in the six countries. Some interesting differences occur between the trends of the different countries. For example, in 1961 the standardized mortality rate for cirrhosis of the liver among French males was 13 times that of the males in England and Wales, and in 1962 the rate for senility in the Federal Republic of Germany was 38 times the rate in the United States. The final chapter gives the number of different kinds of hospitals in the six countries, the number of beds, the number of doctors in each specialty, and the number of medical and auxiliary personnel.

Epidemiologists and medical and vital statisticians interested in the geographical distribution of disease and in the comparability of international mortality statistics will find material in this book that will interest and give rise to speculation. Even for these six countries, chosen because their statistics were thought to be sound, it is evident that any conclusions drawn from international comparisons must be subject to qualifications.

W. J. MARTIN.

Cancer: Diagnosis and Treatment

Progress in Clinical Cancer. Vol. 2. Edited by Irving M. Ariel, M.D., F.A.C.S. (Pp. 375+xvi; illustrated. £5 11s.) London: William Heinemann. 1966.

In the total effort to gain the mastery over cancer the clinician has a vital contribution to make. It is exemplified by the contents of this book, which also demonstrates the fact that progress is being achieved in certain major directions. The editor has grouped the material provided by 49 authors into six sections dealing with general considerations: diagnosis, surgery, irradiation, chemotherapy, and specific neoplasms. Selected references are given and a detailed index provided.

Three important subjects for the clinician are dealt with in the opening section. Under the title "The Molecular Biology of Cancer" attention is focused on the cancer cell, highlighting the genetic system, including D.N.A., three types of R.N.A., amino-acids, proteins, and enzymes. Suggestions emerge concerning possible therapeutic approaches, including chemotherapy, when substances might be found with specific inhibitory action on various parts of the genetic apparatus. Such a discussion points the way to rational cancer chemotherapy. Immunity is discussed in a short chapter where the theoretical excitement of its possibilities is sensed without perhaps present practical foundations; in fact the author advances as "perhaps the most cogent reasons for optimism about the future of immunity in cancer is the possibility that a viral etiology of some malignant neoplasms may be established." But in the case of human cancer this has not yet been done. Will Burkitt's lymphoma be the first? The third subject dealt with in the opening section is blood flow to tumours. This has important practical implications for the clinician using regional perfusion and infusion, and the radiotherapist applying external irradiation or employing radioactive isotope therapy.

Contemplation of the end-results of cancer treatment today cannot engender any complacency with cancer diagnosis, for in so many patients when the tumour is seen or felt dissemination has already occurred. The section devoted to diagnosis is therefore welcomed, for here is the experience of the cancer detection centre at the University of Minnesota established in 1948, which merits careful study and emulation. The value of this work is apparent. The author states, "Our data indicate that routine annual examination by methods in current use will permit detection of the majority of the commonly occurring cancers while relatively early in their course, confined to the organ of origin, and productive of relatively few or no symptoms."

In the section devoted to surgical treatment the editor has chosen six subjects. Rectal cancer in the female creates practical problems because of the close proximity of the vagina, uterus, and ovaries, leading to residual cancer in the pelvis after the Miles operation. An anatomical study is described of the rectal lymphatics and the radical operation which was evolved for rectal cancers 2 to 4 in. (5–10 cm.) above the anal verge.

Other subjects include partial hepatectomy, exarticulation of the innominate bone, immediate ambulation following amputation, cordotomy, and adenomammectomy. The reviewer cannot entirely approve the latter chapter concerning a "technical procedure for biopsy, fibrocystic disease, plastic repair, and breast hypertrophy." There are so many aspects of breast cancer which should be discussed, so why introduce other subjects into a cancer book? Is a cancer still "suspicious" with peau d'orange present? And in this stage a drill biopsy is surely better than "a wide elliptical excisional biopsy."

Important aspects of radiotherapy are considered in five chapters: split-dose radiotherapy; preoperative irradiation for bronchogenic carcinoma (where evidence of its value is given in superior sulcus syndrome carcinomas); hyperbaric oxygen as an adjuvant to radiotherapy; treatment of cancerous effusions; and radioactive microspheres in advanced cancer. Only hyperbaric oxygen as an adjuvant to systemic chemotherapy represents the chemotherapy section; the author believes the results have been improved to a small degree. The remainder of the book is devoted to specific neoplasms, showing the progress made in diagnosis and treatment. The editor and his large team of collaborators have made a valuable contribution to cancer literature; this book repays study, and it is pleasing to read the tribute to Owen H. Wangensteen, to whom the book is dedicated.

RONALD W. RAVEN.

Scoliosis

Scoliosis. By Robert Roaf. (Pp. 147+xi; illustrated. 37s. 6d.) Edinburgh: E. & S. Livingstone. 1966.

The first half of this monograph is concerned with an analysis of scoliosis under the headings of anatomy and mechanics, followed by a discussion on the author's concept of the basic causes of the progressive deformity. This part of the book is often challenging and controversial and a considerable stimulus to thought. The current conventional ideas on conservative and operative treatment are reviewed and the serious shortcomings noted. The author's attempts to reverse the forces causing an increasing lateral deformity by epiphysiodesis of the vertebral bodies on the convex side in children are described. When considering treatment Professor Roaf emphasizes the work of Chaklin in Moscow on partial vertebral body resection in reducing lumbar scoliosis and lumbar lordosis, which he considers an important cause of progressive deformity.

This book is no pedestrian reprinting of accepted textbook ideas about the aetiology and treatment of scoliosis, but a statement of personal individualistic views on a subject that has interested Professor Roaf for a number of years. I can thoroughly recommend this monograph to all surgeons and physicians concerned with scoliosis—both to read now and to have at hand for future reference.

C. W. MANNING.

Using a Health Visitor

The Principles of Health Visiting. Edited by P. J. Cunningham, B.A., S.R.N., S.C.M., H.V.Cert. (Pp. 262. 25s.) London: Faber & Faber. 1967.

"In modern health visiting the whole spectrum of family experience is the province of the health visitor," writes Dr. J. G. Howells in one of the two excellent chapters he contributes to this book. "The health visitor and the general practitioner see illness in the community as it is."

The general practitioner certainly does, but the health visitor under the present tripartite system doesn't get the chance. *Family Needs and the Social Services* (P.E.P., 1961),[1] to which two of the health-visitor contributors refer, brought out this point. Only 55% of all the families surveyed—and they included only families with one or more children under 5—had ever used the health visitor, compared with the 99% who had used the general practitioner. A much smaller percentage of the elderly and of families with grown up children and teenagers can have used her, yet they also have social problems which the health visitor might help solve. Dr. Lumsden Walker in another chapter on "The Family" delineates some of them. It is left to Miss Greta Flack, who had the unusual advantage of working with both an enlightened medical officer of health and enlightened general practitioners, to show how, by attaching her to a group practice, the health visitor can come into her own. It took a little time for everyone to realize that the basic essential—a room to work in—could be provided by the simple expedient of using one of the partner's consulting-rooms when he wasn't there. When she really did become part of the practice the advantages stood out. She increased her scope of work in all spheres, but especially in mental health, care of the aged, and social difficulties. "You really know us," said the patients.

The book is uneven. Some of the chapters are textbook descriptions of symptoms and procedures rather than accounts of how to apply principles to modern conditions. Too many administrators contribute standard chapters which might have been appropriate before the last war. For example, under scarlet fever, "if the patient is nursed at home isolation and concurrent disinfection should be rigidly enforced"—but no general practitioner describes co-operation with health visitors. Dr. Harry Levitt, in an admirable survey of the situation, refers to papers from all parts of the country about successful attachments of health visitors (as well as district nurses and midwives) to practices, but none of the authors is included.

This is a commendable first shot at defining the principles of health visiting, but in the second edition the editor should impose her stamp upon the whole. It may be true, as she says in the preface, that no one person can write about the complexities of the health visitor's work, but a better selected and more disciplined group of contributors could produce a unified book about them.

ANDREW SMITH.

REFERENCE

[1] Published by George Allen and Unwin, for Political and Economic Planning, London, 1961.

Books Received

Review is not precluded by notice here of books recently received.

Psychology in Relation to Medicine. 2nd edition. By R. M. Mowbray, M.A., Ph.D., F.B.Ps.S., F.A.Ps.S., and T. Ferguson Rodger, C.B.E., B.Sc., M.B., F.R.C.P.(Ed. and Glasg.), F.B.Ps.S., D.P.M. (Pp. 412+vii; illustrated. 36s.) Edinburgh and London: E. & S. Livingstone. 1967.

The Depth of Cold. By A. R. Meetham, D.Sc. (Pp. 173; illustrated. 25s.) London: English Universities Press. 1967.

Annual Review of Medicine. Vol. 18. Edited by Arthur C. de Graff. (Pp. 559. $9.00.) Palo Alto, California: Annual Reviews. 1967.

Ficatul Si Hormonii. By St.-M. Milcu, L. Vaisler, and Emma Costiner. (Pp. 371. Lei 33.) Bucharest: Editura Academiei Republicii Socialiste Romania. 1967.

Deadly Harvest. A Guide to Common Poisonous Plants. By John M. Kingsbury. (Pp. 128; illustrated. 21s.) London: George Allen and Unwin. 1967.

Milk Production in Developing Countries. By R. O. Whyte. (Pp. 240. 50s.) London: Faber and Faber. 1967.

First Aid in the Factory. 3rd edition. By Lord Taylor, B.Sc., M.D., F.R.C.P. (Pp. 150+ix; illustrated. 12s. 6d.) London: Longmans, Green. 1967.

The Chemistry of the Gonadotrophins. By Wilfrid R. Butt, Ph.D., F.R.I.C. (Pp. 116+xi. $7.50.) Springfield, Illinois: Charles C. Thomas. 1967.

Advances in Anesthesiology: Muscle Relaxants. Edited by Lester C. Mark, M.D., and E. M. Papper, M.D. (Pp. 118+viii; illustrated. 54s.) New York: Harper & Row. 1967.

Internationaler Kongress für Geburtshilfe und Gynäkologie. Edited by Prof. Helmut Kraatz. (Pp. 894+76 pages illustrations. No price given.) Berlin: Akademie. 1966.

Chirurgie de l'Intestin Grêle et du Mésentère. By Marcel Roux. (Pp. 451+x; illustrated. 95F.) Paris: Masson. 1967.

Cancer of the Naso-pharynx. Edited by C. S. Muir and K. Shanmugaratnam. (Pp. 259; illustrated. Dan.kr.105.) Copenhagen: Munksgaard.

Les États de Mal Épileptiques. Edited by H. Gastaut, J. Roger, and H. Lob. (Pp. 383; illustrated. 90F.) Paris: Masson. 1967.

Actualités Hématologiques. Edited by Jean Bernard. (Pp. 160; illustrated. 30F.) Paris: Masson. 1967.

Actualités en Transfusion Sanguine. Edited by R. Waitz. (Pp. 183; illustrated. 46F.) Paris: Masson. 1967.

Actualités Neurophysiologiques. 7th series. Edited by A.-M. Monnier. (Pp. 327+vii; illustrated. 110F.) Paris: Masson. 1967.

Specific Tumor Antigens. Edited by R. J. C. Harris. (Pp. 366; illustrated. Dan.kr.126.) Copenhagen: Munksgaard. 1967.

Regional Cerebral Blood Flow. The Intra-Arterial Injection Method. By Kai Høedt-Rasmussen. (Pp. 79; illustrated. Dan.kr.25.) Copenhagen: Munksgaard. 1967.

Kurzgefasstes Lehrbuch der Physiologie. Edited by Prof. Wolf D. Keidel. (Pp. 502+xii; illustrated. DM.39.80.) Stuttgart: Georg Thieme. 1967.

Diabetes Mellitus. Theorie-Klinik-Therapie. Edited by Prof. G. Mohnike. (Pp. 405; illustrated. £2 19s. 9d.) Berlin: Volk und Gesundheit. 1967.

A Guide to Dissection in Gross Anatomy. 2nd edition. By Prof. Russell T. Woodburne. (Pp. 150+iv; illustrated. 28s.) London: Oxford University Press. 1967.

Club-foot. By Alfred T. Fripp, M.B., B.Ch. Oxon., F.R.C.S., and Norman E. Shaw, Ch.M. Sheffield, F.R.C.S. (Pp. 122+viii; illustrated. 35s.) Edinburgh and London: E. & S. Livingstone. 1967.

First International Conference on Vaccines Against Viral and Rickettsial Diseases of Man. Pan American Health Organization Scientific Publication No. 147. (Pp. 695+xxviii; illustrated. $7.00.) Washington: Pan American Health Organization. 1967.

Basic Medical Virology. Edited by James E. Prier, Ph.D. (Pp. 715+ix; illustrated. £5 16s.) Edinburgh and London: E. & S. Livingstone. 1967.

Autoimmunity. Clinical and Experimental. By J. R. Anderson, W. W. Buchanan, and R. B. Goudie. (Pp. 485+xv; illustrated. $19.50.) Springfield, Illinois: Charles C. Thomas. 1967.

The Neurological Examination. 3rd edition. By Russell N. DeJong, M.D. (Pp. 1151+xv; illustrated. £11 16s.) Ned York: Harper & Row. 1967.

Dictionary of Symptoms. By Joan Gomez, M.B., B.S.(Lond.) (Pp. 383+xxiv; illustrated. 45s.) Arundel, Sussex: Centaur Press. 1967.

The Control of Infections in Hospitals. With Special Reference to a Survey in Ontario. By W. Harding le Riche, M.D., M.P.H., Carolee E. Balcom, R.N., B.S., and Gerald van Belle, M.A. (Pp. 341+xviii. 72s.) Toronto: University Press. London: Oxford University Press. 1967.

Mastocytosis and the Mast Cell. By Felix Sagher, M.D. and Zvi Even-Paz, M.B., Ch.B. (Pp. 427+xiv; illustrated. sFr./DM.76.) Basel: S. Karger. 1967.

Cardiac Stimulant Substances. By Roland H. Thorp and Leonard B. Cobbin. (Pp. 288+x; illustrated. 96s.) New York and London; Academic Press. 1967.

Drug Dependence. By Antony J. Wood, M.B., B.S., D.P.H. (Pp. 26. 2s. 6d) Obtainable from Health Department, Tower Hill, Bristol 2.

Studies in Anaesthetics. Including Intravenous Dental Anaesthesia. By J. G. Bourne, M.A., M.D.Cantab., F.F.A.R.C.S. (Pp. 166+vi; illustrated. 20s.) London: Lloyd-Luke. 1967.

Practical Management of the Acute Abdomen. By Nigel C. Keddie, M.A., B.M., F.R.C.S. (Pp. 120. 12s. 6d.) London: Lloyd-Luke. 1967.

Cunningham's Manual of Practical Anatomy. Vol. 3. Head and Neck and Brain. 13th edition. Revised by G. J. Romanes, B.A., Ph.D., M.B., Ch.B., F.R.C.S.Ed., F.R.S.E., (Pp. 310+vii; illustrated. 40s. Paper 30s.) London: Oxford University Press. 1967.

Theory of Psychoanalytic Therapy. By Benjamin Wolstein, Ph.D. (Pp. 210+ix. $8.00.) New York and London: Grune & Stratton. 1967.

The Harvey Lectures. Series 61. Delivered under the auspices of The Harvey Society of New York. 1965–1966. (Pp. 269+xiv; illustrated. 76s.) New York and London: Academic Press. 1967.

Methods in Cancer Research. Vol. 1. Edited by Harris Busch. (Pp. 612+xvi; illustrated. £11 4s.) New York and London: Academic Press. 1967.

Middle Articles

IS THERE AN ALTERNATIVE?

The possibility of a large extension of private insurance schemes for health in Britain has often been raised. What schemes are already in existence, in Britain and elsewhere? What problems would be involved in applying them more widely? What are their advantages and disadvantages? In his article Mr. Arthur Seldon discusses the answers to these and some other questions.

Prospects for Private Health Insurance

ARTHUR SELDON*

Brit. med. J., 1967, 3, 166–168

Insurance, private and voluntary, is increasingly discussed in Britain as an indispensable method of paying for health services at rising standards because it would introduce additional finances not otherwise available for higher payments to doctors, nurses, and administrators; larger expenditure on treatment, training, and research; and increased outlay on equipment, buildings, and land.

Private insurance could supplement the three other methods of financing medical care—namely, fees, taxation, and charges. Firstly, fees for some services will be increasingly practicable for more people as incomes rise. Secondly, the belief that taxation, with the compulsory national insurance contributions that are more a tax than a premium, will yield the required growing sums is fading.[1] To satisfy Professor Henry Miller's eloquently argued proposal[2] that £500 million more would have to be found almost immediately from taxation to give medicine in Britain "the relative priority" it enjoys in the United States—that is, to raise expenditure on the N.H.S. from around £1,500 million to £2,000 million—the Government would have to raise tax revenue by a much larger amount, perhaps by £1,500 million, since it could not allocate £500 million more to the N.H.S. and nothing more to State education,[3] school welfare services, housing, pensions, family allowances, unemployment, disability and sickness benefits, other social benefits, and neglected public services such as the police. Even if national income grew by 3% a year, which is not yet certain, tax revenue would not rise enough to provide State welfare for the increasing number of dependants, children, and old people, or to remove poverty. Tax *rates* would therefore have to be raised, a policy which diminishing numbers in all parties now think is either economically desirable or politically acceptable.

Politicians in all parties are discussing realistic charges for State health services: not only for medicines and appliances but also for consultation and treatment. Mr. Houghton and Mr. Walden have been most explicit in recent weeks. If charges drew substantial sums of additional revenue into the N.H.S., they might enable it to provide the rising standards of services expected by people with growing incomes, and the demand for private medicine might run down. But the more charges are designed to raise revenue and not only deter over-use, the more they would reduce the gap between the cost of State and independent medical care, and the more they might accelerate the growing demand for private services. (If the choice is between a free N.H.S. and paying the full cost of private medical care, only a few will pay; if the choice is between charges for the N.H.S. and paying for private medical care, more will pay.) Which of these two effects would be the stronger is impossible to forejudge. The economic dilemma of charges is that if they are low they will not draw in much revenue, and the N.H.S. will not improve very much or continue to deteriorate; and if they are at or near the market cost they may encourage private practice and insurance.

Whether charges are introduced or not, and whether they are at nominal or market levels, private health insurance will be able to draw on substantial funds that would not otherwise be attracted to medical care by fees, taxes or charges. Hence the case for examining the scope for private insurance.

Principles of a Practicable Scheme

Private insurance for the costs of consultation, treatment and/or income in sickness is provided for about two million people by the British United Provident Association, the Hospital Service Plan, the Western Provident Association, the Bristol Contributory Welfare Association, Independent Medical Services and several smaller schemes. About four million families (perhaps 15 million people) are insured for supplements to State health services by the Hospital Saving Association and similar organizations that could expand to cover private medicine.

---

* Editorial Director, Institute of Economic Affairs (I.E.A.), London S.W.1.

[1] The reasons, empirical, analytical, and institutional, are indicated in the author's "Which Way to Welfare?" *Lloyds Bank Review*, October 1966. Briefly: expenditure on medical care has been rising faster than income in the U.S.A. and elsewhere but not in Britain; citizens are not prepared to pay as much in taxes for services shared with others as they demand for themselves; taxes are regarded as deductions from income, not as payment for services. The academic analysis is elaborated in a growing literature on public finance and the economics of medical care by Professor J. M. Buchanan, *The Inconsistencies of the National Health Service*, Occasional Paper 7, I.E.A., 1965; Professors John and Sylvia Jewkes, *Value for Money in Medicine*, 1963, Blackwell; Professor D. S. Lees, *Health Through Choice*, Hobart Paper 14, I.E.A., 1961; Professor R. A. Musgrave, *The Theory of Public Finance*, 1959; a doctoral dissertation at the University of Virginia by Mark Pauly; and others. The argument has also been spreading to the politicians: Messrs. Desmond Donnelly (*Hansard*, 9 June 1967, column 1468), Douglas Houghton (*Paying for the Social Services*, Occasional Paper 16, I.E.A., 1967), and Brian Walden (*Sunday Times*, 25 June 1967).

[2] "In Fitness and in Health: A Doctor's View of Medicine in Britain," *Encounter*, April 1967.

[3] The President of the Association of Education Committees said at its conference on 21 June 1967 that state education had to have £550 m. a year for essential improvements.

[4] Arthur Seldon, *Pensions in a Free Society*, I.E.A., 1957.

[5] Discussed in *Paying for the Social Services*.

[6] Mr. Patrick Gordon Walker, Minister Without Portfolio, speaking to a seminar of the University of Cambridge Board of Extra Mural Studies, 18 June 1967.

And a small number are insured by a dozen or so insurance offices for medical costs or income during disability. In all private insurers assemble perhaps £15 million a year in subscriptions and premiums. However much the N.H.S. may be able to supplement its £1,500 million by charges, there would seem substantial scope for tapping the £15,000 million spent on everyday or household consumption.

The experience of private insurance in Australasia, North America, Europe, and even Africa could also indicate lessons and warnings—provided differences in national economic and social conditions are allowed for in adapting methods and machinery. Australia seems to offer examples of insurance schemes with attractive characteristics; schemes adopted in Britain might incorporate some features of Australian schemes and adapt features of schemes in the U.S.A., Canada, Norway, France, Ireland and other countries. At this stage it would seem possible to discern several generally desirable characteristics.

Market Price

All services, State and private, should work towards charging the full market price to cover current and capital costs. It is here—in charging less than market price—that the two main weaknesses, under-supply and over-demand, originate. For a time it may be necessary for the State, centrally or locally, to provide capital at less than market rates of interest. Ultimately, prices or charges should be sufficient to cover capital costs at market rates of interest.

State Subsidy to Consumer

State "subsidies," to replace the insurable parts of the free N.H.S., should be paid not to the suppliers of health services but direct to consumers in the form of cash or vouchers with which to insure for State or private services. There is no problem of the "deprived" who cannot pay or the irresponsible who will not pay. Other health services would continue to be provided by public authority.

Payment By Patient

Payment to the doctor or hospital for individual units of service should be made, so far as is administratively possible, and except in emergency, by the patient—as it has been in France, Sweden, and Norway, not by the insurer—as in Denmark, Germany, and Switzerland. Machinery for rapid reimbursement, or better still prepayment, of the patient would be desirable.

Patient's Fraction ("Deductible")

The patient should bear part of the cost of each bill—a larger proportion of small bills, a smaller proportion of large bills. In Australia the patient's fraction has been at least 10 per cent. In France it has been 20 per cent. (recently proposed at 30 per cent.) and in Sweden 25 per cent. The "deprived" would pay less or nothing. An income coding to yield a reverse tax—i.e., an automatic supplement to low incomes, discussed in principle by the American economist, Henry C. Simons, advocated in Britain for at least 10 years,[4] persuasively urged by Mr. Houghton recently,[5] and now examined by the Government,[6] would identify people with low incomes, mostly pensioners but also heads of larger families and others, to whom the State could return the patient's fraction as expeditiously as private insurers the amount covered by insurance.

Specialist or Composite Insurers

There could be specialist or composite insurers for (*a*) costs of general-practitioner consultations, medicines, and treatment; (*b*) specialist consultation; (*c*) hospital treatment; and (*d*) income during disability.

State as "Long-Stop"

Private insurers would cover a growing range of risks (in Switzerland poliomyelitis has been added), but some claims for long-term treatment for physical or mental ailments might have to be reinsured with the State as "long-stop."

Competition

Insurers should be both mutual and commercial, profit-making and non-profit-making, State (but not subsidized) or private, provided they satisfy State standards. The aim should be to facilitate competition so that the schemes with lowest costs and highest consumer preference can be discovered.

Experience Rating

Insurance premiums would probably emerge as a mixture of "community rating" (average for varying risks) and "experience rating" (refined to the risks of individual groups) according to the size of the insurers, the degree of competition, and the form of State subsidy as producer or consumer subvention. "Community rating" in a private scheme may be essential or desirable in a small or growing country, but in operating a "private welfare state" the organization may be vulnerable to State influence or control. The danger has been avoided in Australia but it might not be in Britain.

Publicity

Insurers should be encouraged to advertise their schemes by any means allowed under law. If health insurance is desirable there should be no inhibition in publicizing the premiums and benefits of individual schemes.

Compulsory Insurance?

Since 95% of people in Britain have never experienced voluntary insurance for private medical care it is arguable that private insurance should be compulsory for an initial period of five to seven years. Thereafter it could be voluntary, as in Denmark and Australia.

Advantages

The advantages and disadvantages of a scheme of private insurance as outlined, particularly the voucher component, could not be learned until it is established. Results observed in other countries might not be reproduced in the sometimes dissimilar British setting. The general assumptions made by economists about human motives, administrative organization, and the working of markets suggest a number of advantages:

Private insurance would go as far as is feasible to take medicine out of politics. The State would continue to provide environmental paramedical services; it would require preventive consultation and treatment; it might provide personal services—for fees or charges—in competition with private services, as it now does in transport and fuel; and it would finance consumers by vouchers, reimbursement of "patients' fractions," and the full costs of long-term treatment. But the doctor and the hospital would be paid by the patient for the mass of medical care.

Patients and doctors would know the full costs of the services they bought and sold. The tendency of patients to over-use free or partly free medical services and of doctors to over-prescribe for importunate patients would be checked.

The maximum practicable choice of doctor by patient and patient by doctor would be facilitated. The doctor–patient relationship would become more flexible. Doctors could vary charges according to individual and local circumstances. Less satisfactory doctors would go out of practice. More troublesome patients would pay more.

Private insurance financing would strengthen the independence of the general practitioner. Technical advance will continue to make medicine more "scientific," but social advance will stimulate the expectation of personal service, attention, consideration, choice, timing, convenience, and comfort. And these are largely the province of the general practitioner.

Doctors and patients could make any of a wide variety of arrangements they prefer. Doctors could organize themselves into loose federal arrangements for payment by capitation, case, period (salary), or unit of service.

The transformation of every patient, irrespective of original income, except the mentally or otherwise incapable, from a "beneficiary" into a buyer armed with purchasing power would remove the social divisiveness of a system in which—as now in Britain—the few pay for private services and the many receive a free State service.

Choice, competition, and variety would stimulate voluntary addition of purchasing power to the voucher. The underlying technical standard of medical care would rise as salaries and fees rose, equipment and buildings were improved, and new health centres and hospitals were built; but there could be as many standards of personal service as people were prepared to pay for.

In time independent training and research institutions could be established to diminish the risk of error resulting from the over-centralization of Government forecasting, recommendation, and decision. A repetition of the 1957 Willink error would be less likely.

Disadvantages

The main disadvantages or risks of private insurance would appear to be the following.

Administrative costs would probably be higher—8 per cent. or more—than in a centralized State system—5 per cent. or less. Doctors and hospitals would be paid by hundreds or thousands of patients instead of by one State department. Servicing costs are necessarily higher for a personal than for a standardized service. Moreover, the uncertainty of doctors' income would increase, but this is the obverse of the coin of independence.

The bulk of the patient's payment would be by annual premium out of income supplemented by State cash or voucher unrelated to a specific unit of medical service at the time it is received and experienced. Indirect payment at second hand is a second best to direct payment at first hand as a means of inducing patients to think twice before using a doctor. Indirect payment by annual premium divorced from individual bills also weakens the discipline on medical fees and medicine prices. Complaints of increasing costs outrunning insurance benefits are common or frequent in the U.S.A. and elsewhere. Doctors can alienate the goodwill of the public on whom their livelihood depends if they appear to act as an organized trade association. The remedy is commonly a State schedule of fees and costs; but it may tend to be inflexible and to invite political influence. A better remedy would be competitive pricing by individual doctors and hospitals, perhaps required by a general law against collusive restrictive practices, and possibly larger "deductibles" for smaller bills so that patients would be more sensitive to increases in fees.

Selling costs would be higher than in a uniform State system; but competition would encourage improvement. Voluntary insurance in Britain has low selling costs but also a slow rate of expansion. Field studies conducted for the Institute of Economic Affairs and B.U.P.A. suggest that far more than two million would have become subscribers by now if private insurance had been publicized more thoroughly.

Initiation of General Private Health Insurance

Health insurance may spread rather faster in the next few years now that there is a little more marketing effort and competition between B.U.P.A. and its smaller competitors. But even if the annual rate of expansion were 20 per cent, it would be 1971 before the number of subscribers rose to 4 million—still only 8 per cent. of the population. Health insurance could be sold by "mutual" and commercial insurance underwriters and brokers. Private beds could be made available in State hospitals, and new private hospitals and nursing homes could be built with endowed and/or commercial capital. The blockage is not so much in supply as in demand. There is no shortage of men or women to train as doctors or nurses, or of bricks, concrete, steel, wood, or glass to erect buildings and equip them with wards, kitchens, and operating theatres. Supply would appear as if from nowhere if the demand were created.

The demand could be stimulated by income tax rebate on insurance premiums or fees—as in Australia and Ireland—or by notional rebates to everyone, income-tax payers or not. But in Britain these methods would probably be too slow, and a more fundamental, dramatic method is required. State payments direct to the consumer, in cash or preferably in vouchers, are the prerequisites for a rapid growth in private health insurance to pay for competing State or private services.

The voucher principle is simple in essence.

Instead of a free State service everyone would have a coupon with which to insure with the medical insurer and service of his choice. If the State hospital service costs £20 per head a year, the "hospital voucher" could be, say, £15 per head to insure for most forms of treatment, leaving £5 with the State to cover long-stay, abnormal maternity, mental and geriatric treatment. If general practitioners cost £3 a head and prescriptions £3 10s., the "family doctor voucher" could be £6 10s. Dental and ophthalmology service could be paid in cash, with remission by income code (although B.U.P.A. insures orthodontic treatment). Local health services, which may cost £4 a head, would continue to be financed out of taxes, unless they could be provided more efficiently by private suppliers.

Vouchers could be varied with income by being taxed: they could vary with regional hospital costs; they could differ for children, adults, and the over 70s.

If people are prepared to pay more for better food, clothing, furnishings, motoring, holidays, it should be possible to enable them to pay more for better medical care. In 1965 23% of a sample of 1,660 people aged 16 to 65 said they would accept a £5 voucher per head of the family and add £5 to pay for private health insurance costing £10 a head; in all they would add £45.4 million. In time it is reasonable to suppose that experience, competition, and rising incomes would raise the amounts added to the voucher out of current expenditure on everyday household consumption.

SELF-HELP IN THE HOSPITALS

St. Christopher's Hospice

[FROM A SPECIAL CORRESPONDENT]

St. Christopher's Hospice dates its foundation from the first gift—left in 1948 by a young Pole who died of cancer in a ward of 50 patients. He discussed with the almoner the possibility of establishing a small institution for patients with problems such as his, and when he died he gave £500 to provide a window if such a home was built. Since then almost half a million pounds has been raised for St. Christopher's Building Fund Appeal. The first stage of the hospice is nearing completion; it will have received its first patient by the time this article appears. The young Pole's window round the front entrance stands out among the many parts of the building that are named for particular gifts.

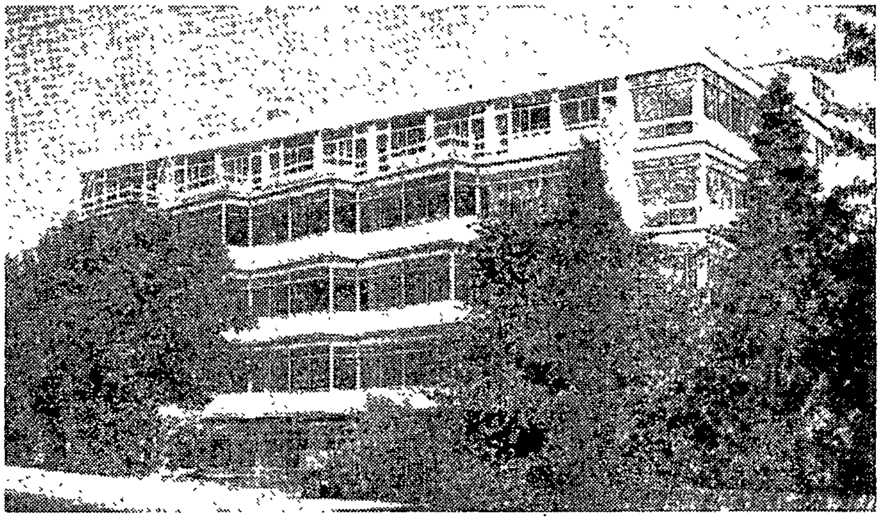
Aims of the Hospice

St. Christopher's Hospice is planned, as its Medical Director, Dr. Cicely Saunders, once said, "as something between a hospital and a home—combining the skills of the one with the warmth and welcome that belong to the other." It will care for people in pain and distress who cannot be cared for satisfactorily at home. Many of them will be the terminally ill, with a prognosis of no more than three months, who will probably spend the last weeks of their life at the hospice; others will be admitted with long-term illness and chronic pain and are likely to stay much longer. Both types of patients may be enabled to return to their homes. An outpatient clinic and an experimental domiciliary service will become part of the work of the hospice.

The basic aim of the hospice is to give these patients a real chance to live their lives, short or long, as fully and as peacefully as possible. Moreover, the hospice also has a broader aim—it wants to stimulate the growth of skill and interest in the care of these patients. Research and teaching will therefore be one of the prime functions of the hospice from the beginning. It will, for example, carry out further work into the relief of pain and distress, believing that this must include the understanding and treatment of mental as well as physical pain and also of all the other discomforts of such illness.

St. Christopher's is a religious foundation of an unusually broad character and it is difficult for such a foundation to retain its essential character as part of a public service; that is why it will remain an independent body. This independence will also help the hospice to remain freely adaptable to new ideas and to pioneer effectively in this new field. From the beginning this has been discussed with the Ministry of Health and the regional hospital board, and contractual arrangements have been made with the latter, so that for most of the patients care will be free.

Late in 1962 a suitable site for building the hospice was found in the London Borough of Bromley. The committee did not know the exact cost of the project at this stage—only that it would amount to some hundreds of thousands of pounds and that this could be raised only from private sources, both from the large charitable foundations and from individual donors. In fact financial help had been promised a year before the site was found, the City Parochial Foundation having promised a grant of £50,000 when developments assured the establishment of the hospice. The first grant actually paid to the hospice came from the King Edward's Hospital Fund for London, which gave £27,000 and the expenses involved in purchasing the site in 1963.



St. Christopher's Hospice.

In March 1964 the St. Christopher's Hospice Building Fund Appeal for the first stage of building was launched with "The Week's Good Cause" appeal on the B.B.C. Home Service. Shortly afterwards the Drapers' Company promised £50,000 for the old people's wing, and without this grant the latter could not have been included in the first stage.

In December 1964 the Nuffield Foundation granted £60,000 for a ward and the Sembal Trust £22,680 for a section of a ward. A legacy from the U.S.A. enabled a second site near by also to be acquired. To date over £400,000 has been received for the hospice, and only about £70,000 is still required to complete and equip the first stage of the building.

A Local Appeal

In 1967 the London Borough of Bromley set up a local appeal committee to raise money locally. The appeal was officially launched by the Mayor in February 1967 at a public meeting in the uncompleted building. Bromley people have organized their fund-raising functions to contribute to this appeal, while, in addition, those interested are beginning to form the nucleus of a volunteer department, which will help to make the patients feel part of the local community. Some of the several hundreds who already comprise the Friends of St. Christopher's Hospice will be joining them in what it is hoped will develop as an integral part of the work of the hospice.

The first stage of the building includes: ward accommodation for 54 patients, together with very ample day space and facilities, the Drapers' Wing for 16 elderly people, some staff rooms, and the outpatients' clinic. The ward block will finally accommodate 75 patients; the regional hospital board will have contractual arrangements for 40 of the original 54 beds, and these will therefore be free to patients. Money will be raised in various ways for the other patients and residents.

The hospice illustrates very forcibly the important and valuable part that voluntary institutions can still play in a country whose medical needs are almost entirely met by a State service. The practical realization of the vision for St. Christopher's demonstrates also how by hard work and dedication very large voluntary projects indeed can start from the smallest beginnings and come successfully to fruition even in these supposedly complacent days of the Welfare State.

Radio Communication and the Emergency Department

M. H. HALL,* M.R.C.S., L.R.C.P.; R. S. GARDEN,† M.B., M.CH.ORTH., F.R.C.S.ED.

Brit. med. J., 1967, 3, 170–171

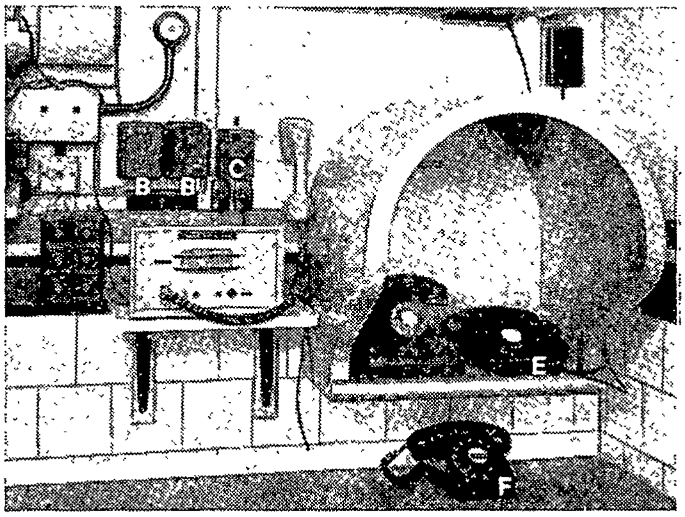
Several years ago it was decided to investigate the use of radio communication between the Emergency Department and the ambulances serving the Preston Royal Infirmary (Garden, 1962). The telephone line already existing between Lancashire County Council ambulance headquarters and the hospital was used to complete the radio link, but technical problems arising from the length of the land lines caused some delay in the early stages. Improvements made by the radio department staff of the Lancashire County Constabulary, however, enabled the ambulance headquarters operator to monitor the signal and switch from transmit to receive as required. At the hospital the telephone line terminating in the ambulance officers' room was extended into the Emergency and Accident Department (Fig. E). An ordinary bell-push beside the telephone in the ambulance officers' room was installed to ring a warning bell in the emergency department when an ambulance attendant wished to communicate by radio with the medical officer on duty during the day (Fig. A). At other times an indicator relay worked by the telephone circuit was used as a warning device (Fig. B).

This experimental arrangement proved to be of immediate value in alerting the hospital staff of the impending arrival of seriously ill or injured patients, and in maintaining contact between the hospital and the flying squad dealing with motorists or workmen trapped as a result of road or industrial accidents.

The Emergency and Accident Department is extremely cramped; over 30,000 new patients are treated annually within a total floor area of only 956 square feet. During a large part of the day there is little unused space, but the information that a seriously injured patient is on his way to hospital allows time for room to be made available and resuscitation equipment to be set out. If several patients are expected, confusion and delay in treatment are avoided by calling extra help to the department before the patients reach the hospital.

It soon became apparent that if advantage was to be taken of this early warning it was essential to set out full resuscitation equipment before each patient arrived. This required the design of new types of equipment and the development of fresh methods of instrument storage to overcome the inherent difficulties under which the department is required to work.

Because the results of this initial experiment were so successful, radio-link facilities were extended to the Borough ambulance vehicles, using a remote-control unit installed in the Emergency Department (Fig. D). This unit was connected to the tie-line between the hospital and the Borough ambulance headquarters (Fig. F), the telephones being disconnected from the tie-line by a switch (Fig. C) when the radio link was in operation. This arrangement proved easier to operate than the County system, because the send-receive switch was incorporated in the handset of the control unit. Warning devices similar to those in use for the County system were installed for use during the appropriate hours (Fig. A^1, B^1).



The radio-link installation. A, County, and A^1, Borough daytime warning bells. B, County, and B^1, Borough nighttime indicator relays. C, Radio/telephone switch for Borough system. D, Remote control unit for Borough transmitter. E, Tie-line telephone to County ambulance headquarters. F, Tie-line telephone to Borough ambulance headquarters.

To ensure that all members of the staff are able to use the equipment a short test transmission is made every morning. This has proved helpful in overcoming the strangeness felt by most people using radio communication for the first time.

Results

One of the most gratifying and highly welcome by-products of the early warning system has been the unexpected competition that has arisen between the ambulance personnel and the departmental staff to ensure immediate attention for seriously injured patients.

It has clearly emerged that the avoidance of even a minute's delay in starting resuscitation can preserve lives which even a few years ago would have been lost. As an example, 97 patients suffering from severe multiple injuries have been treated in the department during the past three years. Of these patients 68 had sustained crush injuries of the chest and 32 showed paradoxical respiration. The overall mortality was 20%, and many patients who were in extremis on arrival would certainly not have survived if the department had been inadequately equipped or unprepared for the immediate relief of respiratory embarrassment.

---

* Senior Accident Officer, Preston Royal Infirmary.

† Consultant Orthopaedic Surgeon, Preston Royal Infirmary; Lecturer in Clinical Orthopaedic Surgery, University of Liverpool.

Discussion

Apart from its value in the management of trauma, the radio link enables advice to be given direct to the ambulance personnel. This facility is greatly valued, as they no longer feel cut off from medical aid when faced with difficult problems, especially during the transport of seriously ill or injured patients to the Accident and Emergency Department. On occasion it is tempting to shorten the journey by taking the patient to the nearest hospital, but this is not always in the best interests of the patient, and radio contact with the accident centre can help to relieve the anxiety of the ambulance personnel in these circumstances.

Abuse of the flying squad is prevented by avoiding call-out when the information received over the radio link makes it clear that little or no benefit can be expected.

The radio link enables the most efficient use to be made of the available nursing staff during the night, because the senior nurses can continue their normal duties in other departments and need not be summoned to the emergency unit until the patients are expected to arrive.

When the emergency team is summoned to an accident messages can be sent back to the hospital with information about the patient's condition and the estimated time when he is likely to be brought to the hospital (Hall, 1965).

> The emergency team was called out at 4 a.m. to deal with a lorry driver trapped in the cab of his vehicle after a motorway accident. A message was sent to the hospital stating that his release would take a long time.
>
> Subsequent messages asked for two pints (1.14 l.) of Group O Rh-negative blood to be sent to the scene of the accident. A transfusion was begun while the driver was still trapped, and a short general anaesthetic was needed before he could be extricated at 6.30 a.m. A message was then sent with the information that the patient would reach the hospital in 30 minutes' time.
>
> Because the patient was receiving a blood transfusion, and because his fractures were immobilized, a slow and steady journey to the hospital was possible. There was no need for haste, and when he arrived in the emergency department his condition was appreciably better than it had been when he left the scene of the accident.

Future Developments

The radio link at Preston Royal Infirmary operates over the normal telephone cables, but this is not necessarily the best arrangement under every circumstance. The use of a radio transmitter under the department's control would provide additional facilities, although tie-lines would still be needed to avoid constant monitoring by the hospital staff (Collins, 1966). A transmitter with several channels would allow the department to contact direct not only the ambulances but also the police and fire services. This would be helpful on many occasions, and discussions are now being held with a view to the acquisition of suitable apparatus. Adjacent ambulance services, using different radio frequencies, could then contact the hospital during the transference of, for example, neurosurgical patients coming for treatment from hospitals some distance away. Should the condition of these patients cause anxiety, direct contact with the receiving hospital would permit advice or active help to be given during the journey. Unfortunately this is not generally practical at the present time because of the widely differing frequencies and types of modulation used in the radio installations of various ambulance authorities. It is hoped, however, that the committee now considering the equipment of the ambulance services will make recommendations which will enable a standard type of communication set to be used in emergency departments throughout the country.

Experiments are now being undertaken to transmit electrocardiographic information by radio link from the ambulance. If this proves to be practicable it will allow monitoring of the cardiac state of patients with severe injuries or collapse after coronary thrombosis, and by giving advice to ambulance personnel the survival rate, especially from coronary infarction in the younger age groups, might possibly be increased.

Messages from a mountain rescue team several miles away have been relayed directly into the emergency department, and there is no obstacle now to the provision of similar facilities for air-sea helicopters or other rescue services. Indeed, it is only by enabling all rescue services to collaborate at an early stage that significant advances will be made in the treatment of casualties before they reach a hospital. With this in mind, it would seem logical that the allocation of a common national rescue radio-frequency should be considered by the General Post Office.

Little thought has been given in the past to the care of patients before they reach hospital, but the attention of the ambulance services has now been drawn to this deficiency (Working Party Report, 1966). Emergency departments should likewise appreciate the expanding part they have to play in this direction. Although the next ten years will doubtless see an expansion of the facilities for the early management of the seriously injured greater than has ever occurred before, the ideal of medical help for the patient from the moment of injury will remain a physical impossibility. An adequate communication network, however, will at least ensure that medical advice is available at the earliest possible moment.

We wish to acknowledge the enthusiastic help we have received from the staff of the Preston Borough and Lancashire County Council ambulance services and the radio department of the Lancashire County Constabulary.

REFERENCES

Collins, J. (1966). *Brit. med. J.*, 2, 578.
Garden, R. S. (1962). In *Modern Trends in Orthopaedics (Fracture Treatment)*, edited by J. M. P. Clark, 3, 59. London.
Hall, M. H. (1965). *Lancet*, 1, 904.
Working Party Report on Ambulance Training and Equipment (1966). Part I, Training. H.M. Stationery Office, London.

WITHOUT PREJUDICE

A friend sent me the other week a copy of an address given to the Wigan Division of the B.M.A. in April this year by Sir Harry Platt, a youthful octogenarian. The title of his talk was "Medicine and Authority"—full of vigour and wisdom. He asked at the end of his talk the question whether the doctor of the future would remain a man of authority and independence. Both are being challenged in more than one country. "I have no doubt," Sir Harry said, "that the education and training of the doctor during the last fifty years, throughout all its changes, turned him out as a man of affairs well able to face the contemporary problems of society. . . ."

There must have been a lot of virtue in our medical community during this century. The training and education doctors received were thorough, the standards they set themselves and set others were remarkably high. They made great contributions to clinical medicine. And they engaged in public life while still active in their profession. Medicine seems to attract a good share of such men. I think the biologist is probably more versatile, more adaptable than other scientists. And as a scientist the medical man is a biologist, a student of human biology. In this capacity he has much to give the community in which he lives. The late Lord Brain was a remarkable example of the medical man in authority in the society in which he lives. And then there is Sir Arthur Porritt, a youthful surgeon now approaching his 67th birthday, soon off to New Zealand as its Governor-General, the first medical man, I believe, to be appointed to such a great position of trust.

I often wonder whether the new kind of authoritarianism in Medicine that seems to be the underside of our State medical service will stunt the growth of the independent mind that is such a valuable feature of the professional man at his best. It is something society can ill afford to lose in a world of shifting values.

"In all countries where highly organized health services have become the direct concern of central government," Sir Harry Platt says, "the doctor, irrespective of the source of his remuneration, must now fight to retain his position as an independent leader and adviser." I believe that the independence and resourcefulness of the outstanding men in our profession during, for example, the present century were very much part of their way of life as private doctors who have had to fight their way up with courage, initiative, hard work, and a competitive thrust to excellence. If the sole source of remuneration for the doctor is the State, then Sir Harry's fight will be a hard one. The State does not like too much independence in its servants.

* * *

I have just been looking through the volume *Fifty Years of Medicine* brought out by the *B.M.J.* in 1950. What a remarkable and magnificent story it is! What we inherit today is the result of the pioneering work of men who grew up in the much harder world of free enterprise. We owe a great deal to them, and should not underestimate our inheritance.

Just look at the picture the late Professor G. Grey Turner painted in the *B.M.J.* symposium! What an advance the old pioneers—as they must seem to us now—made and in what circumstances! Some measure of their difficulties, and of the distance we have moved since 1900, may be gauged from Grey Turner's description of surgery in his younger days. Operations were often enough carried out in most difficult circumstances in the patient's home. Most surgeons, Grey Turner says, took little equipment with them. Most of it, or all of it, would go into a Gladstone bag. A baking bowl from the patient's kitchen would serve as a "reservoir for Lister's strong mixture in which to soak towels clean from the wash. . . ." A meat dish served as an instrument tray.

Illumination was a hazardous affair of lamps and candles. "No one knows," wrote Grey Turner, "how feeble is the light from candles unless he has tried to do a strangulated hernia or remove an appendix with its aid." And when he was recollecting his experience for the *B.M.J.* symposium, published only 17 years ago, he remarked, "In retrospect I am prepared to reiterate that I have not yet seen the surroundings in which I could not operate with assurance, provided always that I personally superintended every detail of the arrangements."

* * *

I think that in decency we might recall the virtues of private practice before we exorcise it with bell, book—and candle. It had its bad sides, and these are the only sides the "Statist" can see. But the stimulus was productive of excellence. In his *Lancet* article last year Henry Miller said of the generation of neurologists just retired from hospital practice that a number were physicians of international stature, "well able to stand comparison with their great predecessors of the nineteenth century." He paid a neurologist's tribute to them. "In the intervals of exacting hospital work, undergraduate and postgraduate teaching, and busy private practice, they made major contributions to the study of the nervous system and nervous diseases. To these outstanding individuals the milieu in which they worked was a stimulating one, and it is improbable that any would willingly have abandoned it to become full-time academic physicians."

But Miller is surely right in seeing the future bound up with the establishment of academic units of clinical neurology "closely integrated with internal medicine and with the laboratory departments" if it is not to be left behind in the race for excellence.

There was a lot of truth in Clifford Allbutt's saying, made I believe at the Cambridge meeting of the B.M.A. in 1919, that Harley Street was the graveyard of clinical research. Private specialist practice is to all intents and purposes out in the Scandinavian countries, and surgeons I have talked to there would not have it back.

* * *

It is economics as much as anything else that has forced the change of direction. And it is economics that will determine the growth and development of Medicine in Britain. Sir Harry Platt, in his Wigan address, made an effective plea for reinforcing the State contribution by active voluntary contribution. He noted that in the U.S.A. and Canada the success of this depended "on the existence of an intelligent tax system whereby modest annual contributions are tax free, and large gifts are immediately free from estate duty." Surely we might imitate what appears to be a good model!

In the U.S.A. I was interested to learn from the *New England Journal of Medicine,* third-party payments, in 1964, met 82% of all costs for hospital care, most of it coming from insurance. And the author of the article, Professor Somers, estimates that some 43% of the cost of services of the physician in private practice was also met by third-party payments—from private insurance, combined with payment from governmental agencies. He sees Medicare as a stimulus to private insurance, and the two of them as being mutually supportive. "In short," he says, "the years ahead will witness a massive increase in both public and private financing of health services, although the public portion will be greater. The nation [U.S.A.] is now committed to assuring that all medical needs will be met and paid for."

We reached that decision twenty years ago. We have now got to tap private sources of money in order to keep the pledge. The public must put its hand into its private pocket to make the N.H.S. a success by contributing to it directly as well as through taxation. In this way the public would show that it really believes in the N.H.S., and wants it to prosper.

PERTINAX

Correspondence

Letters to the Editor should not exceed 500 words.

Nature of the Scrapie Virus

SIR,—It has recently been suggested[1, 2] that scrapie—a transmissible disease of the central nervous system in sheep, goats, and mice—may be related to multiple sclerosis, and so a study of the nature and mechanism of action of the infective agent of scrapie could be important in the understanding of the human disease. A similar pathogenesis may also be attributed to other obscure degenerative diseases of the central nervous system in man, one of which, kuru, has recently been transmitted experimentally to chimpanzees.[3]

Although many of the properties of the scrapie agent are consistent with the supposition that it is a slow virus, there have been many reports of its exceptional stability to the action of heat, ultraviolet and *x*-irradiation, chemical agents such as formalin, and enzymes. There is also a growing body of evidence suggesting that the scrapie agent is of extremely small size, perhaps as small as 3 mμ,[4] and that the infection does not result in the production of antibody by the host.[5]

Recent evidence, particularly that concerning its stability, has led to speculations that the scrapie agent may represent a new class of replicating particles.[6] Its resistance to irradiation led Alper and her colleagues[7, 8] to suggest that the scrapie agent might be a replicating particle not containing nucleic acid; Pattison and Jones[9] proposed that it might be a histone, while Field[2] mooted the possibility of its being a replicating polysaccharide.

However, it seems to us that such radical departures from conventional virus theory are not essential to explain the many exceptional properties of the scrapie agent if certain assumptions are made concerning the nature of the viral coat. Although it is generally assumed that viral nucleic acid is sheathed with protein (possibly mixed with some lipid), there appears to be no a priori reason why this should invariably be so. We would like to suggest tentatively that the scrapie agent consists of a small nucleic acid core enclosed in a mucopolysaccharide or even polysaccharide coat, and further that the nucleic acid core is stabilized structurally by covalent bonds with the sugar residues in the coat. Such a model might be expected to be very resistant to energy disruption, to be weakly or non-antigenic, and to carry enough coding information even with a relatively small nucleic acid core for the small amount of protein which may be present in the coat structure.

Further detailed considerations of a theoretical model are in progress and attempts are being made to obtain experimental verification of this hypothesis.—We are, etc.,

D. H. ADAMS.
E. A. CASPARY.

M.R.C. Research Unit in
Demyelinating Diseases,
Newcastle upon Tyne 2.

REFERENCES

[1] Pálsson, P. A., Pattison, I. H., and Field, E. J., in *Slow, Latent, and Temperate Virus Infections*, NINDB Monograph No. 2, 1966, p. 49, edited by D. C. Gajdusek, C. J. Gibbs, jun., and M. Alpers, Bethesda.
[2] Field, E. J., *Brit. med. J.*, 1966, **2**, 564.
[3] Gajdusek, D. C., Gibbs, C. J., and Alpers, M., *Nature (Lond.)*, 1966, **209**, 794.
[4] Pattison, I. H., and Sansom, B. F., *Res. Vet. Sci.*, 1964, **5**, 340.
[5] Chandler, R. L., *Vet. Rec.*, 1959, **71**, 58.
[6] *Nature (Lond.)*, 1967, **214**, 755.
[7] Alper, T., Haig, D. A., and Clarke, M. C., *Biochem. biophys. Res. Commun.*, 1966, **22**, 278.
[8] Alper, T., Cramp, W. A., Haig, D. A., and Clarke, M. C., *Nature (Lond.)*, 1967, **214**, 764.
[9] Pattison, I. H., and Jones, K. M., *Vet. Rec.*, 1967, **80**, 2.

Future of Mental Hospitals

SIR,—Your leading article on the future of the mental hospitals ends on a very gloomy note (24 June, p. 781). It suggests that there is no alternative between the "living graveyards for increasing numbers of senile patients and repositories of . . . 'long-stay' schizophrenics" and the social chaos which might occur if the older mental hospitals suddenly disappeared.

You seem anxious to justify the retention of the old mental hospitals and the system they represent. The fact that there is variation in bed needs from area to area hardly undermines the thesis that the total bed numbers will be reduced, nor does the unfortunate fact that there are insufficient community facilities available alter the need to plan for a future when such facilities will be available. Hundreds of patients still in mental hospitals do not need to be there. In the case of many patients they share the attention of one nurse with fifty others, see their doctor once a year for a routine annual examination, and may have no medication whatever and the most elementary daily routine. These patients may indeed need some measure of supervision and accommodation but it can hardly be claimed that they are having *hospital* care now or, indeed, need this level of provision. The old mental hospital service was intended to isolate and institutionalize and it did this very successfully with large numbers of inadequate people.

No one wishes to see social chaos, any more than most psychiatrists can feel contented with our present "living graveyards." Like many others, I had thought that we were planning for a future where the patient needing admission and treatment would be treated within the acute general hospital system, while the longer-stay patient needing nursing care and rehabilitation would be treated in the longer-stay hospital, catering for the longer-stay patients from medicine, neurology, and other specialties. There seems no good reason for providing a separate mental hospital, any more than there are good reasons for providing a separate hospital for patients with rheumatic disorders, for example. Many patients have multiple disabilities, particularly the more chronic patient and, as studies have shown, to attempt segregation of patients is usually to the detriment both of those who have psychiatric disabilities with a physical accompaniment and the many patients who have physical disabilities and some psychiatric accompaniment.

The patients staying on in mental hospitals tend to be those who are unwanted by the outside community. Whether they are unwanted is often unrelated to the severity of their illness. It is very rare to find a beautiful woman on the back wards of a mental hospital. It is to be hoped that our society, which is gradually coming to understand the problems of the mentally ill and showing a greater willingness to tolerate and accept these patients, will not replace them with the geriatric patient, who suffers just as much by being rejected and isolated away from their home community as the psychiatric patient. Neither the schizophrenic nor the senile patient wants to end his days in the "living graveyard."—I am, etc.,

Banstead Hospital,
Sutton, Surrey.

A. A. BAKER.

Trismus Following Inferior Dental Nerve Block

SIR,—A considerable number of cases of severe trismus have been seen recently which followed inferior dental nerve block injections. In most instances local analgesia had been given merely to carry out conservative dentistry procedures, such as fillings, and not in order to perform surgery. According to the operators the injection was painless and uneventful, but later a progressive trismus developed over a period of three or four days, resulting eventually in complete inability to open the mouth.

On examination of such a case no tenderness or swelling is present and the only physical sign is extreme limitation of opening. Gentle pressure on the mandible gives a feeling of mechanical locking of the jaw and causes slight pain in the region of the medial pterygoid muscle. No improvement in mouth opening occurs with the passage of time, and in one instance the limitation of jaw movement had been present for three months. However, once established the condition does not appear to deteriorate. Active jaw opening exercises achieve little improvement and there is no relaxation of the masticatory muscles upon giving a general anaesthetic.

If the mandible is gently prised open under general anaesthesia, using a mouth gag between the teeth on either side of the jaw, a characteristic cracking sensation is detected in the region of the medial pterygoid muscle as the impediment to movement is overcome. Following this action normal mouth opening is restored. The patient does not experience any postoperative pain and there is no tendency to recurrence. Care must of course be taken not to exert excessive force when opening the mouth in this manner, and a wide-bladed instrument, such as a Featherstone gag, should be used in order to avoid damage to the crowns of teeth or the accidental displacement of an upper second premolar into the maxillary sinus.

The cases examined appear to have had no common aetiological factor in so far as the injection technique and the nature of the analgesic solution is concerned. The most likely cause appears to be that with the modern, thin, sharp hypodermic needle there is a greater risk of penetrating a small artery. Rupture of the vessel would then cause haematoma formation with subsequent organization of a band of fibrous tissue in the vicinity of the medial pterygoid muscle. This would explain the gradual onset of the trismus and the mechanical locking effect achieved, and also account for the recent increase in the condition.—We are, etc.,

H. C. KILLEY.
L. W. KAY.

Eastman Dental Hospital,
London W.C.1.

Guanoxan

SIR,—We were interested to read the paper by Dr. V. Vejlsgaard and his colleagues (3 June, p. 598) in which they reported a double-blind trial of four hypotensive drugs. One of these drugs, guanoxan, we have used in an extensive clinical trial for more than two years, and the results of this trial are soon to be reported in detail elsewhere.[1] In our series we also found that severe lassitude is an important side-effect in some patients on guanoxan.

Vejlsgaard remarks that they found no evidence of a hepatotoxic effect of guanoxan. We would suggest that this was partly because in their trial the number of patients was small and they were observed for a short period of time (40 patients observed for from two to six months). In our trial we had 96 patients observed for periods from 2 to 27 months; 54 of these patients were observed for over one year. In our series 26 patients (27%) had some derangement of liver-function tests at some time and 10 patients (10%) had severe abnormalities of their liver-function tests—that is, very high serum transaminases with raised serum alkaline phosphatase. Four of these 10 patients developed frank jaundice and one of the four died with acute on chronic hepatic necrosis. Further details of these cases will be published.[1]

Since our trial was officially closed further cases of liver-function-test abnormalities have occurred among the patients who remain on the drug. One of these patients had severe derangement of his liver-function tests. We do not claim that the incidence of abnormalities in liver-function tests that occurred in our trial is necessarily the true overall incidence, but we do think that it represents a fairer picture than that of Dr. Vejlsgaard's trial, as the occurrence of liver-function-test abnormalities from patients on guanoxan in other centres has been at roughly the same level as in our trial, as reported in your correspondence columns (14 January, p. 111).

Finally, we would also like to draw attention to the fact that a systemic lupus erythematosus syndrome has also been observed in patients on guanoxan. One such patient was reported in the letter referred to above and a further case is reported in our paper.—We are, etc.,

SUSAN G. COTTON.
E. MONTUSCHI.

Whittington Hospital,
St. Mary's Wing,
London N.19.

REFERENCE

[1] Cotton, Susan G., Lovel, T. W. I., and Montuschi, E., *J. clin. Trials (Lond.)*, 1967. In press.

Lead Absorption in Children

SIR,—We have read with interest the paper by Dr. N. Gordon and colleagues (20 May, p. 480) on lead absorption in children, with particular reference to its association to mental retardation. In that paper it is stated that we claimed that "lead was a greater factor in producing mental retardation than previously thought" and that a "raised blood lead level is a common finding among mentally retarded children and that this is of aetiological significance." It is true to say that in comparison with our own control group, in which the upper limit of normal for blood lead was 36 μg./100 ml., 55% of the mentally retarded children did have elevated blood lead values, but it was never at any time claimed that this was of primary aetiological significance so far as the mental retardation was concerned, and thus Gordon and his collaborators are quite mistaken in their assertions. What was claimed, and this was the whole point of the paper, was that mentally retarded children with pica (to which many are prone) are clearly more liable to lead poisoning if there is lead in the environment, and in such circumstances the neurotoxic effect of lead could further impair their functioning.

The authors also assert that we claimed improvement with treatment of a child with a blood lead of 48 μg./100 ml. on clinical grounds alone. Again, this is a misrepresentation of our statement. The improvement was assessed clinically and also by formal psychometric assessment as detailed in the paper.

During childhood, the detection of lead poisoning before clinical toxicity is apparent still remains a difficult problem. It is not unreasonable to assume that lead can interfere with intermediary metabolism long before the classical clinical symptoms are produced. The choice of normal subjects is always difficult in clinical medicine, particularly in paediatrics. It is surprising that Gordon's controls included children that, by any standards, had significantly elevated blood lead values and that these children showed no signs at all of toxicity. It is also surprising that the authors found such variability in levels of repeated examinations.

Our original plea was not that lead poisoning caused much more retardation than was generally thought, but that mentally retarded children who have pica and who ingest lead could possibly deteriorate even further. It remains our considered view that the clinicians should do their best to detect and treat lead poisoning before the onset of severe symptoms. It is important that the parents should be aware of the dangers of pica, especially chewing paint in old houses. It may be that we will never know at what level lead becomes actively toxic until we have an accurate test of a biochemical nature to assess this.—We are, etc.,

A. A. MONCRIEFF.
B. E. CLAYTON.
G. E. ROBERTS.

Hospital for Sick Children,
London W.C.1.

The Scabies Epidemic

SIR,—As Service dermatologists abroad we see a small but constant number of cases of scabies, but certainly not the epidemic proportions described in your pages as occurring in Great Britain (18 March, p. 669).

I was impressed on returning to Britain after two years abroad by the vast increase in the number of youths wearing long hair, to which syndrome is usually added a failure to wash. The present-day soldier, whether he likes it or not, is obliged to wash regularly and keep himself smart, which I believe is one reason why the scabies epidemic has not affected the Services in my own experience.

Lack of precise instructions on the use of benzyl benzoate is no doubt another cause of failed treatment. All patients with scabies attending our clinics are given a simple but detailed typed proforma on treatment, which they are made to read before taking it home with them. Attention to the patient's environment and activity during the treatment period is important. It is unlikely, for example, that an old-age pensioner living on his own will be able to apply lotion "everywhere below the neck."

Here in the tropics, where all Europeans sweat, even at rest, it is impossible to keep an application on the skin for more than a few hours before sweat washes it off. For this reason we frequently admit our patients to air-conditioned rooms during treatment. While this procedure is obviously unnecessary in the United Kingdom, one can visualize that manual workers, miners, blast-furnace operators, athletes, etc., are unlikely to be able to carry out treatment successfully while remaining at work, and unless all aspects of the patient's environment are considered at the consultation treatment is less likely to be effective.—I am, etc.,

T. C. HINDSON.

Dermatology Department,
British Military Hospital,
Singapore.

SIR,—I have read the recent articles and correspondence on the subject of scabies, and it seems that our experience of this problem may be of interest to others.

Our work involves child health in remote villages in central Tanganyika. Scabies is a serious problem, and in some villages almost 100% of children over 6 months old are affected. In some cases the lesions are so extensive and the secondary infection so severe that it is a factor contributing to the very high child mortality in this area.

I have found benzyl benzoate effective in hospital use but quite useless in the village setting. The patients treated in hospital are promptly reinfected on returning home. The result was that after nine months' work in the villages there was no significant change in the incidence of scabies.

About a year ago we stopped using benzyl benzoate and started using monosulfiram soap, advising the patients to allow the soap to dry on the skin. In this way an effective concentration of monosulfiram is built up on the skin and in the clothes and bedding.

The results have been quite remarkable, and scabies has almost disappeared in some villages. The only obstacle to complete eradication seems to be the cost of the soap at 2s. each in a country where a manual worker earns only 6s. a day when he can find work.

I was surprised to see no mention of monosulfiram in the copies of the *B.M.J.* which have reached me so far.—I am, etc.,

R. W. SMITH.

Save the Children Fund,
P.O. Box 15,
Dodoma, Tanzania.

SIR,—Dr. J. O'D. Alexander's two cases (17 June, p. 766), in which he found acari from scrapings but no recognizable burrows, raise the interesting question whether *Sarcoptes scabiei* may sometimes behave atypically. There are of course occasions when the acarus does not produce a burrow—or not a typical one; this is in fact true of the male and of the larva, but obviously in established scabies there are likely to be burrow-producing adult females as well. Another possibility to be considered is whether the acarus is perhaps of animal origin; sarcoptic mange of dogs is transferable to humans as a follicular rash without burrows.

I am not of course suggesting that this must be the explanation of Dr. Alexander's cases—this would be tantamount to asserting that human scabies cannot occur without burrows, and this kind of negative is unprovable. I cannot myself recall seeing a case of human (as opposed to animal) scabies in which no burrow could be found *somewhere in the family*. In particular an examination of the soles and ankles, which are relatively protected from scratching, is often rewarding.

I heartily agree with Dr. Alexander's last paragraph, and would only add the suggestion that in the case of infants the face and scalp should be included in the treatment. Typical burrows may occur on these sites.—I am, etc.,

Winchester. LIONEL J. BACON.

Problems of Antenatal Care in the Tropics

SIR,—Mr. S. Haroon's article on the problems of antenatal care in the tropics (3 June, p. 617) highlights some of the difficulties confronting the Western-trained doctor who works in these regions. Yet, although the basic problem in the tropics appears to be poverty, there is considerably more clinical variation in different regions than his article suggests. Clinical experience in Western Nigeria,[1] for example, would appear to differ greatly from Mr. Haroon's.

However, despite this clinical diversity, I believe that there are some basic generalizations that can be applied to antenatal care and that these should have had more emphasis in his article. All of them require some reorientation of thought in the Western-trained doctor.

(1) The doctor must learn to delegate authority. He should not regularly undertake routine tasks that can be done by others under his supervision. This means in practice that most of the work of an antenatal clinic is done by the nurses and that the nurses themselves may give some routine work—for example weighing and urine testing—to unqualified helpers. The doctor, therefore, is much more an organizer, supervisor, and teacher than he would be in the West.

(2) The doctor will need to turn his thoughts towards preventive medicine. This will bring him to the realization that one of his major functions is teaching. Antenatal mothers provide a captive audience who are particularly receptive to health teaching. If this teaching can be linked with, and continued through, the postnatal and paediatric clinics it provides one of the most successful ways of raising the standard of health in a community. In my opinion health teaching is one of the most important functions of an antenatal clinic and all members of staff from the top to the bottom should take part in it.

(3) The doctor will have to think very carefully about the cost of the care he is providing. If he wishes to help the people among whom he works he must provide care that all can afford, for the provision of an expensive service to an affluent minority does little to help the community at large. This may mean pruning some hallowed antenatal procedures.

(4) The doctor must believe sufficiently in the importance of clinical research to do some himself. The medical needs in a tropical area are often unknown. An efficient obstetric service cannot be created until these needs and their relationship to the local culture have been discovered. For example, in my own area it is more important to estimate the haemoglobin regularly than to weigh the patient, or even to take her blood pressure routinely. Antimalarials are of far greater benefit than iron tablets.

(5) The doctor must stray purposefully outside his specialty. A recent editorial sums this up particularly well.[2] A mother will see little profit in good clinical care in pregnancy and labour if her child soon dies of malnutrition or endemic disease.

In the poor countries of the tropics the family's first contact with modern ideas on health is often through the antenatal clinic. If the mother accepts the teaching she receives there she is likely to apply it to the whole family. This may help to bring under control the enormous loss of life in infancy and early childhood from readily preventable conditions.—I am, etc.,

V. J. HARTFIELD.

Wesley Guild Hospital,
Ilesha, Nigeria.

REFERENCES

[1] Cannon, D. S. H., and Hartfield, V. J., *J. Obstet. Gynaec. Brit. Cwlth*, 1964, 71, 940.

[2] *Lancet*, 1965, 1, 791.

Treatment of Choriocarcinoma

SIR,—May I reply to the letter on this topic sent to you by Professor W. S. H. Tow and Dr. W. C. Cheng (17 June, p. 764)? Again, as before, my primary concern is with logic and pathology. Thus:

(1) Untreated choriocarcinoma is a metastasizingly malignant lesion, equally lethal in young and old, nullipara and multipara. For its eradication hysterectomy is either believed to be optimum basic treatment or it is not. If it is believed to be so hysterectomy will always, when practicable, be performed; and it necessarily follows from this that if, in these circumstances, hysterectomy be *not* performed either optimum treatment is not being used or the therapist is not translating his belief into practice. To withhold what is believed to be optimum treatment for the eradication of a cancer just because the patient is young or nulliparous seems to me illogical.

(2) It is surely of the essence of medical or any other science that comparison be continually made between thought, method, and result in one centre and another. Professor Tow and Dr. Cheng say that they do not consider such comparison to be fruitful at present, and this I think most strange.

(3) It is a prime necessity for interchange of opinion that agreement on terminology be achieved as far as possible. To be sure, there is still room for debate in the case of lesions of trophoblast, but in using the (by current standards) self-contradictory term "villous choriocarcinoma" Professor Tow and Dr. Cheng stand virtually alone. In the histopathology of neoplasia diagnosis is prognosis; by this tenet "villous choriocarcinoma" as a diagnosis fails.

(4) I cannot have expressed myself clearly enough in criticizing the use of the term "a trophoblast" to designate a cell. Instead, may I ask what kind of cell do Professor Tow and Dr. Cheng consider "a trophoblast" to be?—I am, etc.,

W. WALLACE PARK.

Department of Pathology,
Queen's College,
Dundee.

Varicose Veins, Oral Contraceptives, and Thromboembolism

SIR,—Mr. G. Fegan in his letter (24 June, p. 838) comments on our report (3 June, p. 637) of fatal thromboembolism following injection of varicose veins. We are at this clinic comparing the injection/compression technique with a conventional scheme of operative treatment in a trial supported by the Ministry of Health, and therefore followed the method used by Mr. Fegan himself. We would like to take this opportunity to thank him for teaching us at his clinic in Dublin.

The case reported was treated by one of us personally. Only 5 ml. of sodium tetradecyl sulphate was injected. The bandages were undisturbed when embolism occurred the following day.

We apologize again for stating the dose as 10 ml. When this error was discovered we reported it at once to you (17 June, p. 778) and to Mr. Fegan. We agree that personal attention to detail is essential for safe and successful treatment, and that ascending great saphenous thrombophlebitis should not occur. We have seen this complication only twice, each time after the patient has removed the bandages contrary to firm instructions given both verbally and in writing.

We think it may be significant that the opposite leg of this patient had been treated successfully and without complication at a time when she was not receiving hormone therapy.—We are, etc.,

H. O. JONES.
J. C. F. TOWNSEND.

Cardiff Royal Infirmary,
Cardiff.

Lyell's Toxic Epidermal Necrolysis

SIR,—We were very interested to read the article on Lyell's disease by Dr. J. Jefferson (24 June, p. 802), particularly as we admitted a similar case on 12 June which caused a great deal of diagnostic difficulty.

This was a 2-week-old female child who had been restless and irritable for two days. On the day of admission the mother had taken her to the local child welfare clinic, where it was noted that she had a blepharitis, and was given sulphacetamide eye ointment to apply. Five hours later the mother noticed the skin was peeling off the child's buttocks and brought her to hospital. The main clinical findings were a temperature of 99° F. (37.5° C.), general erythema of the skin (boiled lobster appearance), patchy areas of moist erythema with yellow crusts on the face, particularly around the mouth, nose, and eyes, and large patches of what appeared to be scalds of the perineum, buttocks, and trunk. In view of the appearance of the child's skin and the state of agitation of the mother (who was 17 years old, and this was her first child) it was suspected that she had been accidentally scalded, but the mother was emphatic that there was no possibility of this. In addition, the child showed no evidence of shock, dehydration, or systemic disturbance. A swab from the facial lesions yielded a heavy growth of *Staphylococcus aureus* resistant to benzylpenicillin.

Treatment was on the same lines as that described by Dr. Jefferson, except that the child was nursed in a gallows splint to keep the perineum exposed. All the skin lesions healed completely within two weeks, and at no time throughout her stay did the child show any evidence of systemic disturbance.—We are, etc.,

W. S. JAMIESON.
I. CAPPERAULD.

Royal Herbert Hospital,
London S.E.18.

SIR,—I was interested to read the article by Dr. J. Jefferson (24 June, p. 802), as in my experience as a consultant physician in Aden in the last two years epidermal necrolysis is not uncommon in European infants there. Although minor degrees of the condition are seen, some 15 infants and young children had lesions extensive enough to need hospital admission.

Staphylococci were isolated from the great majority of the children, although no facilities existed for phage typing. Localized skin sepsis preceded the characteristic "scalded" appearance in some patients, and several had received tetracycline orally or topically before admission. It is not possible entirely to exclude this drug as a sensitizing agent, but it is most unlikely both from the time interval and the fact that it was common to a minority of patients with a similar clinical picture. Progress was generally towards complete skin healing in 10–11 days, and typically the neck and perioral areas were slowest to heal. Our treatment regimen was similar to that of Dr. Jefferson, but I am not convinced that treatment ever significantly shortened the time taken for the skin to heal.

The disease was fatal in one 9-week-old male infant who had 75% skin involvement and required replacement of considerable fluid losses as in a burn of similar extent. Terminally this infant developed digital gangrene, and necropsy showed a necrotizing endarteritis with gangrenous dermatitis and little inflammatory response.

In other particulars our cases resembled others described, and I would emphasize the distress and irritability of the affected infant which is almost certainly due to widespread skin tenderness.

Apart from this picture, staphylococcal skin lesions are commonly bullous in Aden and other parts of the Middle East, and it is tempting to suggest that climatic conditions potentiate the action of a specific staphylococcal lysin, perhaps by increasing skin permeability in a non-immune subject.—I am, etc.,

D. J. STOKER.

Royal Air Force Hospital,
Wolverhampton, Staffs.

Heavy Uterine Bleeding

SIR,—Both your expert (20 May, p. 494) and Mr. J. M. Gate (1 July, p. 47) have given a somewhat misleading reply to the questioner who asked about uterine bleeding and abnormality of the clotting mechanism.

While a non-gynaecological cause for uterine bleeding occurs in less than 1% of cases, because of the frequency of consultations for this symptom considerable numbers of haematological disorders present to the gynaecologist and obstetrician. Many of these are cases of idiopathic thrombocytopenic purpura, and less commonly, as Mr. Gate indicates, other disorders are present such as aplastic anaemia or leukaemia. Thus thrombocytopenia from any cause may be responsible.

In von Willebrand's disease uterine haemorrhage is often far more of a problem than your expert suggests. I have seen catastrophic haemorrhage at menarche, several severe postpartum haemorrhages, and prolonged heavy menstrual bleeding causing severe iron deficiency, not controlled by progestogens, and requiring hysterectomy. Rarely patients with pseudo-xanthoma elasticum and the Ehlers–Danlos syndrome suffer menstrual disturbances, but this has not been a prominent aspect of the cases seen here.

Your expert further states that deficiencies of coagulation factors do not cause uterine haemorrhage; this is usually true for congenital afibrinogenaemia, but patients deficient in factors V, VII, X, and XI sometimes suffer frequent heavy periods and also postpartum haemorrhage.—I am, etc.,

J. J. TAYLOR.

Queen Elizabeth Hospital,
Birmingham 15.

"Swallowed" Endotracheal Tube

SIR,—Following Mr. J. A. S. Dickson and Mr. G. C. Fraser's recent article on "swallowed" endotracheal tubes in neonates (24 June, p. 811), may I report a further similar case transferred to this hospital?

The infant was born by lower segment caesarean section following a trial of labour for disproportion. Birth weight was 8 lb. 11¾ oz. (4 kg.), and the Apgar score was 2. Resuscitation was carried out and included intubation with a Portsmouth tube. The child rapidly improved and remained well until the fifth day, when he began to vomit. Vomiting at first occurred two or three times per day, but became more severe and frequent. Between vomiting the child was retching forcibly. On the tenth day the vomitus contained bile, and he was transferred here. His weight was found to be 8 lb. 3 oz. (3.7 kg.), but there were no abnormal physical signs except the repeated retchings, which occurred approximately every 30 minutes. A test feed was carried out. The child took the feed eagerly, the stomach became moderately dilated, and small peristaltic waves were seen. X-ray revealed a Portsmouth tube, the lower end impinging on the greater curvature of the stomach, the upper end lying in the upper end of the oesophagus. The tube was removed easily under general anaesthetic, using a straight laryngoscope and a pair of tonsil-holding forceps. The child made an uneventful recovery, and vomiting ceased immediately.

In retrospect it was remembered that during resuscitation of the infant the anaesthetist had been recalled to the mother urgently.

The interesting feature of this case was the length of time between "intubation" and the removal of the tube. In all Dickson's cases removal appears to have been carried out soon after birth, when the child's condition had improved. In this case removal was carried out on the tenth day. Despite this the child's general condition had remained good and his weight was only 8¾ oz. (250 g.) below the birth weight. No long-term effects are anticipated.—I am, etc.,

MICHAEL G. PRINN.

Queen Elizabeth Hospital for Children,
London E.2.

Enuresis and Psychiatry

SIR,—I have recently been asked to see an 18-year-old enuretic boy who originally attended a child guidance clinic 10 years ago for that complaint, for which he received psychotherapy for a while, but no attempt was made to deal with the symptom specifically. The family has been in touch with the clinic ever since, during which time the mother must have had to cope with over 3,000 wet beds, yet the clinic thought it best to ignore the problem (easier for them than for the mother to do). Last year the boy's sister, now aged 8, also began psychotherapy there for enuresis, but the indirect approach has again been adopted.

In certain psychiatric circles it is regarded as disastrous to tackle a symptom directly, however unpleasant it may be. The reason usually given is that the symptom is only the visible part of the iceberg, and the greater, more important part lies below the surface; unless this is dealt with other symptoms will replace the one that is removed. As if unable to tolerate any challenge to this kind of dogma, some psychiatrists have been known to warn the parents of enuretics that successful treatment (with the buzzer) may give rise to impotence later in life. On reflection, it is apparent that this form of therapeutic nihilism is unhelpful, to say the least, to the patient, and borders on the unethical. It seems to me:

(1) Substitution symptoms have never been shown to develop in a significant proportion of enuretics successfully treated.

(2) Even if they did develop they might well be less humiliating and upsetting to all concerned.

(3) And there is no reason why the underlying iceberg should not be treated concurrently with the direct attack on the wetting or other symptoms anyway.

Asthma, enuresis, epilepsy, and migraine all have much in common. They are all inherited, usually improve with age, reflect emotional tension, and respond to symptomatic treatment. Now that the latter is so much more effective than it used to be, it seems that to withhold it is to do a disservice to one's patients.—I am, etc.,

IAN G. WICKES.

North Middlesex Hospital,
London N.18.

Ophthalmic Graves's Disease

SIR,—In relation to your leading article "Ophthalmic Graves's Disease" (6 May, p. 329) and Mr. Kenneth C. Wybar's letter (24 June, p. 836), may I point out that Henderson[1] has obtained excellent results (in several cases of lid retraction in Graves's disease) by the procedure of severing the attachment of Mueller's tarsal muscle from the tarsal plate.

This is a significant pointer as to the aetiology of lid retraction in Graves's disease.—I am, etc.,

D. K. RAY.

Blackwood, Mon.

REFERENCE

[1] Henderson, J. W., *Arch. Ophthal.*, 1965, 74, 205.

Carbenoxolone Sodium

SIR,—It has been pointed out to us that in our medical memorandum (18 February, p. 412) we have described carbenoxolone sodium (Biogastrone) as the disodium salt of β-glycyrrhetinic acid. This should have read the disodium salt of the hydrogen succinate derivative of β-glycyrrhetinic acid.

Some confusion also appears to have arisen owing to the fact that certain methyl groups and double bonds were omitted from the formulae of β-glycyrrhetinic acid, aldosterone, and cortisone. The formulae as presented were simply to demonstrate a similarity in the basic structure of the three compounds.—We are, etc.,

Victoria Infirmary, Glasgow S.2. — N. MACKAY.

Royal Infirmary, Glasgow. — CHARLES FORBES.

Cervical Smears

SIR,—For over a year I have been carrying out cervical smears on all my female patients between the ages of 25 and 65 years. Now that the Minister of Health has recognized the need for this service,[1] and has agreed to the payment of 7s. 6d. per smear, the lower age limit has been raised to 35 years. I recently carried out smears on two of my patients under the age of 35, and my claims for payment were rejected.

I am wondering on what grounds this age limit has been applied. If the Minister has been informed that women under the age of 35 do not get cervical cancer his information is not in accord with the experience of the pathologist who has kindly read the smears for me, and who tells me that 20% of all his positive smears occur in women under the age of 35. If, on the other hand, the Minister has been told that there is a shortage of readers and pathologists I can only point out that since January 1966 I have taken smears whenever I have considered it necessary, and they have been read without question. (For this help I should like to record my thanks to Dr. C. H. Wrigley, of the Royal Hampshire County Hospital at Winchester.)

I feel that the decision about when a cervical smear should be taken should be left to the patient's personal physician, and not be dictated by someone in Whitehall. I hope that the British Medical Association may be able to persuade the Minister to accept this view.—I am, etc.,

MICHAEL B. CARSON.

Lymington,
Hampshire.

REFERENCE

[1] *Statement of Fees and Allowances Payable to General Medical Practitioners in England and Wales*, Part II, October 1966, p. 14.

Live Donors for Renal Transplantation

SIR,—In your leading article (11 March, p. 581) on "Dilemma of Irreversible Renal Failure" you refer to the ethical problems of taking a kidney from a healthy person. After consideration of the use of the kidneys taken from cadavers, you say "Close relatives of compatible tissue group might still wish to donate kidneys, since the results would probably be better than those from unrelated donors." With the exception of identical twins, the statistical chance of transplantation succeeding is not overwhelmingly greater in the case of compatible relatives than of cadavers. The use of a 10-year-old boy as a donor for his identical twin has recently been discussed by Murray and by Lynch.[1] We feel that it is only very rarely that the use of a young live donor can be justified, and cite the following personal experience with identical twins in support of this view.

On 3 October 1962, a 23-year-old girl was admitted suffering from terminal renal failure. She was referred to us because her general practitioner had read a leading article in your journal referring to successful kidney transplantation between identical twins.[2] She was very ill on admission, with generalized oedema and a blood pressure of 260/210 mm. Hg. Vision was very poor and she could see faces only as a blur. There was detachment of the lower one-eighth of both retinae, which by the following day had progressed to a funnel-shaped detachment of both retinae, the central area remaining attached though oedematous. The blood urea was 438 mg./100 ml.; plasma sodium 125 mEq/l., potassium 4.6 mEq/l., chloride 79 mEq/l., and alkali reserve 12 mEq/l., haemoglobin 5.2 g./100 ml. The hypertension was energetically treated with Apresoline (hydrallazine) and Vegolysen (hexamethonium bromide), and she had a three-and-a-half-hour dialysis on the twin-coil kidney on the day following admission. After this treatment the blood pressure was 210/130, and the blood urea was 195 mg./100 ml.

The patient's twin was found to resemble her physically, and was willing to act as a donor for her sister. The blood groups of the two girls were identical in the ABO, Rh genotype, MN, S, P, Le^a, Kell, and Fy^a groups.

At this point the parents of the two girls asked whether, if a kidney was successfully transplanted from one girl to the other, the patient's sight would recover. If this was not likely to happen they were reluctant for the transplant to take place. The potential donor herself was willing to give a kidney. Mr. E. C. Cowan kindly saw the patient and expressed the view that if the patient's general condition could be improved there was at least a possibility the retinae might reattach and useful sight return. Accordingly it was decided that the patient should be treated by further dialysis to prepare her for transplantation at a later date. Investigation of the healthy twin was planned, to ensure that she had two normally functioning kidneys, and that the renal vessels were suitable.

Three days after the first dialysis the blood urea had risen to 275 mg./100 ml., and a second dialysis on the twin-coil kidney was commenced. After three hours a rise in blood pressure and pulse rate caused us to discontinue the dialysis. Despite this tachycardia increased to 180 per minute, and one hour later she had a convulsion, during which she died.

On 27 January 1967, the healthy twin was referred to one of us complaining of urinary incontinence. She had been delivered of a healthy infant by caesarean section on 3 September 1966, after a 34-hour labour. Within a short time following she became incontinent and used a sanitary pad every hour. She had never previously had any urinary symptoms.

On examination she was perfectly normal in every respect except that there was a continual leakage of urine from the vagina. Apart from the presence of occasional pus cells, her urethral urine was free from protein, and sterile on culture. The blood urea was 31 mg./100 ml. Intravenous pyelography showed marked hydronephrosis of the left kidney. There appeared to be an irregular filling defect in the left upper aspect of the bladder outline. Apart from being a little low in position, the right kidney was radiologically normal. On 9 February vaginal examination showed that urine high in the vault appeared to be coming from the cervical os. Cystoscopy revealed a normal bladder with two normally placed ureteric orifices: a catheter could not be induced to pass up more than 2 cm. into the left ureter. Injection of dye produced no useful information. Abdominal exploration revealed that the left ureter, 1 cm. in diameter, was involved in a fibrotic process as it passed the cervix. The fistula was clearly seen entering the cervical canal and the distal ureter was normal.

The damaged ureteric segment was excised and continuity was re-established, leaving a T-tube above the anastomotic site through a proximal uterostomy. Subsequently, a second laparotomy was carried out because dye could not be coaxed downwards into the bladder. The distal limb of the T-tube was blocked by sticky debris. A number 10 ureteric bougie passed easily from the ureterostomy across the anastomosis to the bladder.

Unfortunately, about 10 days later she developed ileus with peritoneal signs. At a third operation urine was found to have extravasated intraperitoneally from the ureterostomy site despite external drainage. The opportunity was taken again at this time to confirm the adequate patency of the distal repaired ureteric segment. By adequate extraperitonealization of the ureterostomy site with external drainage the patient's wound was completely dry over the next 10 days.

The further convalescence was complicated by a coliform infection of the urine. The organism was resistant to sulphonamides, ampicillin, nitrofurantoin, and tetracycline, but was sensitive to nalidixic acid. Despite the in-vitro resistance to nitrofurantoin, the infection cleared following treatment with this for two weeks, and at review one month later the urine was free from protein, cells, and organisms. During the period when urine collected within the pelvis the blood urea rose to 61 mg./100 ml., but subsequently fell to well within normal limits.

If this patient had given a kidney to her twin sister there is every likelihood that it would have been the left one which would have been used. It could therefore be argued that if she had been used as a donor she would have been spared the lengthy illness described above, as there would have been no left kidney to form a fistula into the cervix. However, what if the ureter to be damaged by the caesarean section had been a right and only ureter because the left one had previously been removed? There is also the fact that this patient had a urinary infection with hospital type of coliform organisms resistant to several antibiotics commonly used in the treatment of urinary infections, and this may recrudesce to give further trouble. Late stenotic complications following ureteric anastomosis are not unknown. We feel thankful that this patient had not been used as a kidney donor, although at the time that this was considered we did not think that there was any ethical objection to the use of an identical twin as a kidney donor.

In view of this experience and the fact that it has been reported many times that glomerulonephritis can recur in a transplanted kidney we would now have reservations to the use of any young person, even if an identical twin, as a donor.—We are, etc.,

MARY G. MCGEOWN.

Department of Nephrology,
Belfast City Hospital,
Belfast.

JOSEPH A. KENNEDY.

Department of Urology,
Belfast City Hospital,
Belfast.

REFERENCES

[1] Murray, J. E., and Lynch, J. J., *J. Amer. med. Ass.*, 1967, 200, 187.
[2] *Brit. med. J.*, 1962, 2, 532.

Radioactive Corpses

SIR,—With reference to your leading article on Radioactive Corpses (6 May, p. 331) the method in use at this institute for warning the mortuary attendant that a body is radioactive is as follows.

For all large radioisotope therapy doses the patient is admitted for an appropriate time dependent on the nature of the isotope, and its biological half-life, and a note is sent to the pathologist to the effect that "If patient X presents for necropsy before a certain date he is to be regarded as a radioactive hazard and the physicist called." This note is pinned behind the mortuary door and discarded after the given date. The responsibility for the issue of this note lies with the senior staff of the radioisotope unit.—I am, etc.,

Cancer Institute,
Melbourne, Australia.

K. H. CLARKE.

Health of Students and Soldiers

SIR,—I read your leading article "Health of University Students" (20 May, p. 457) with considerable interest, and would heartily endorse the policy advocated regarding the state of rapprochement required in the staff/student complex.

I must, however, take issue—if I have interpreted the wording aright—with the suggestion that the control of health in the armed Forces carries a lesser personal touch than that in universities. Certainly, so far as the Army is concerned, and I believe that similar principles apply in the other Services, great emphasis is laid on this very aspect of man-management. If control is to be exercised in any context, then responsibility must be defined. In the Army, responsibility for health devolves on its commanders (in the broadest sense), advised or assisted by the medical services.

While it would obviously be unrealistic to expect a divisional commander and his assistant director of medical services to be *au fait* with the health problems of every man in the division, it is a very different story when one comes down to regimental or battalion level. By tradition, and in practice, this is a close-knit, almost a family community. It would be absolutely wrong to judge that the "usual channels," as might be implied by the less well-informed reader of your leading article, inevitably lead to an impersonal approach to matters of health.

The regimental officer is fitted by training and by situation to be qualified, perhaps uniquely so, to observe, to advise, and generally to care for the men under his command. And associated with the regimental officer in the field of health, and in their common goal of conservation of highly and expensively trained military manpower, is the regimental medical officer. He is the man who must fulfil many roles, both advisory and executive. He does not necessarily wait to be asked for advice, although he must be freely available for consultation. It is his duty to identify himself with his unit, to know its role, to acquire a knowledge of the tasks undertaken by its members, and to help seek out weak or potentially weak links in the health chain, whether these are personal or environmental.

It might indeed be postulated that any university planning a health service could do very much worse than to base this on the practice of the nearest regular battalion of one of our county regiments.—I am, etc.,

Royal Army Medical College,
London S.W.1.

H. G. SKINNER.

Smoking and Atherosclerosis

SIR,—In a previous letter on this subject (16 April 1966, p. 984) I suggested that smoking and dietary sugar affect the arteries in a similar way. Further work with the help of heavy-smoker volunteers indicates that the atherogenic effect of smoking might lie in its ability to induce hyperinsulinism. This conclusion is based on the following experiment.

Twelve male and seven female volunteers were chosen with the only criterion in their selection that they habitually smoked 20 cigarettes, or more, per day. Their ages ranged from 25 to 57 years. After explaining the purpose of the trial, the subjects were asked to fast overnight and abstain from smoking until a fasting blood sample was taken. Each subject then smoked two cigarettes in succession while talking to each other or reading magazines. A second specimen of blood was then withdrawn. After this, each subject was given 100 g. glucose in water, and further specimens of blood were collected at set intervals for blood glucose and serum insulin estimations. According to the original plan, subjects volunteered to abstain from smoking for 14 days after the first part of the experiment, but only three males and two females were able to do so. The above test was then repeated on these subjects. Glucose levels were estimated by the method of Folin and Wu, and serum insulin by immunoassay.

In the accompanying Table are shown the blood glucose and serum insulin levels in the fasting state, before and after smoking two cigarettes, and during the glucose tolerance test. The values found during the period of heavy smoking and after the cessation of smoking for 14 days may also be compared.

Comparison of Blood Glucose and Serum Insulin Levels

Subject and Sex	Stage of Trial	Glucose (mg./100 ml. Blood)					Insulin (μu./ml. Serum)				
		Fasting		30 min.	60 min.	120 min.	Fasting		30 min.	60 min.	120 min.
		Before Smoking	After 2 Cigarettes				Before Smoking	After 2 Cigarettes			
1 M	30 cigarettes/day ..	92	100	151	112	90	87	96	150	156	102
	Stopped 14 days ..	73	78	136	105	70	29	32	54	67	47
2 M	30–40 cigarettes/day	85	90	127	103	84	52	58	112	100	61
	Stopped 14 days ..	66	83	112	100	80	35	40	63	57	38
3 F	25–30 cigarettes/day	98	95	134	119	88	99	96	145	158	98
	Stopped 14 days ..	54	81	126	102	80	86	88	112	110	91
4 F	20–30 cigarettes/day	90	98	145	120	87	33	30	95	84	40
	Stopped 14 days ..	73	108	141	118	80	8	11	26	22	13
5 M	50 cigarettes/day ..	78	84	135	100	89	53	50	149	124	80
	Stopped 14 days ..	69	87	137	99	90	30	34	86	72	66

If excessive insulin response can be defined as insulin levels rising above 100 microunits per ml. serum during an oral glucose tolerance test[1] then subject No. 4 may not be considered to have hyperinsulinaemia. However, the marked drop in insulin response after she stopped smoking for 14 days indicates a relative hyperinsulinism during the period of heavy smoking. The view that hyperinsulinaemia is atherogenic is well documented.[2–5] The suggestion that it is the factor responsible for the liability of heavy smokers to develop atherosclerosis is an expansion of this theory.—I am, etc.,

STEPHEN SZANTO.

Department of Nutrition,
Queen Elizabeth College,
London W.8.

REFERENCES

[1] Grodsky, G. M., Karam, J. H., Pavlatos, F. C., and Forsham, P. H., *Lancet* 1965, 1, 290.
[2] Nikkilä, E. A., Miettinen, T. A., Vesenne, M. R., and Pelkonen, R., ibid., 1965, 2, 508.
[3] Peters, N., and Hales, C. N., ibid., 1965, 1, 1144.
[4] Vallance-Owen, J., *Quart. J. Med.*, 1965, 34, 485.
[5] Welborn, T. A., Breckenridge, A., Rubinstein, A. H., Dollery, C. T., and Fraser, T. R., *Lancet*, 1966 1, 1336.

"Escape from Sanity"

SIR,—On the night of Friday, 9 June, I viewed a television programme entitled "Escape from Sanity" from beginning to end.

As nearly everyone will know, the subject dealt with was schizophrenia, and I regret to say that I consider the presentation to have been an appalling exercise in bad taste. In my opinion it also sailed very near the wind ethically, for I remain to be convinced that all the patients shown were in a condition to give free and comprehending consent to taking part.

As a medical officer of health I am concerned with health education, but the public exhibition of personal suffering and anguish has no place in my concept of this subject. The programme as shown appeared to me to be of very little practical value as an educational project directed towards the lay public, and should never have been mounted on a medium where it is impossible to divorce education from entertainment.

One of the less pleasing features was towards the end, when an apparent member of our profession made a public confession of almost complete ignorance of the subject, which was surely quite unnecessary, and can hardly have done much to improve our image in the eye of the man in the street, or to increase his faith and confidence in us.

Lest any of our more "progressive" colleagues, or members of the staff of the B.B.C., may think that this was an enlightened venture I would remind them that in the eighteenth century lunatic asylums (Bedlam) were opened to the populace for their entertainment by our barbarous and reactionary forebears. Now in the second half of the twentieth century we put patients suffering from mental disorders on television for the edification of the citizens of the Welfare State—such is progress.—I am, etc.,

Littleborough,
Lancashire.
R. G. MURRAY.

Research in General Practice

SIR,—It is becoming increasingly clear that one of the most fruitful remaining fields in which the general practitioner can contribute to the advancement of medicine is in epidemiology. This is particularly true in relation to the regular outbreaks of well-circumscribed "influenzal-like" illnesses which afflict every practice throughout the year. Some of these illnesses, though self-limiting, produce a surprising degree of debility, especially among young adults, and with the advent of specific anti-viral agents perhaps in the foreseeable future it would seem important for us to begin to map out recognizable clinical patterns and relate them to specific viruses.

In this connexion I have been prompted to report one such outbreak in my own practice. The clinical picture was quite distinct. Typically, the patient was a young adult between 25 and 35 years of age who complained of a severe headache of sudden onset accompanied by a characteristic sharp pain in the ocular muscles made worse by any eye movements. There was photophobia, nausea and anorexia, and slight neck stiffness in most cases. The illness generally lasted about 48 hours, but a few patients were ill for periods of up to two weeks, and these had gross muscular weakness and a curious relapsing pattern to the illness. The temperature was elevated in the severe cases, but many remained afebrile throughout. In most cases where there were children in the house they were either unaffected or had only very mild symptoms.

Owing to the enthusiastic co-operation of the local public health laboratory I was able to have stool cultures tested for viruses from most of the cases, and they succeeded in isolating E.C.H.O. virus type 9 from 11 out of 16 cases.

Perhaps the most enlightening feature of this piece of elementary research was the ease with which it could be carried out during routine visiting even when under fairly heavy pressure of work. The patients were uniformly delighted that something positive was being done apart from soothing words and aspirin, and were happy to collect, label, and post their own specimens. Complicated apparatus and time-consuming procedures are simply not required for this sort of study, which I feel might, if sufficiently intensified, produce something of real value.—I am, etc.,

L. P. MARTIN.

Gravesend,
Kent.

Coroners' Jurisdiction

SIR,—Your correspondent Mr. H. A. Kidd (3 June, p. 642) seems to have lost sight of the true function of the coroner in his suggested reforms, and to have ignored the fact that the interests of the medical profession are not the only consideration which should guide the Crown and its officers in the discharge of their obligations to the community.

The fact that there has been criticism of the coroners' jurisdiction "not only by doctors but also by members of the legal profession" does not prove anything, more especially when one remembers that it is a minority of each profession which is involved, that in each case the grounds of criticism differ, and that the remedies suggested by each profession are quite different and only suited to their own particular purposes.

The Crown has a constitutional obligation to protect life, and in discharging that obligation it relies upon coroners to investigate publicly all deaths due to unnatural causes. As a preliminary to this, the coroner must be informed of all deaths which are not known to be natural, so that he can decide upon which he must hold inquests, and as a result of it he must ensure that steps are taken "to prevent the recurrence of fatalities similar to that in respect of which the inquest is being held."[1]

The premises, therefore, upon which the jurisdiction is based are quite simple, and, I would suggest, unassailable from the point of view of the public interest. Difficulties mainly arise out of the fact that, whereas elaborate rules of procedure have been laid down for the guidance of coroners, no official attempt has yet been made to define what are "unnatural causes."

At present each coroner uses his own criteria in considering this fundamental matter, and I would suggest that herein lies the main point of confusion as far as the medical profession is concerned. If Mr. Kidd is interested in this subject it is discussed in some detail in an article to which I have contributed.[2]

In making his arrangements a coroner should consider: firstly, his duty to the Crown; secondly, the convenience of bereaved relatives; thirdly, his other essential commitments; fourthly, the convenience of witnesses, among whom doctors form an important minority; and, finally, his own personal convenience. It is inevitable, therefore, that not everyone can be satisfied.

The suggestion that a coroner should meet or discuss with medical staff before deciding whether to hold an inquest is vague. If the meaning is that a coroner should be thoroughly acquainted with all the circumstances of a case, and in particular with the medical aspects of deaths arising in hospital—for example, prognosis with or without treatment, inherent risk of treatment etc.—then I would readily accept it. If, however, Mr. Kidd expects the coroner to be influenced by the views of a surgeon on the desirability of holding an inquest then he must surely consult also the drivers of cars and the owners of factories, who in other cases are equally liable to embarrassment. This would be a complete abdication of his responsibilities.

No system is perfect, and isolated occasions will always arise in which doctors by folly or by lack of sophistication fail to do justice to themselves in the witness-box, but the publicity is soon forgotten provided that they themselves do not draw attention to it or prolong it. This is surely one of the hazards of medical practice and is more than compensated by the esteem in which those are held who adhere to their ethical and professional standards. Those who appear to have neglected these standards only make news because the vast majority of their colleagues maintain them, and in so doing have nothing to fear from appearing at an inquest.—I am, etc.,

H. H. PILLING,
H.M. Coroner.

Maltby,
Nr. Rotherham, Yorks.

REFERENCES

[1] *The Coroners Rules*, 1953, Rule 27, Statutory Instruments, 1953, No. 205.

[2] Pilling, H. H., *Med. Sci. Law*, 1967, 7, 59.

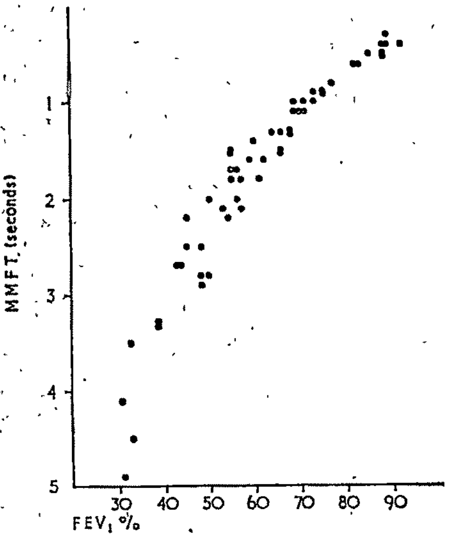
Maximal Midexpiratory Flow Time

SIR,—The first-second forced expiratory volume (F.E.V.$_1$) expressed as a percentage of the forced vital capacity (F.E.V.$_1$%) or unforced vital capacity (F.E.V.$_1$/V.C.%) is widely used as a test for airflow obstruction. The maximal midexpiratory flow rate (M.M.F.R.) and maximal midexpiratory flow time (M.M.F.T.) were introduced by Leuallen and Fowler[1] as tests of ventilatory capacity that were particularly sensitive to obstruction; attention has hitherto been given mainly to the M.M.F.R. We have recently studied the M.M.F.R. and M.M.F.T. in relation to the F.E.V.$_1$ and F.E.V.$_1$%. The measurements were carried out on 54 subjects (46 patients with chest diseases and 8 normal subjects) using a dry recording spirometer (Vitalograph). The M.M.F.T. was found to correlate closely with the F.E.V.$_1$% ($r = -0.94$), except in very severe obstruction, when an M.M.F.T. longer than 3.5 seconds was not matched by reduction in F.E.V.$_1$% below about 30 (see Figure). The

M.M.F.R. did not correlate well with the F.E.V.$_1$%.

We believe there are a number of advantages in including the M.M.F.T. in clinical spirometry:

(1) It can be read quickly from the spirogram, and the presence and severity of airflow obstruction are immediately apparent from its duration.



(2) It may be a more accurate index of obstruction than the F.E.V.$_1$% in severe cases (M.M.F.T. greater than about 3 seconds).

(3) There is no need to use either the F.E.V.$_1$% or the F.E.V.$_1$/V.C.% in the assessment of those cases in which the two percentages differ markedly.

(4) A discrepancy between the M.M.F.T. and the F.E.V.$_1$% can bring to light a faulty forced expiration, particularly when an inaccurate F.E.V.$_1$% is due to a slow start or an incomplete F.V.C. (the M.M.F.T. being less affected).

The forced expiratory time (F.E.T.), which can be estimated spirometrically and clinically, also correlates well with the F.E.V.$_1$%.[2, 3] However, the spirometric F.E.T. cannot be recorded in patients with moderate or severe airflow obstruction with a spirometer such as the Vitalograph, which runs for six seconds only. Moreover, the F.E.T. may be an exhausting procedure for some patients with severe obstruction; or, if they are not required to complete the expiration fully, it is underestimated. Such incomplete expiration does not affect the M.M.F.T. and F.E.V.$_1$% when the negligible volume of airflow is reached towards the end of the expiration.

In the same 54 subjects we found that the M.M.F.R. correlates moderately well with the F.E.V.$_1$,[4] but that the M.M.F.T. does not do so. Our investigation is continuing and we hope to report on it fully in due course.—We are, etc.,

J. J. SEGALL.
B. A. BUTTERWORTH.

Finchley Chest Clinic,
London N.20.

REFERENCES

[1] Leuallen, E. C., and Fowler, W. S., *Amer. Rev. Tuberc.*, 1955, 72, 783.
[2] Rosenblatt, G., and Stein, M., *New Engl. J. Med.*, 1962, 267, 432.
[3] Lal, S., Ferguson, A. D., and Campbell, E. J. M., *Brit. med. J.*, 1964, 1, 814.
[4] Bates, D. V., Woolf, C. R., and Paul, G. I., *Med. Serv. J. Can.*, 1962, 18, 211.

Fees for Health Certificates

SIR,—It is constantly happening that firms instruct actual or prospective employees to seek medical examinations and certificates concerning fitness for special tasks. Here are quite recent extracts from letters:

(1) From a firm of architects to the general practitioner: "Would you be good enough to supply a certificate stating that Mr. X is in good health and able to undertake a tour of duty in the tropics."

(2) From a large nationalized public utility concern to a youth accepted as apprentice: "Will you please arrange to obtain from your National Health Doctor a certificate as to the general state of your health and your ability to undertake the training we propose to give."

The architects were paying for their employee to fly to and travel in West Africa. The nationalized company's representative told us that the training would cost them £2,000. In both cases they refused to consider the extra of the doctor's fee, which they expected the employee to meet. We believe that fees for such medical services should be the responsibility of the firm which has made the demand. Also that a general practitioner should refuse to examine and to certify unless he has obtained the firm's written agreement to pay.

We should be grateful if this letter were published so that the views of our colleagues could be invited.—We are, etc.,

A. S. PLAYFAIR.
W. M. B. STRANGEWAYS.

Cambridge.

Appointment Systems in General Practice

SIR,—Dr. J. S. K. Stevenson's paper (24 June, p. 827), as excellent and as informative as his previous ones, provides answers to questions about how patients use his appointments system. They ring true and are probably valid for most practices, with one notable exception: the number of patients who are prepared to wait for a day or two to see a particular doctor. He found it less than 2%. In our group practice, larger than his and with a higher proportion of patients in social class two, it is much higher. In April I took three days' holiday and missed four surgeries on Thursday, Friday, and Saturday. To test the hypothesis that any partner can miss occasional surgeries without overburdening the others, I asked the receptionists to count the number of patients wanting an appointment with me who were not prepared to wait until Monday, when I would if necessary see all who had. Only one patient made an appointment with my partners. It is difficult to express this as a percentage, because we do not know how many would have made appointments had I been there, but the average for the Thursday, Friday, and Saturday of the three subsequent weeks was 70, the lowest being 54. If we assume that 54 would have made appointments in the week in question the proportion of those who would wait at least two and at most four days was 98%.

That patients will wait for their own doctor is so much accepted by us that if one decides to miss a surgery he need not notify the others, because he knows their work will be infinitesimally affected. At the end of an average-sized surgery last Wednesday the receptionist told me there was a casual—that is, someone who had not made a prior appointment. I said that he was not my patient but Dr. X's, and her reply that he was at Durham Regatta was my first intimation that he had not been steadily consulting in the next room for the past two hours.

I suspect that the explanation lies in different attitudes to family doctoring. Dr. Stevenson and his partners do not attach importance to the doctor–patient relationship; we do. Not, as he suggests, because we are egotistical or think ourselves infallible but because it is more efficient. If you know a patient—his medical history, personality, family relationships, attitude to his occupation, reaction to stress, pain threshold—it is easier to get the history of his complaint, it takes less time to make a diagnosis and prescribe treatment, and it is simpler to explain the prognosis in words appropriate to his temperament and intelligence than if he is a stranger. An established doctor–patient relationship is more efficient. That, and not the incidental satisfaction it may give the doctor, is the justification for personal doctoring.—I am, etc.,

ANDREW SMITH.

Newcastle upon Tyne.

SIR,—I read with considerable interest the article by Dr. J. S. K. Stevenson (24 June, p. 827) describing the experiences of a practice of four partners working by appointment only.

My experience in a single-handed practice working by appointment for over three years is so similar as to be worth recording.[1] Of the appointments 98% are made by telephone. The number of patients attending without an appointment fell rapidly to 9% in 1965, 3½% in 1966, and less than this so far this year. The consultation rate has varied very little, but the fall in visiting is quite dramatic. After the introduction of the appointment system the visits in the first two quarters of 1965 were 841, of 1966 714, and of 1967 560. During this period the list has risen by 225 to 2,400.

Among the reasons for this fall in visiting is a much greater preparedness by mothers to bring fractious babies, knowing that waiting-time will not exceed 11 minutes, and that the waiting-room will be almost empty.

We have in fact heard this so often that we are prepared to put some little pressure on patients to bring children when visits are requested. "Are you not able to bring him up?" is a remark often overheard from the receptionist's desk.

The outstanding advantage to me has been our ability to spread the work load to a much greater extent to suit myself and fit my other commitments. All but a small handful of patients have welcomed the system.—I am, etc.,

C. TAYLOR.

Liverpool.

REFERENCE

[1] Taylor, C., *Medical World Newsletter*, 1967, 2, No. 6, 12.

Obituary Notices

Sir ALEXANDER MACGREGOR, K.B.E., LL.D., M.D., F.R.C.P.GLASG., D.P.H.

Sir Alexander Macgregor, a former medical officer of health for Glasgow, and chairman of the Western Regional Hospital Board (Scotland), died suddenly in a Glasgow hospital on 29 June. He was 86.

[Universal Pictorial

Alexander Stuart Murray Macgregor was born in Arbroath on 7 April 1881, and was educated at Hutchesons' Grammar School, Glasgow, and Glasgow University, graduating M.B., Ch.B. in 1904. He spent four years of resident service in the Royal Infirmary and Belvidere Hospital, gaining the M.D. with honours and gold medal in 1908. A year later he took the Cambridge D.P.H. Thereafter he was formally appointed to the staff of the Public Health Department of the City of Glasgow, already notable for the work of two outstanding medical officers of health, to the second of which he was in due time to become the successor. As a major in the R.A.M.C.(T.A.) he served in the first world war, principally at Gallipoli, and in Egypt, Palestine, and Syria ; and the public health problems, military and civilian alike, which confronted him in these theatres of war so stimulated his interest, ingenuity, and enterprise that he was confirmed in his conviction that the field in which he might best exercise his energy was that of preventive medicine. He was mentioned in dispatches four times, and in 1919 was appointed O.B.E. in recognition of his work in combating malaria in Palestine during the war.

After demobilization he returned to Glasgow, and—first as a senior medical officer, and later as deputy medical officer of health—became deeply immersed in the thronging and complex public health problems of a great community faced with the urgent need for enlightenment, advance, and change. He was particularly preoccupied with such things as general sanitation, sewage disposal, slum dwellings, the activities of port medical officer, the provision of adequate hospital facilities for infectious diseases, tuberculosis and the like, and, perhaps above all, with the challenge of infant mortality and the establishment of sound and progressively efficient maternity services. The last was to remain a principal ingredient of his thought until the end of his life.

A member of the British Medical Association, he was honorary secretary of the section on naval and military medicine at the Annual Meeting in 1920, honorary secretary of the tuberculosis section in 1922, and president of the section of preventive medicine in 1930. In 1926 he was elected Fellow of the Royal College (then Faculty) of Physicians and Surgeons of Glasgow.

In 1925 he succeeded Dr. A. K. Chalmers as medical officer of health, a post which he held until his retirement in 1946. The intervening years were spent in unremitting toil, which tended to occupy him into the hours of darkness, and in the inculcation of the basic principles of his profession into the minds of his subordinates. Practice rather than precept was a telling feature of his habit in this regard. Under his guidance, in which details as well as policy governed his actions, all the services for which he was responsible were so shaped as to become models of their kind. This fact was recognized when, in 1941–2, he was elected president of the Society of Medical Officers of Health, an event which coincided with the conferment of the honorary degree of LL.D. by Glasgow University in 1940, and of a knighthood in the following year. He was an honorary physician to the King in Scotland from 1937 to 1940.

The transference to the custody of the Public Health Department of four large general hospitals—Stobhill, Merryflats, Duke Street, and Oakbank—previously administered by the old Parish Council, gave Sir Alexander an opportunity to begin the transformation of what had been indifferent institutions into what have now become the first-line hospitals of Stobhill, the Southern General, the Eastern District, and the Western District respectively. The experience thus gained proved to be of great moment when, in 1947, Sir Alexander emerged from his retirement on being called upon by the Secretary of State for Scotland to assume the chairmanship of the Western Regional Hospital Board, over which he presided for some seven years. For this work he was honoured in 1955 by the appointment of K.B.E. He maintained a keen interest in public health, and in the organization of the health services, to the end of his life, and his book *Public Health in Glasgow, 1905–1946,* appeared only a few weeks before his death.

There are many who in a personal way will remember Sir Alexander as essentially a fertilizer of the mind of youth, and as one who sought consistently to maintain and enhance the dignity of the medical profession. He was a great humanitarian, and his interest in and enthusiasm for the National Health Service was particularly centred in the possibilities which it presented for providing for clamant human needs.

He married in 1910 Miss Margaret Whyte, who died in 1965. He is survived by two sons and two daughters, all of whom are members of the medical profession.—A. K. B.

Sir ARTHUR MACNALTY writes: Sir Alexander was not only appreciated in Glasgow ; he was rightly regarded universally as one of the most progressive and enlightened of public health administrators. His counsel and advice were valued by us at the Ministry of Health and by other health authorities. In the present century great contributions have been made to the progress of public health by eminent medical officers of health like Shirley Murphy, J. C. Thresh, of Essex, John Robertson, of Birmingham, J. Niven, of Manchester, Arthur Newsholme, at Brighton, and William Savage, of Somerset. Macgregor was of this illustrious company. Sir Alexander's chief recreation was golf. He had a kindly and friendly disposition, and was liked by his acquaintances and beloved by his friends. When he was constructing the municipal hospitals of Glasgow he offered me the medical superintendency of one of them. I was inclined to accept, but my chiefs at the Ministry dissuaded me. Sir Alexander has passed on, full of years and honours, with the satisfaction of a life well spent for the betterment of mankind.

Professor FERGUSON ANDERSON writes: With the death of Sir Alexander Macgregor the last of a generation of great Glasgow doctors, famous not only in their own city but throughout the world, comes to an end. He will be remembered for his pioneering work in the Public Health Department in Glasgow, where his advanced and brilliant policy resulted in the development of a first-rate hospital and outdoor clinic service for the city. His broad interpretation of the various relevant Acts of Parliament, and his wide experience of administration, gave Glasgow a range of medical and surgical facilities second to none throughout the land in the corporation hospitals of that time. His lifetime of work in public health enabled him to portray in a most interesting way the conquest of disease in recent years in his book *Public Health in Glasgow 1905–1946.* This clear and vivid account of change and progress in the city has been widely acclaimed. Innumerable consultants in the west of Scotland owed their start in their specialist career to his foresight and his ability to choose his medical staff wisely. His inspired vision of a link between the corporation hospitals and the university came to be, and made possible the great advances in teaching and research which were to come under professors like the late Noah Morris.

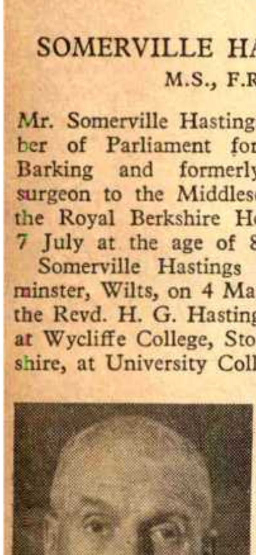
Always of a happy and pleasant disposition, Sir Alexander had a wonderfully cheerful and refreshing faith in human nature which made him a delightful companion. His unique characteristic of charming the opposition into accepting as their concept his own ideas endeared him to those watching with admiration. Although gifted with insight into the frailties of the citizens, especially of his own city, he was unable by nature to speak ill of any man, and he had only friends. Privileged as few are with the possession of a most active mind, he had a retentive memory and outstanding intelligence, and inevitably his advice was sought by great numbers of people from all walks of life.

Sir Alexander married in 1910 Miss Margaret Whyte, who died in 1965, and together this remarkable man and his charming wife enjoyed a long-enduring bond of happiness. The frank and pawky humour of this dear lady made the day-to-day episodes of a busy life an occasion for much laughter and deep understanding between them. Both delighted in being Scots, and the friendly atmosphere of their home allowed no place for humbug or pomposity. Blessed with an alert manner, an upright carriage, and a handsome appearance, Sir Alexander never grew old. In his mature years he would still attract glances from those who saw him as an upstanding and charming gentleman. Throughout his life despite the well-deserved honours he received he remained the most modest of men, anxious wherever possible to remain in the background and with his quiet smile play the part of the interested spectator. Glasgow will not see his like again, and there will be many sad hearts in that great city which has lost a noble servant and an illustrious citizen.

SOMERVILLE HASTINGS, M.B.
M.S., F.R.C.S.

Mr. Somerville Hastings, successively member of Parliament for Reading and for Barking and formerly consultant aural surgeon to the Middlesex Hospital, died in the Royal Berkshire Hospital, Reading, on 7 July at the age of 89.

Somerville Hastings was born at Warminster, Wilts, on 4 March 1878, the son of the Revd. H. G. Hastings, and was educated at Wycliffe College, Stonehouse, Gloucestershire, at University College, London, and at the Middlesex Hospital. While at University College he won the gold and silver medals in botany, a subject which became a life interest, and he was an entrance scholar and governor's prizeman at the Middlesex Hospital. He qualified M.R.C.S., L.R.C.P. in 1902, taking the London M.B. in the same year and the B.S. in 1903. He obtained the F.R.C.S. in 1904 and proceeded M.S. in 1908. At the Middlesex Hospital he was demonstrator of physiology, a cancer research scholar, and house-surgeon, casualty surgical officer, and surgical registrar. He also held the posts of assistant surgeon at the East London Hospital for Children and at the London Throat Hospital. For many years he was surgeon to the ear, nose, and throat department at the Middlesex Hospital, ultimately becoming consultant aural surgeon and lecturer in his old department. He was associated with the hospital for well over sixty years. Hastings served as a captain in the R.A.M.C. during the first world war and in the Emergency Medical Service in the second world war.


[" Illustrated "

Hastings retired from practice in 1945. In that year he was again returned to Parliament as the first member for the Barking constituency, having previously represented Reading in the House of Commons in 1923–4 and 1929–31. He retained the Barking seat at the general elections of 1950, 1951, and 1955. He did not stand for re-election at the 1959 General Election. In 1960 the freedom of Barking was conferred on him. His election in 1923 made him the first Labour member for Reading, and in the first Labour Government of 1924 he was Parliamentary private secretary to the Board of Education. A member of the London County Council from 1932 to 1946, he became chairman of the hospitals and medical services committee of the council in 1934, and occupied the chair for ten years until he became chairman of the council itself in 1944. In the following year he was elected an alderman. He was the second medically qualified occupant of the chair, the other being Sir William Collins, who was present in 1944 to see Hastings take office.

Hastings assisted in the formation of the Socialist Medical Association in 1929, and in that year joined with other medical M.P.s in promoting the idea of a national health service. Elected first president of the S.M.A. he held that office until 1951. He was also a member of the public health advisory committee of the Labour Party. Always interested in the needs and care of children, he was a member of the Curtis committee and vice-chairman of the children's committee of the L.C.C. He was a member of the Medical Planning Commission which presented its draft interim report in 1942.

He had been chairman of the boards of governors of the Hammersmith, West London, and St. Mark's Hospitals and of the North-east Metropolitan Regional Hospital Board, and a member of the Standing Medical Advisory Committee and of the board of governors of Middlesex Hospital. When the British Medical Association held its Annual Meeting at Portsmouth in 1923 he served as a vice-president of the section of laryngology, and he was president of the section of otology of the Royal Society of Medicine in 1928–9.

In addition to surgical papers in his specialty Hastings published *Summer Flowers of the High Alps, Wild Flowers at Home, Toadstools at Home, Alpine Plants at Home,* and *First Aid for the Trenches.*

Hastings married Bessie, fourth daughter of the late W. C. Tuke. They had one son and one daughter. Mrs. Hastings died in 1958.

LADY SUMMERSKILL writes: The idea of a National Health Service germinated in the hospitable atmosphere of Somerville Hastings's Devonshire Street home. It was there that Somerville with his selfless dedication gathered around him a few socialist doctors who felt that medical advice and treatment should be freely available to all. It was known that thousands of people failed to seek treatment because they could not afford to pay fees. At that time we did not approach the future with great confidence, but our meetings were exhilarating. Somerville was a shy man without personal ambition, and he was greatly revered by his colleagues in the Labour Party. He was the complete tolerant Christian. Although a teetotaller, he felt it his duty as a host to provide the type of refreshment which some of his less enlightened friends desired. He was a doctor who was not content with exercising his particular skill upon his patient, but was broad enough in outlook to realize that his whole environment had to be considered. His professional life was restricted to the narrow confines of the ear, nose, and throat, but he sought to impress upon the public the relationship between good health and satisfactory social conditions. Nearly 40 years ago he organized a team of doctors to make a survey of the living conditions of some of the poorer people in Hammersmith, and this showed that poverty and bad housing resulted in physical and mental inferiority. It is pleasant to think that much of what this exceptional man fought for has been achieved, at least in this country.

Lieutenant-Colonel W. C. GRAY, M.B.
CH.B., F.R.C.S.ED., M.R.C.P.GLASG.
I.M.S.(RET.)

Lieutenant-Colonel W. C. Gray, late of the Indian Medical Service, died in Jersey on 2 June 1967. He was 88.

William Cowan Gray was born on 4 October 1878, and received his medical education at the University of Aberdeen, graduating M.B., Ch.B. in 1901. After holding several resident posts he entered the Indian Medical Service in 1905, and served most of his time in the Madras presidency. He held several of the larger and more onerous of the civil surgeoncies in South India, and on two occasions filled a leave vacancy as professor of obstetrics at Madras Medical College and superintendent of the women and children's hospital in that city, where his competence and kindly disposition are still remembered. During periods of study leave he became F.R.C.S.Ed. and F.R.F.P.S.Glasg. On the reorganization of the faculty he became M.R.C.P.Glasg. He had lived in retirement in Jersey for many years.

Sir CLAUDE FRANKAU, C.B.E.
D.S.O., M.B., F.R.C.S.

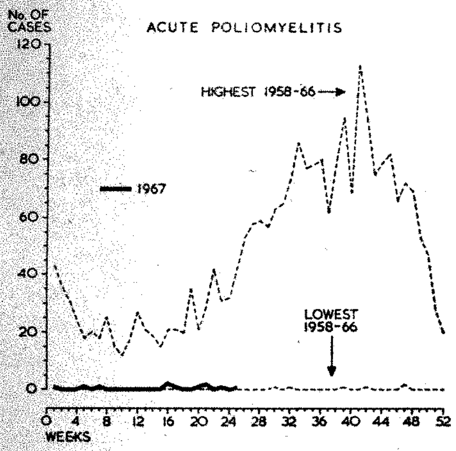
Mr. H. F. ANDERSON writes: Claude Frankau (obituary, 8 July, p. 116) was one of the great general surgeons. He was a towering personality, both surgically and physically. As students we all wanted to be on Claude's firm, and when we qualified we all wanted to be his house-surgeon. The lucky ones became his registrar. He was a superb and courageous surgeon, undertaking anything that was asked of him provided he believed that surgical intervention offered his patients relief from their symptoms. He was also the "doctor's doctor," for it was to Claude Frankau that his colleagues turned when in search of surgical help. He was the most sought-after teacher of his time. His teaching rounds on Tuesday afternoons, always starting punctually at half past one, were open not only to his firm but to anyone in the hospital. His rounds were attended by a large following comprising surgical dressers, more senior students, and housemen and registrars who were working for higher examinations. Secondly, his teaching was simple and direct and above all clinical. His passing will be mourned by generations of students at St. George's Hospital who had the privilege of benefiting from the humanity of his surgery and the greatness of his teaching.

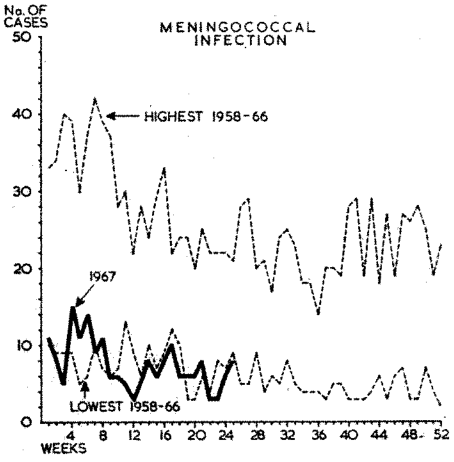
News and Notes

EPIDEMIOLOGY

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of acute poliomyelitis and meningococcal infection in England and Wales. Figures for 1967 are compared with the highest and lowest figures for each week in the previous years shown.





Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available.

	Week Ending 23 June	Week Ending 30 June
Dysentery		
Bedfordshire	15	27
Bedford M.B.	5	17
Greater London	58	58
Wandsworth	4	14
Lancashire	126	92
Northumberland ...	29	32
Suffolk	12	19
Warwickshire	58	62
Yorkshire West Riding ...	47	39
Edinburgh	36	36
Glasgow	26	34
Food-poisoning		
Greater London	58	43
Lancashire	25	20
Blackpool C.B. ...	0	10

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **24 June** (No. 25) and corresponding week 1966.

Figures of *cases* are for the countries shown and for Greater London. Figures of *deaths* and *births* are for the whole of England and Wales (London included) Greater London, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The Table is based on information supplied by the Registrars General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0		0	0	1	0	
Dysentery ..	514	58	80	22	2	542	151	75	15	9
Encephalitis, acute.. ..	4	3		0		3	2			
Enteric fever: Typhoid ..	1	1	0	0		4	0	0	0	
Paratyphoid..	2	2	0	0		4	0	0	0	
Food-poisoning	140	58	13	27		206	27	27	1	
Infective enteritis or diarrhoea under 2 years				19	25				15	36
Measles* ..	6,205	419	31	150	139	6,867	717	77	111	117
Meningococcal infection ..	8	1	4	0		7	0	5	2	
Ophthalmia neonatorum..	29	1	0	0		15	0	1	0	
Pneumonia† ..	97	12	47	1	2	81	13	52	0	2
Poliomyelitis, acute: Paralytic ..	0	0	0	0		0	0	0	0	
Non-paralytic	1	1	0			0	0	0		
Puerperal fever§	75	28	1	0		87	38	9	0	
Scarlet fever ..	307	57	9	13	8	375	37	39	14	11
Tuberculosis: Respiratory ..	211	40	47	0		256	54	33	11	
Non-respiratory ..	56	4	10	0		57	15	12	2	
Whooping-cough	612	99	61	8	47	403	68	30	18	2

DEATHS	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0		0	0	0	0		0	0	0
Dysentery ..	2	0		0		0	0		0	
Encephalitis, acute.. ..					0					0
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	5	0	4	1	1	7	1	0	0	1
Influenza ..	2	0	0	0	0	2	0	0	0	0
Measles ..	0		0	0	0	0		0	0	0
Meningococcal infection ..			0					0		
Pneumonia ..	539	71	19	13	9	418	74	19	12	10
Poliomyelitis, acute.. ..	0	0		0	0	0	0		0	0
Scarlet fever ..	0		0	0	0	0		0	0	0
Tuberculosis: Respiratory ..	28	4	5	0	5	34	5	2	0	5
Non-respiratory ..				0	0				0	0
Whooping-cough	0	0	2	0	1	1	0	0	1	0
Deaths 0-1 year	288	55	22	9	18	304	55	14	8	9
Deaths (excluding stillbirths)	9,256	1460	519	113	172	9,083	1427	510	111	128
LIVE BIRTHS	16,676	2751	894	288	363	16,255	2727	909	254	
STILLBIRTHS	228	32	13			244	39	20		

* Measles not notifiable in Scotland, whence returns are approximate. † Includes primary and influenzal pneumonia. § Includes puerperal pyrexia.

PARLIAMENT

Hospital Treatment Facilities for Drug Addicts

[FROM OUR PARLIAMENTARY CORRESPONDENT]

The extent to which hospitals will be ready to treat drug addicts when the Dangerous Drugs Bill, with its restrictions on prescribing except by licensed medical practitioners, has become law is still the subject of persistent questioning to Government departments. There was more of it when the Bill was discussed on the committee stage in the House of Lords on 5 July.

LADY PHILLIPS, speaking for the Government, told the House that the Government had it in mind to bring the notification regulations into operation in the autumn. Before then it hoped to have set up a panel to advise doctors who were in doubt whether a patient was an addict; to have introduced in connexion with the central records of addicts a special scheme for the identification of heroin addicts which would be used by the treatment centres; and to have introduced, also in the treatment centres, new precautions against the misuse of prescriptions.

It was hoped, she continued, to bring the prescribing regulations into operation early next year. Before then adequate treatment facilities must be provided, arrangements made for the transfer of addicts from general practitioners to hospitals, and for the licensing of doctors at treatment centres to administer, prescribe, or supply restricted drugs.

Assurances Sought

All this came at the end of a general discussion of the operation of the Bill begun by **LORD SANDFORD**. Accepting the special case for starting with heroin and cocaine, he nevertheless contested an impression he thought was gaining ground that other drugs were somehow less dangerous, and he asked the Government to make a public authoritative statement now about the dangers of cannabis and other drugs not included in the Bill.

He also wanted firmer assurances about the provision of treatment centres—the linchpin of the whole scheme—and plans for ensuring the provision of rehabilitation hostels to match them. The Minister of Health had said in the Commons on 3 July that inpatient services for heroin addicts were available in all regional hospital board areas and outpatient services in 12. He hoped it was true, but what did the services consist of; how many addicts were receiving regular treatment; when would the centres be able to cope with the 650 heroin addicts known to the Home Office in January of this year. If a doctor telephoned a hospital and asked that an addict be admitted, could he be accepted straightaway?

There would be a critical stage when the Bill became law and before the regulations were brought into force. The handful of dedicated general practitioners doing their best to treat these demanding patients believed their right to prescribe for heroin and cocaine addicts would be taken away; the Minister had stated that general practitioners would not be licensed under the regulations. Was it sensible to jettison all the skill and experience that had been built up? It was not readily available in the hospitals. There was good reason for considering their point of view, to see whether it was possible to find some framework in which they could co-operate with the treatment centres.

LORD AMULREE, carrying this a stage further, asked if a consultant psychiatrist treating a patient would be allowed to continue treatment, or if the patient would be automatically transferred to a treatment centre. **LORD SEGAL** took the view that the problem was of such extreme urgency that the first emphasis must be on control by means of notification. He suggested that licences should be issued as liberally as possible, so that an appreciable number of general practitioners who already had experience with addicts might receive them. It might be necessary to grant them on a temporary basis, to tide over the immediate phase when the number of notifications might be so high that the specialists designated and licensed by the central authority might not be sufficient to cope with the flood.

Study of Cannabis

LORD STONHAM, Under Secretary for the Home Office, deprecated any suggestions that cannabis was not a serious question. There was probably more traffic in and consumption of cannabis than of any other drug under international control. Smoking it had become extensive only recently. Before the war it was no problem; last year there were over 900 convictions. It was a drug about which there was a considerable area of "no knowledge." The Government were convinced that the essential starting point before action was a careful assessment of all that was known about the drug. Two months ago an advisory committee on drug dependence under the chairmanship of Sir Edward Wayne began a study of the pharmacological, legal, and social aspects. Until they had reported it was premature to consider what, if any, amendment should be made to the law. But the study was evidence of a determination to ascertain the facts and do whatever was necessary.

Hospital Memorandum

LADY PHILLIPS, who speaks for the Ministry of Health, repeated the assurances previously given that regulations prohibiting prescription by general practitioners would not be brought in until the Ministry were satisfied that hospital facilities were adequate. The memorandum of guidance issued to hospital authorities last March recommended inpatient treatment for the withdrawal of heroin in small groups, not more than 12, in mental illness hospitals or psychiatric units of general hospitals. It might be considered desirable to treat separately heroin addicts and others, or to separate younger heroin addicts from older ones. Arrangements for treatment were a matter for clinical discretion.

For addicts unwilling to accept withdrawal treatment, expected to be the majority, the memorandum recommended outpatient services. The load must be shared, and the plan was for psychiatric hospitals in and around London to provide most of the inpatient services, and for the teaching hospitals and psychiatric departments to provide most of the outpatient services, though some hospitals would provide both. There were now in operation 11 outpatient clinics in London, and plans for four others were under urgent consideration.

Describing the results which the Ministry hoped to see, she said that authority to administer, prescribe, and supply heroin would be confined to licensed doctors at a relatively small number of centres. Addicts would be checked against central records to ensure they were not being treated at more than one centre. New precautions would be adopted to prevent the misuse of prescriptions dispensed by retail chemists.

The addict unwilling to accept withdrawal treatment would usually be invited to enter hospital for a short period in which dosage could be accurately assessed. By these means excessive prescribing should be reduced, and perhaps eliminated, and the spread of addiction checked. There was clearly a need for some form of treatment after withdrawal in hospital, but the form it should take was less certain.

The problem of providing effective rehabilitation was very difficult. The Minister had arranged two conferences on the subject—one with psychiatrists, and the other with voluntary bodies and local authorities. There seemed to be support for the idea that after completing withdrawal treatment addicts would benefit from staying in hostels where they could receive some social support and medical supervision. It also seemed, unfortunately, that only a small minority could be expected to complete a period of rehabilitation. In view of this it seemed appropriate to make no initial large-scale provision of hostels, but instead to build on the experience of a few experimental hostels. Several of these had been started by voluntary bodies, and the Government welcomed this initiative.

New Clauses

The new clauses authorizing the Home Office to impose a unified code for the safe-keeping, record keeping, and packaging of drugs (hard and soft), and giving the police powers of search on suspicion, were added to the Bill.

MEDICAL NEWS

University of Birmingham

Professor R. B. HUNTER, F.R.S.(Ed.), has been nominated Vice-Chancellor and Principal of Birmingham University in succession to Sir ROBERT AITKEN, who is to retire in September next year. He is professor of materia medica, pharmacology, and therapeutics at St. Andrews University. Professor Hunter, who is 52, graduated at Edinburgh University in 1938. After service in the R.A.M.C. he was appointed lecturer in therapeutics at Edinburgh and assistant director of the Edinburgh Postgraduate Board for Medicine. In 1948 he went to his present post at St. Andrews. He was dean of the faculty of medicine from 1958 to 1962 and is director of postgraduate medical education. In 1965 he was visiting professor of medicine in the postgraduate school of the University of Adelaide. He is a member of the General Medical Council, a member of the Committee on Safety of Drugs (chairman of the Clinical Trials Subcommittee), and an editor of the *Quarterly Journal of Medicine*. Since 1964 he has been a member of the University Grants Committee and last year he was appointed chairman of the medical subcommittee.

[Viking Studios

Appointments to Chairs

Dr. D. B. BREWER has been appointed to the first chair of morbid anatomy in the pathology department at the Medical School, Birmingham. Dr. Brewer graduated M.B., B.S. at the Welsh School of Medicine in 1943. After service in the R.A.M.C. he worked in the pathology department at Cardiff, first under Professor J. B. DUGUID and later under Professor J. GOUGH. He obtained the M.D.(Lond.) in 1947. In 1948 he was appointed lecturer in pathology at Birmingham University, and after two years as lecturer with the late Professor J. R. SQUIRE in the department of experimental pathology he became senior lecturer in the pathology department in 1953 and reader in 1955. He is a founder member of the College of Pathologists and was admitted to fellowship in 1965.

Professor P. G. H. GELL has been appointed to the chair of experimental pathology at Birmingham University from 1 August. He has held a personal chair in immunological pathology in the same department since 1960. Professor Gell was educated at Stowe School, Trinity College, Cambridge, and University College Hospital Medical School. After qualifying he worked in the Emergency Public Health Laboratory Service and later on the staff of the National Institute for Medical Research. He was appointed reader in experimental pathology in 1948. A research group in basic immunology was established in the department under Professor Gell's direction by the Medical Research Council in 1964 (see *B.M.J.*, 15 August, p. 456).

Naming of Chairs

The chair of obstetrics and gynaecology has been named the Lawson Tait Chair of Obstetrics and Gynaecology. The chair of paediatrics and child health has been named the Leonard Parsons Chair of Paediatrics and Child Health. The chair of pathology has been named the Leith Chair of Pathology. (The Leith chair was previously that of experimental pathology, held by the late Professor J. R. SQUIRE.)

Health Service Report

There was a " striking measure of success " in 1966 according to the Ministry of Health report for that year (Cmnd. 3326, H.M.S.O., 19s. net). Evidence is found in the hospital building programme, use of hospital resources, the " vigorous growth " of the local authority health and welfare services, and the family doctor service.

In general practice the number of prescriptions increased by 7.2% and their cost by 9.8%. At the end of the year there were 536,000 patients waiting for admission to National Health Service hospitals as inpatients, the majority seeking admission to surgical and gynaecological departments. Despite progress, the average length of stay in beds for the acutely ill remained " appreciably higher " than in many other advanced countries, and there was marked variation between hospital regions in England and Wales.

A further fall (183) is recorded in the number of principals providing full general medical services. On the other hand, during the year ended July the number of newly qualified doctors increased by over 130. In the medical schools the intake rose to a level about 30% higher than in 1960–1. Attendances at refresher courses went up from 7,156 to 8,953, some 5,740 doctors taking part. The Ministry's Regional Medical Officers made 1,300 visits to discuss prescribing costs, 100 more than the previous year.

Eight new health centres were opened, giving a total of 31 in England and Wales ; 13 were being built and plans for a further 27 were approved. Though the number of hospital beds fell by 1,468, inpatients treated rose by 2%. A total of 717 more beds were made available for geriatric and chronic sick cases. The number of medical laboratory technicians trained in techniques for testing for cancer of the cervix increased from 382 to 545. By the end of the year 112,849 women a month were being screened, compared with 64,000 a month in 1965. On hospital building the report comments that the most important single lesson learned from the previous five years' work was that the rate of achievement depends directly on the intensity with which planning and design manpower is utilized. The ability to manage hospital building on a national scale, it observes, is the envy of many other countries.

Expenditure on the health and welfare services for the 1965–6 financial year was £1,241m., over 4% of the national income. The cost for the current year is put at £1,367m.

University of Newfoundland Medical School

Dr. IAN E. L. H. RUSTED has been appointed dean of the new medical school at the Memorial University of Newfoundland. He is physician to the General Hospital and chairman of the department of medicine at St. John's and director of the Memorial University medical research unit. Dr. Rusted received his training at Memorial University College, as it then was, Trinity College, University of Toronto, and Dalhousie University. He took the M.Sc. at McGill, and has held a fellowship in medicine at the Mayo Clinic. He is a Fellow of the Royal College of Physicians (Canada), a Fellow of the American College of Physicians, and Vice-President - elect of the Royal College of Physicians and Surgeons of Canada. His main research interests are thyroid disease and hypertension. He has also worked on mitral-valvular disease and diabetes.

Lord TAYLOR has taken office as President of the University (see *B.M.J.*, 1966, 18 June, p. 1550).

New Research Building at Hammersmith

A building to house the Medical Research Council's cardiovascular research unit was opened on 10 July at the Royal Postgraduate Medical School. It has been presented by Mr. JOSEPH COLLIER in recognition of the benefit he has received from medical science. In a short speech after visiting the building Mr. ANTHONY CROSLAND, M.P., Secretary of State for Education and Science, referred to the work of the unit as " extraordinarily impressive."

Kent Postgraduate Medical Centre

On 8 July, following a dedication by the Lord Bishop of Dover, Professor Sir JOHN MCMICHAEL, F.R.S., opened the new building of the Kent Postgraduate Medical Centre at Canterbury. The Centre, which is on the main drive of the Kent and Canterbury Hospital, occupies a total area of 5,400 sq. ft., and together with equipment cost £26,000. Besides offices and a kitchen, it contains a common room, a museum–demonstration room, the Linacre library, a tutorial room, and the Harvey lecture hall. The last two rooms can be thrown together to provide accommodation for a total audience of 140.

In his opening address, Sir John McMichael quoted Sir Francis Fraser's dictum to medical teachers: " Never let your pupils see you doing anything second-rate." Sir John reminded his audience that many of the young doctors who were taking part in programmes of vocational and continuing education at present would still be practising in the twenty-first century, and he emphasized that much of the responsibility for the competence of future doctors lay with the postgraduate medical centres attached to peripheral hospitals.

The organizers of the Centre hope that the new building will enable the already flourishing programme of postgraduate education (see *B.M.J.*, 1966, 2, 295)—which besides medicine includes dental and veterinary surgery and the related sciences—to continue and to be expanded. The opening scientific lecture in the new building, on myelomatosis by Professor Jan Waldenström, was due to be given on 12 July.

British Association of Urological Surgeons

The following have been elected officers for 1967–8: *president*, Mr. A. W. Badenoch; *vice-president*, Mr. W. S. Mack; *honorary secretary*, Mr. J. F. R. Withycombe; *honorary treasurer*, Mr. Howard G. Hanley.

People in the News

▶ Captain J. S. Cox, Royal Army Medical Corps, has had the M.B.E. conferred on him for gallant conduct in Aden.

Grants and Awards

Dr. Trevor H. Howell has been awarded the Willard O. Thompson gold medal by the American Geriatrics Society for distinguished contributions to geriatric medicine.

Coming Events

British Academy of Forensic Sciences.—Scientific meeting, "The Hazards of Modern Life," 21–22 July, Institute of Psychiatry, Maudsley Hospital, London S.E.5. Admission by ticket. Application to Secretary-General, British Academy of Forensic Sciences, 37 Welbeck Street, London W.1.

Israel Medical Association.—Congress, "Human Genetics," 1–9 August. Details from office of Seventh World Assembly of the Israel Medical Association, Beth Harofe, 1 Heftman Street, Tel Aviv.

British Council for Rehabilitation of the Disabled.—Residential seminar on rehabilitation engineering services, 4–6 August, Digby-Stuart College, London S.W.15. Details from B.C.R.D., Tavistock House South, Tavistock Square, London W.C.1.

Societies and Lectures

For attending lectures marked ● a fee is charged or a ticket is required. Applications should be made first to the institution concerned.

Monday, 17 July

Institute of Laryngology and Otology.—5.30 p.m., combined staff consultation clinical meeting.

Royal Free Hospital.—5.15 p.m., Professor T. Doxiades (Athens): Modern Aspects of Amoebiasis.

Tuesday, 18 July

B.B.C.—2 Television.—1.15 p.m., medicine today: Heart Failure. (Sponsored by A.S.M.E.)

London Jewish Hospital Medical Society.—8.15 p.m., Dr. S. Weinberg (New York): Bullous Diseases of Infancy and Childhood.

Royal Postgraduate Medical School.—4 p.m., Mr. G. C. Knight: Stereotactic Tractotomy in Mental Illness.

Wednesday, 19 July

Royal College of Surgeons of England.—4 p.m., Pocklington memorial lecture by Professor L. E. Zimmerman (Washington, D.C.): Cancerous, Precancerous, and Pseudocancerous Lesions of the Cornea and Conjunctiva.

Stoke Mandeville Hospital.—(1) 12.15 p.m., Dr. R. Spalding Smith: Barium Enemas. (2) 6 p.m., Dr. A. Stephen Hall: *X*-ray Quiz.

Thursday, 20 July

Royal Postgraduate Medical School.—4 p.m., Professor T. Doxiades (Greece): Amoebiasis.

Friday, 21 July

Royal College of Surgeons of England.—3 p.m., Charles Tomes lecture by Dr. F. A. Henny (Detroit): An Evaluation of High Mandibular Condylectomy for Temporomandibular Dysfunction.

Royal Postgraduate Medical School.—(1) 10.15 a.m., Mr. J. P. M. Clark: Peripheral Surgery in Spastic Paralysis; (2) 11.30 a.m., Mr. W. H. Stephenson: Clinicopathological Conference.

Appointments

Brigden, W. W., M.D., F.R.C.P. (consulting cardiologist to the Royal Navy).

Knyvett, A. F., M.B., M.R.C.P., M.R.A.C.P. (medical superintendent, Royal Brisbane Hospital, Queensland).

Liverpool Regional Hospital Board.—C. F. Conway, M.B., F.F.A. R.C.S., D.P.H. (consultant anaesthetist to Chester Royal Infirmary); S. M. Hart, M.B., F.F.A. R.C.S. (consultant anaesthetist to Broadgreen Hospital); P. Harper, M.B., D.P.M. (consultant psychiatrist to Rainhill Hospital); Phyllis E. D'Netto, M.R.C.P.Ed., D.C.H. (consultant geriatrician to Deva and Moston Hospitals).

New Issues of Specialist Journals

Obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London W.C.1.

ANNALS OF THE RHEUMATIC DISEASES

Contents of the July issue are as follows:

Immunocytology in Arthritic Joints. M. L. Barnhart, J. M. Riddle, and G. B. Bluhm.
Components of the Fibrinolytic System in Synovial Joints. D. E. Caughey and T. C. Highton.
Significance of Antinuclear Factor in Older Persons. R. F. Willkens, R. R. Whitaker, R. V. Anderson, and D. Berven.
Salivary Flow Rates and Iodide Trapping Capacity in Patients with Sjögren's Syndrome. D. K. Mason, R. McG. Harden, J. A. Boyle, M. K. Jasani, J. Williamson, and W. W. Buchanan.
Intra-articular Hydrocortisone in Osteoarthrosis. K. D. Shah and V. Wright.
Changes in the Antigenic Properties of Connective Tissue in the Skin of Embryonic Rats during Development. D. G. Scott and N. R. Rowell.
Rheumatoid Changes in the Metacarpophalangeal Region as a Cause of Bunnell's Sign. K. Vainio.
Blood Groups ABO and Rh(D) Factor in the Rheumatic Diseases. I. Stoia, R. Ramneantu, and M. Poitas.
Antiglobulin Factors in Sera from Patients with Rheumatoid Arthritis and Normal Subjects. G. Torrigiani and I. M. Roitt.
Heberden Society. Book Reviews. Notices. Abstracts.

Volume 26, No. 4. Yearly subscription (6 numbers) £4 4s., abroad £4 15s.

BRITISH JOURNAL OF INDUSTRIAL MEDICINE

Contents of the July issue are as follows:

Individual Variations in Sickness Absence. P. J. Taylor.
Mortality in a Movie Projectionist Union in Boston, 1910–64. B. G. Ferris, jun., and J. Worcester.
Physique and Serum Lipids of Young London Busmen in Relation to Ischaemic Heart Disease. R. M. Oliver.
Use of the Albino Guinea-pig to Detect the Skin-sensitizing Ability of Chemicals. M. A. Stevens.
Early Signs of Lead-exposure: A Comparative Study of Laboratory Tests. A. de Bruin and H. Hoolboom.
A Cooling System for Impermeable Clothing. J. P. Gleeson and J. F. Pisani.
Effects of Pulsed Currents on Respiration and the Heart. W. R. Lee, S. Zoledziowski, and S. Temiyachol.
Investigation of a Minor Asbestos Hazard. M. C. S. Kennedy and R. Routledge.
Miscellanea:
  Protection of Employees with Defective Vision. J. P. W. Hughes and M. A. Cooke.
  Apparent Onset of Coal-workers' Pneumoconiosis after Leaving the Mines. N. K. Coni.
  A New Method for Calibrating the Kofranyi-Michaelis Respirometer. C. T. M. Davies and D. S. Shirling.
Book Reviews.

Volume 24, No. 3. Yearly subscription (4 numbers) £3 3s., abroad £3 10s.

Universities and Colleges

BIRMINGHAM

The title of university clinical lecturer has been conferred on the following: Mr. R. L. Edwards, part-time consultant obstetrician and gynaecologist to the United Birmingham Hospitals, from 1 May 1967; Dr. J. Insley, part-time consultant paediatrician to the United Birmingham Hospitals, from 1 March 1967; Dr. R. E. Nagle, part-time consultant cardiologist to the United Birmingham Hospitals and the Regional Hospital Board, from 1 April 1967; Dr. J. Stuart, consultant haematologist to the United Birmingham Hospitals, from 1 July 1967.

The title of senior clinical tutor has been conferred on the following: Mr. M. B. Stanton, consultant ear, nose, and throat surgeon to the Birmingham and Midland Ear and Throat Hospital, from 1 January 1967; Mr. R. S. Sneath, consultant orthopaedic surgeon to the Royal Orthopaedic Hospital and Selly Oak Hospital, from 1 October 1966.

Appointments.—Mr. J. R. Geddes and Mr. D. A. K. Woodward (clinical tutors in surgery for dental students).

ROYAL COLLEGE OF SURGEONS OF EDINBURGH

At a meeting of the College held on 12 May, the following candidates having passed the requisite examinations were admitted Fellows:

P. M. Atkinson, H. A. M. H. Badran, D. L. Bailey, R. S. Bartholomew, S. K. Beshara, S. L. Biddulph, W. E. Birkenstock, W. N. F. Boughey, G. A. Bunch, V. W. Burton, D. W. Cairns, J. M. Cairns, I. B. Chakravarti, A. Wing-Tai Chan, M. A. Choudry, A. A. Chowdhury, P. I. Condon, B. Cruickshanks, Abdul-Razzak S. Dabbagh, K. R. De, Caroline M. Doig, J. B. Garston, A. D. Garud, Y. V. Ginde, L. H. Grundlingh, M. A. Hamoud, G. El D. M. Hamza, A. Higham, N. J. B. Hitchcock, J. A. B. Hokin, E. G. Holmes, E. M. Holt, B. N. Irani, S. Jamal, S. Jawaheer, R. F. Jones, C. P. Joseph, E. Kabir, A. M. Karmody, B. Z. Katalinic, (Mrs.) Mahmooda Khan, M. I. Khan, P. E. Kiely, U. T. Kosalge, (Miss) Piloo D. Kotwal, T. D. Kretzmar, W. S. P. McGregor, R. A. McWilliam, F. Ma, C. J. Magarey, N. Majumdar, M. J. R. Marsh, G. S. Martinez, M. A. Matin, T. S. Maung, M. A. Mirza, R. Mustafa (Al Kattan), K. K. Nair, M. Y. Najjar, J. P. O'Brien, C. A. Quick, K. C. Rankin, W. J. C. C. Rich, E. S. Rosen, R. C. Sahu, S. Selvarajah, J. H. Shah, K. Shanmuganathan, G. A. Sheikh, M. J. Simcock, J. T. Snow, R. S. Sodhi, J. A. Spencer, E. A. Sue-A-Quan, J. J. Talati, M. Tasleem, Ll. A. Toft, B. A. Trevitt, M. J. Troy, A. R. Undre, A. J. V. M. Van Merwyk, C. S. Viswanathan, S. M. Vitharana, A. C. Warr, R. H. Weeks, B. Wheatley, J. Winch, J. D. Wisheart.

Deaths

Roberts.—On 5 July 1967 in hospital, Kenneth Roberts, L.M.S.S.A., D.A., of Droitwich, aged 77.

Correction

The appointment of Dr. Edward Cooper at Leeds University, announced in the issue of 1 July, is the Harold Mackintosh Professor of Cancer Research and Director of Cancer Research.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON W.C.1. TELEPHONE: 01-387 4499. TELEGRAMS: *Aitiology, London W.C.1.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.
Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs.
ADVERTISEMENT AND SUBSCRIPTION ORDERS should be addressed to The Manager at B.M.A. House, London, or at 415 Bourke Street, Melbourne, Victoria, Australia.
MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the British Medical Association, B.M.A. House, London, or to the Scottish Secretary, B.M.A. Scottish Office, Drumsheugh Gardens, Edinburgh.

BRITISH MEDICAL JOURNAL

LONDON SATURDAY 22 JULY 1967

Pointers

Bristol Annual Meeting
Scientific Proceedings (pp. 227–236).
A.R.M. (*Supplement*, pp. 69–98)
Lord Cohen's Gold Medal (*Supplement*, p. 99).
Leader (p. 192), letter (p. 245).

Management of Ulcerative Colitis: Favourable results of early radical surgery reported by Professor J. C. Goligher and colleagues (p. 193). Leader at p. 188.

Dwarfism: Acute metabolic response to injected human growth hormone was greater in patients with hypopituitarism investigated by Dr. K. E. W. Melvin and colleagues (p. 196). Leader this page.

Chronic Intestinal Ischaemia: Mr. J. Kennedy Watt and colleagues report successful revascularization in proved cases (p. 199).

Chronic Bronchitis: New long-acting sulphonamide is more valuable in prophylaxis than in treatment of acute exacerbations, according to Dr. A. Pines (p. 202).

Augmented Histamine Tests: Mr. R. J. Abernethy and colleagues found differences in expressing results of test responses unlikely to alter conclusions derived therefrom (p. 205).

Dangers of Thorotrast: Dr. A. O. Langlands and colleagues consider progressive loss of splenic function may occur as a result of this irradiation (p. 206).

Unexplained Digital Ischaemia: Mr. P. R. Hawley and colleagues demonstrated occult neoplasm in six patients presenting with "Raynaud's disease" (p. 208).

Unusual Sunburn: Dr. A. E. A. Ridgway reports retinopathy from eclipse exposure (p. 212).

E.S.R. and the Pill: Dr. J. Ll. Burton found the rate raised in healthy women (p. 214).

Radiation Sickness: Pyridoxine gave good results in the hands of Dr. H. Mattie and colleagues (p. 215).

Case Reports: Englemann's disease (p. 217). Phenindione-induced neuropathy (p. 218).

Medicine Today: Article on heart failure complementing B.B.C. 2 television programme (p. 219).

Today's Drugs: Special article giving advice on prescribing in pregnancy (p. 220).

Pertinax: Without Prejudice (p. 237).

Ortho-dianisidine: Suspected carcinogenic properties for laboratory staff. Letter (p. 238), leader (p. 189).

National Kidney Centre: Letter from Dr. S. Shaldon, the medical director (p. 241).

Abortion: Mr. Steel's Bill through Commons (p. 250).

Children of Short Stature

"Why is he so short? Why won't he grow?" These are questions frequently asked by parents and not always easy to answer. Recently D. W. Smith has given illustrated descriptions of 52 syndromes in which short stature is a feature.[1] The diagnosis of a few of these conditions requires no more than the eye of the experienced clinician who has seen the condition previously, and in future it may often be made with the help of a computer. But sometimes no firm diagnosis can be made even after many investigations.

Conditions for which treatment may be available must be specially sought first. They include malnutrition, depression of appetite due to emotional deprivation, malabsorption, congenital heart disease, and chronic kidney disease. Mild degrees of hypothyroidism may be difficult to diagnose and should be considered in any child with failure of growth. Excess of corticosteroid leads to retardation of growth and is more often due to administration of these hormones than to Cushing's syndrome.

Children with chromosomal disorders such as Down's syndrome (mongolism) and gonadal dysgenesis are short, and in the investigation of a girl of short stature a buccal smear to determine the sex chromosomes is an essential and simple investigation. When, however, gonadal dysgenesis is associated with chromosomal mosaic—that is, cells with different complements of chromosomes—the buccal smear may be normal and the diagnosis can be made only by further investigation of the chromosomes.

In a few children failure of growth antedates birth. They have a birth weight below that expected for the period of gestation and have been called "low birth weight dwarfs." No doubt there are many reasons for retardation of intrauterine growth,[2] and in the individual child the condition often remains unexplained.

In practice the diagnosis of most of the conditions so far mentioned can usually be made or excluded on the basis of a careful clinical history, a physical examination, and with the help of a few carefully selected investigations. Once they have been excluded, the clinician has to decide whether his patient is a normal child but of short status, or has hypopituitarism, or falls into the group of children whose failure of growth cannot be adequately explained.

When hypopituitarism is due to a demonstrable lesion of the central nervous system, such as a craniopharyngioma, the diagnosis is usually but not always easy. But in the idiopathic type it is difficult and in the past was often delayed until, at the expected age, failure of sex hormone secretion gave additional evidence of pituitary failure. Now that human growth hormone is available for treatment, earlier diagnosis has become important. Supplies of this hormone are scarce because it cannot at present be synthesized but has to be extracted from pituitary glands obtained at necropsy. It appears to be of little value in the treatment of short children whose failure of growth is not due to deficiency of the growth hormone. Correct diagnosis is therefore important so that hormone will be given only to children likely to benefit from it.[3]

© *British Medical Journal*, 1967. All reproduction rights reserved.

The June issue of the *Archives of Disease in Childhood* contains four papers on the diagnosis of hypopituitarism as well as an annotation by A. Prader,[4] who with his colleagues in Zurich has contributed so much to the subject. The first three papers come from the Institute of Child Health in Birmingham and evaluate critically certain laboratory tests.[5–7] The fourth paper comes from the Institute of Child Health and the Hospital for Sick Children, Great Ormond Street, London,[8] and stresses the importance in diagnosis of accurate and repeated measurements of height, weight, skeletal maturity, and skinfold thickness.

These studies, and the study by Dr. K. E. W. Melvin and his colleagues from the Royal Postgraduate Medical School at page 196 of the *B.M.J.* this week, show that at present there is no single reliable diagnostic test for deficiency of growth hormone. A battery of tests is required, and some of these are time-consuming and difficult for the patient, the nurses, and the laboratory staff, and ideally should be undertaken only in a metabolic unit. The best and most simple guide in reaching a decision whether to submit a short child to such investigations is the growth curve.[9] Accurate recording of height and weight of these children at regular intervals is essential. Too often these measurements are done inaccurately by inexperienced staff, with unreliable height measures and balances. The charts prepared by J. M. Tanner and R. H. Whitehouse, of the Institute of Child Health, University of London, are satisfactory for the purpose of recording these data, and the height of children in whom a diagnosis of deficiency of growth hormone has to be entertained will fall well below the third centile. In idiopathic hypopituitarism, the growth curve begins to flatten during the first two years of life, and height deviates progressively from the third centile. In small normal children the height is usually only just below that level and with advancing age tends to approach it or at least runs parallel to it. In the child with retardation of intrauterine growth the degree of stunting tends to be intermediate. The bone age tends to be more delayed in the child deficient in growth hormone, even without associated hypothyroidism, than in either the small normal child or the child with retardation of intrauterine growth.[8]

Though spontaneous hypoglycaemia may be a symptom of hypopituitarism, particularly in early childhood, L. Stimmler and G. A. Brown[6] found the response to insulin-induced hypoglycaemia (insulin tolerance test) to be of little value in the diagnosis of growth-hormone deficiency. In some but by no means all children with deficiency of this hormone appropriate tests will show up a deficiency of thyroid-stimulating hormone or corticotrophin (A.C.T.H.) or both, and in a few the level of serum cholesterol is raised without evidence of hypothyroidism.[5]

Probably the two most useful tests for detecting deficiency of growth hormone are the plasma growth-hormone response to insulin-induced hypoglycaemia[10] and the nitrogen-retention test during a short period of treatment with human growth hormone.[11] Stimmler and Brown[6] found that all their seven patients with hypopituitarism failed to produce an adequate increase in the concentration of growth hormone in the plasma in response to insulin-induced hypoglycaemia. However, four other children of short stature but without clinical evidence of hypopituitarism also failed to respond adequately. In other words, a normal response appears to rule out a diagnosis of growth-hormone deficiency, but an abnormal response is not absolutely diagnostic. Though in their patients the intravenous insulin test did not give rise to anxiety, it requires extreme watchfulness. The recent observation of J. J. Gagliardino and his colleagues[12] that vasopressin raises serum levels of growth hormone in normal children and adults but not in those with hypopituitarism may lead to the development of a safer test. At present only few laboratories are getting reliable results with the delicate radio-immunological assay of growth hormone.

As a single test the nitrogen-retention test is probably the most reliable, though time-consuming. Brown, Stimmler, and J. G. Lines[7] determined the nitrogen retention produced by administration of human growth hormone to 22 short children, 10 of whom had hypopituitarism. They found increased nitrogen retention in all but two of the children, but it was greater and longer lasting in the group with hypopituitarism. Dr. Melvin and his colleagues, in their study of the acute metabolic response to injected human growth hormone, also find nitrogen retention to be most marked in patients with hypopituitarism, but regard the fall in blood urea as an even more useful distinguishing feature. That the nitrogen-retention test occasionally gives misleading results has been reported by several groups of workers.[11 13] Prader and his colleagues[4] have shown that when growth-hormone deficient children are given the hormone the serum α-amino-nitrogen increases and the α-amino-nitrogen clearance decreases, presumably because of increased transport of amino-acids into the cells.

The final proof of growth-hormone deficiency comes from a significant growth spurt in response to long-term treatment with the hormone. Children whose short stature is not due to deficiency of this hormone do not respond with a sharp increase in the rate of growth. Unfortunately there are difficulties even with this therapeutic test, because some children with growth-hormone deficiency develop antibodies to human growth hormone during the first few months of treatment which block its effect.[14]

[1] Smith, D. W., *J. Pediat.*, 1967, **70**, 463.
[2] Warkany, J., Monroe, B. B., and Sutherland, B. S., *Amer. J. Dis. Child.*, 1961, **102**, 249.
[3] *Brit. med. J.*, 1967, **2**, 64.
[4] Prader, A., *Arch. Dis. Childh.*, 1967, **42**, 225.
[5] Hubble, D., ibid., 1967, **42**, 228.
[6] Stimmler, L., and Brown, G. A., ibid., 1967, **42**, 232.
[7] Brown, G. A., Stimmler, L., and Lines, J. G., ibid., 1967, **42**, 239.
[8] Clayton, B. E., Tanner, J. M., Newns, G. H., Whitehouse, R. H., and Renwick, A. G. L., ibid., 1967, **42**, 245.
[9] Tanner, J. M., and Whitehouse, R. H., *Brit. med. J.*, 1967, **2**, 69.
[10] Roth, J., Glick, S. M., Yalow, R. S., and Berson, S. A., *Science*, 1963, **140**, 987.
[11] Prader, A., Illig, R., Széky, J., and Wagner, H., *Arch. Dis. Childh.*, 1964, **39**, 535.
[12] Gagliardino, J. J., Bailey, J. D., and Martin, J. M., *Lancet*, 1967, **1**, 1357.
[13] Joss, E., Rossi, E., Zahind, G., and Zuppinger, K., *Minerva pediat.*, 1966, **18**, 1811.
[14] Prader, A., Zachmann, M., Poley, J. R., Illig, R., and Széky, J., *Helv. paediat. Acta*, 1967, in press

Fulminating Ulcerative Colitis

Ulcerative colitis is a common disease, of unknown aetiology and without a completely satisfactory method of treatment. Medical therapy may control an individual attack but has little apparent effect on long-term prognosis. Surgical treatment usually entails a major, if not a radical, operation on what is often a desperately sick patient. Recent careful studies of large series of patients in which the severity and the extent of the disease have been precisely defined have provided important clues to the course and prognosis of the disease, and largely as a result of these some logical approach to therapy may be indicated, especially in the immediate management of an individual attack of colitis.

F. C. Edwards and S. C. Truelove,[1] in a study of 624 patients admitted to hospital in Oxford between 1938 and 1962, showed clearly the close relationship between the clinical severity of an attack and the possibility of death in that attack. The risk rose from 0.7% in a mild first attack to 9% in a moderate and to no less than 38% in a severe first attack. In relapses the figures were respectively 0.9%, 11%, and 2%. These are the overall figures for the total period, and it is of considerable interest that the introduction of the corticosteroids in about 1952 was followed by a considerable fall of mortality in the moderate group but caused little change in the prognosis of the severe cases. J. McK. Watts and his colleagues[2] surveyed 204 patients with ulcerative colitis who presented at the time of their first admission to hospital between 1952 and 1963 and confirmed the close correlation between severity of the attack and mortality—0% in the mild, 2% in the moderate, and 8% in the severe episodes. Prognosis was also clearly related to the increasing age of the patient and the extent of disease in the large bowel.

The usual treatment in severe cases with diarrhoea, bleeding, fever, tachycardia, anaemia, and raised erythrocyte sedimentation rate is intensive medical therapy, which usually includes corticosteroids. Surgery is kept in reserve for failed medical treatment or when there is perforation or uncontrolled haemorrhage. Even in skilled hands the operative mortality in such cases is high. S. O. Aylett,[3] for example, reported nine deaths in 53 fulminating cases (17%). J. E. Lennard-Jones and A. B. Vivian[4] have recorded a rate of 31% and J. C. Goligher[5] 29% in such patients. These figures are from specialist centres, and the mortality for emergency colectomy must be presumed to be higher still in the hands of less experienced surgeons who deal only occasionally with such problems. In such circumstances a good case can be made out for emergency ileostomy or caecostomy with decompression of the colon as a simpler alternative which might tide the patient over into a more satisfactory condition for radical surgery.[6-8]

Would earlier recourse to surgery improve on the disappointing prognosis of the fulminating cases? N. D. Gallagher and his colleagues[9] from Sydney, Australia, reported on 23 patients for whom such a policy was adopted. For 22 surgical operation was performed when there was failure to improve or sudden deterioration in spite of supportive treatment. Marked dilatation of the colon, rebound tenderness, and recurrent hypotension were regarded as urgent indications for operation. There were only two deaths (9%), which compares sharply with eleven deaths in the previous 18 patients when surgery, if it was performed at all, was a heroic measure.

In this issue of the *B.M.J.* (page 193) Professor J. C. Goligher and his colleagues from Leeds report on 74 patients with severe attacks of ulcerative colitis on whom operation was performed unless there was unequivocal evidence of rapid improvement in the patient's condition on conservative treatment. This series is compared with an earlier group of 124 patients managed along more conventional lines during 1952–63. The overall mortality in the more recent series was only 1.3% in contrast with 11.3% previously. Since January 1964 there have been no medical deaths, and the operative mortality in the 44 patients requiring urgent surgery has amounted to only one case. This is in contrast with six medical deaths in 124 cases during the preceding period (a mortality of 4.8%), and the surgical mortality of eight patients (20%) in the 40 treated during the earlier period. Although Goligher and his colleagues freely admit that this is not a fully controlled therapeutic trial, the results strongly suggest that, in special centres where there is extensive experience in both the medical and the surgical approach to the treatment of colitis, early radical surgery may have considerable advantages for patients with fulminating colitis who fail to respond rapidly to thorough medical treatment.

---

[1] Edwards, F. C., and Truelove, S. C., *Gut*, 1963, **4**, 299.
[2] Watts, J. McK., de Dombal, F. T., Watkinson, G., and Goligher, J. C., ibid., 1966, **7**, 16.
[3] Aylett, S. O., *Brit. med. J.*, 1966, **1**, 1001.
[4] Lennard-Jones, J. E., and Vivian, A. B., ibid., 1960, **2**, 96.
[5] Goligher, J. C., ibid., 1961, **1**, 151.
[6] Cachin, M., Pergola, F., and Safavian, A., *Bull. Soc. méd. Hôp. Paris*, 1965, **116**, 249.
[7] Hickey, R. C., Tidrick, R. T., and Layton, J. M., *Arch. Surg.*, 1963, **86**, 764.
[8] Truelove, S. C., Ellis, H., and Webster, C. U., *Brit. med. J.*, 1965, **1**, 150.
[9] Gallagher, N. D., Goulston, S. J. M., Wyndham, N., and Morrow, W., *Gut*, 1962, **3**, 306.

Carcinogenic Hazard

A letter in our correspondence columns this week (page 238) draws attention to the possible dangers of substances chemically related to benzidine, itself a known carcinogen in man and animals. Ortho-dianisidine (dimethoxy-benzidine) and ortho-tolidine (dimethylbenzidine) are likewise suspect as possibly carcinogenic in man. They are used in the manufacture of dyestuffs and in some industrial and chemical laboratories.

There is a clinical suspicion, as yet no more, that tumours of the urinary tract are occurring with undue frequency among laboratory workers. It has not yet been possible to conduct epidemiological studies on makers and users of ortho-dianisidine and ortho-tolidine, because usually workers in the dyestuff industry who have come into contact with them will have had even more contact with benzidine, an extremely potent urinary tract carcinogen in man. Ortho-dianisidine and ortho-tolidine are carcinogenic in animals,[1 2] and metabolites of ortho-tolidine have been found in the urine of men who work with the substance that would appear to be very similar to the carcinogenic metabolites derived from benzidine.[3] Indeed, ortho-tolidine was listed in the Prescribed Industrial Diseases Regulations in 1953 as a urinary-tract carcinogen.[4]

Since trivial exposure to benzidine has been known to be associated with carcinoma of the urinary tract, and since this type of carcinogen cannot be said to have a "safe dose," the handling of such substances must be subjected to stringent precautions. If suitable alternative methods based on non-carcinogenic materials exist they should be adopted. Various organizations, such as the Association of Clinical Biochemists, the Government Chemist's Department, and the Water Research Association, are seeking acceptable alternative techniques to those in current use which are based on the carcinogenic aromatic amines, and it would be helpful if information on the techniques could be collated and published.

---

[1] Scott, T. S., and Williams, M. H. C., *Brit. J. industr. Med.*, 1957, **14**, 150.
[2] Weisburger, J. H., Mantel, N., Weisburger, E. K., Hadidian, Z., and Frederickson, T., *Nature (Lond.)*, 1967, **213**, 930.
[3] Dieteren, H. M. L., *Arch environm. Hlth*, 1966, **12**, 30.
[4] *Statutory Instrument 1740*, 1953. H.M.S.O.
[5] *Statutory Instruments*, No. 879, 1967. H.M.S.O.
[6] *Factories Act, 1961*. 1965. H.M.S.O.
[7] Copies free on request from the Librarian, Chester Beatty Research Institute, Institute of Cancer Research, Fulham Road, London S.W.3.

The problem extends further back than the laboratory use of the reagents, for such materials must already have been manufactured, purified, and packed.

The Carcinogenic Substances Regulations, 1967,[5] have been laid before Parliament, and unless annulled will come into force on 9 December 1967. They will, however, apply only to places covered by the Factories Act, 1961,[6] and will not therefore directly affect research workers, who will not be required by law to submit to a medical examination. The relevant part of the medical examination to be applied to workers who do come under the Act is the requirement to submit a specimen of urine for exfoliative cytological screening every six months. In general it seems unlikely that research workers have been at sufficient risk to warrant such a procedure, but the advice given to inquirers by the Chester Beatty Research Institute is worth repeating here:

"Although it is not possible to say that there is a level of exposure to the carcinogenic aromatic amines below which there is no risk, the hazard to trained laboratory workers must be small, and we do not recommend that such people should be asked to undergo urine screening unless they themselves have read of the risk and become worried, in which case the facility should be provided, and the test carried out at six-monthly intervals at least for the rest of their lives if they so wish." The Harlow Industrial Health Service and the Chester Beatty Research Institute have issued a pamphlet entitled, "Precautions for Laboratory Workers who Handle Carcinogenic Aromatic Amines,"[7] and it is recommended that all laboratory workers become familiar with these precautions and observe them.

Haematology Automated

Automated procedures have been developed and used in industry for many years on an ever increasing scale. More recently they have been introduced into hospitals, particularly in the clinical chemistry laboratories. Now they are spreading into the other branches of clinical pathology, notably haematology.

Automation in haematology formed the theme of a symposium held at the XIth Congress of the International Society of Haematology in Sydney last August. A report of its proceedings has now been published[1] and provides an instructive account of the ways in which work in the haematological laboratory is beginning to be automated. The combination of more work and fewer technicians has spurred the development and application of automation. At the simplest level are machines for mixing blood samples and for automatic staining. There are automatic pipetting devices, electronic cell counters, and continuous-flow devices for estimating haemoglobin, counting cells, and determining blood groups. Machines can indeed provide an integrated system for the processing and analysis of specimens and the storage and reporting of data by computer.

Electronic cell counters are now widely used for counting leucocytes and erythrocytes and in all large laboratories have supplanted manual procedures. The most commonly used instrument, the Coulter counter, operates on the difference in electrical conductivity between blood cells and their suspending medium. A cell passing through the electrical field of an aperture causes an increased resistance, which produces a change in voltage. This voltage signal is converted into a digital count by a computer, and it also provides a measure of cell size. Counting time is 10–20 seconds, and, provided the samples presented to the machine are satisfactory, the results are accurate and highly reproducible. Greater speed and reliability make electronic cell counting generally superior to manual methods for leucocytes and erythrocytes. For counting leucocytes the red cells are first removed by lysis with saponin, but for erythrocyte counts the presence of white cells is unimportant because the latter usually comprise less than 1% of the cell population. The enumeration of platelets by electronic counters has not been entirely successful, and more reliable instruments are required.

Haemoglobin is now determined photometrically as haemiglobin-cyanide (cyanmethaemoglobin), and this procedure can be automated. Electronic methods based on conductance principles are available for determining packed cell volume. More recently, automated electronic systems have become available which will simultaneously count leucocytes and erythrocytes and measure haemoglobin concentration and the packed cell volume. The results can then be printed out in figures. With these more complex machines complete blood counts (with the exception of the white cell differential count) can be obtained rapidly at the rate of 40 an hour.

For ABO grouping by machine the cells are tested simultaneously with anti-A, anti-B, and anti-A+B (to identify the weak subgroups of A), and for Rh typing with anti-D and anti-CDE; the plasma is tested with A, B, and O cells. To increase the sensitivity of the process the red cells are treated with bromelin, a proteolytic enzyme, and formation of rouleaux is induced with polyvinylpyrrolidone (P.V.P.). The treated samples flow through a T-piece and the agglutinated cells are decanted through the lower limb, whence they are propelled on to a moving filter-paper strip on which each blood group is recorded as a line of agglutinates. Samples can be tested at the rate of 120 an hour, and the paper strip can be stored as a permanent record.

The antibody-screening machine is similar in principle to the blood-typing machine. Enzyme-treated red cells containing known antigens are mixed with the test sera and P.V.P. and any agglutinates formed are selectively removed. The residual red cells are haemolysed and the liberated haemoglobin is measured in a continuous-flow colorimeter, the result being recorded on moving paper by a pen recorder, which produces a series of peaks. If no agglutination has taken place all the cells will be haemolysed and the resulting haemoglobin solution will impede the transmission of a light beam (zero transmission). Antigen–antibody reactions will cause the removal of cells as agglutinates, and the haemoglobin solution derived from the unagglutinated cells will be relatively weaker and will allow increased transmission of light. This will be recorded as a peak of variable height depending on the strength of the antibody. While the machine for blood grouping appears to be reliable, that for antibody screening and identification, at least in its present state, is less reliable and requires further improvement. However, for measuring amount of antibody—for example, anti-D—the machine is very sensitive, and it may be useful in predicting the severity of haemolytic disease of the newborn.

Automated techniques have also been developed for measuring the osmotic fragility of red cells and for determining some red cell enzymes, such as glucose-6-phosphate dehydrogenase and pyruvate kinase: deficiency of these enzymes accounts for many cases of non-spherocytic congenital haemolytic anaemia. These methods probably have little place in most routine laboratories but may be more useful for research purposes and for population surveys. The automation of serum vitamin-B_{12} assays should be possible now with radioisotopic methods, the requirements being automatic pipetting and an automatic gamma-ray counter.

---

[1] *Brit. J. Haemat.*, 1967, **13**, Suppl., ed. S. M. Lewis.

While the automated procedures for blood counting are of great value, it remains important not to neglect the study of cell morphology in blood films. All haematologists are familiar with cases in which the blood count was normal but examination of the blood film showed a significant abnormality which led to early diagnosis or to recognition of a condition which would otherwise have been overlooked. It is possible that devices will be developed for automating examination of blood films. But meanwhile it is important not to become lulled into a false sense of security by figures flowing fast and furiously from the clinical laboratory. In the proper use of laboratory tests and the correct interpretation of the results, with its bearing on rational diagnosis and treatment, the haematologist must play an even greater part.

Finally, there is the question, Who shall become fully automated ? All laboratories have some degree of automation. The machines referred to above are expensive. For instance, a multichannel blood-counting and blood-grouping machine costs £5,000 to £6,000. Only the larger hospital laboratories with a big work load could justify their possession—though even if the need exists there may not be the money to buy them. The blood-grouping machine would, for routine purposes, best be sited in a regional transfusion centre, where large numbers of samples are handled. All these matters and more, such as the continued need for even more skilled and psychologically suitable technicians to supervise the equipment, are dealt with in the proceedings of the symposium on automation in haematology,[1] which should be of interest to all workers in this important field.

Hereditary Malignant Melanoma

Cutaneous malignant melanoma may arise either from a pre-existing naevus or else as a result of spontaneous malignant change in the melanocytes present in the basal layer of the epidermis. Little is known about the aetiology of the condition. There is no factual basis for the traditional view that mechanical trauma is a predisposing cause. Sunlight may be of some importance, for the tumour occurs most frequently on the exposed parts, and is seen more often in fair-skinned people living in hot climates than in those domiciled in temperate countries.[1, 2] Extremely rare in childhood, the disease has its greatest incidence in later adult life. Though naevi darken during pregnancy, there is no evidence that they are unusually liable to undergo malignant change during this period.[3, 4]

That malignant melanoma of the skin might have a hereditary basis was first suggested in 1952, when E. P. Cawley described the condition in a father and two of his three children.[5] Since then there have been a number of case reports of melanoma occurring in several members of a family.[6-10] D. E. Anderson and his colleagues have recently investigated 22 such families,[11] and have noted a sufficient similarity in the cases to warrant the recognition of a special category of hereditary malignant melanoma. In one family the tumour developed in fifteen individuals.

The noteworthy features of this type of malignant melanoma, apart from its familial incidence, are the youthful age at which it occurs and the tendency for multiple primary lesions to develop. In these respects it resembles other hereditary neoplastic conditions—for example, polyposis coli, Gardner's syndrome, and xeroderma pigmentosum. In Anderson and his colleagues' series the average age at which the condition was diagnosed was about 40 years, whereas the sporadically occurring melanoma appears more commonly about a decade later. In about 20% of the cases of hereditary melanoma two or more primary tumours were found, a striking contrast to the frequency of 1.3 to 3% in the sporadic type.[11] The mode of inheritance is complicated. In a pedigree investigated by Anderson and colleagues the disease appeared to be transmitted by an autosomal dominant gene showing poor penetrance, but it is possible that more than one gene is involved.

An important clinical implication of these findings is that young patients with malignant melanoma should be examined for similar lesions elsewhere on the skin. A family history should be elicited, and in suspicious cases the relatives should be encouraged to undergo an examination so that early lesions can be removed as soon as possible. Indeed, it may well be that common malignant lesions of other kinds in unusually young people have a similar genetic basis, and that detailed family studies would be valuable in these cases.

---

[1] Lancaster, H. O., *Med. J. Aust.*, 1956, **1**, 1082.
[2] Davis, N. C., Herron, J. J., and McLeod, G. R., *Lancet*, 1966, **2**, 407.
[3] George, P. A., Fortner, J. G., and Pack, G. T., *Cancer (Philad.)*, 1960, **13**, 854.
[4] White, L. P., Linden, G., Breslow, L., and Harzfeld, L., *J. Amer. med. Ass.*, 1961, **177**, 235.
[5] Cawley, E. P., *Arch. Derm.*, 1952, **65**, 440.
[6] Moschella, S. L., ibid., 1961, **84**, 1024.
[7] Miller, T. R., and Pack, G. T., ibid., 1962, **86**, 35.
[8] Schoch, E. P., ibid., 1963, **88**, 445.
[9] Turkington, R. W., *J. Amer. med. Ass.*, 1965, **192**, 77.
[10] Katzenellenbogen, I., and Sandbank, M., *Arch. Derm.*, 1966, **94**, 331.
[11] Anderson, D. E., Smith, J. L., and McBride, C. M., *J. Amer. med. Ass.*, 1967, **200**, 741.

Contaminated Cylinders of Nitrous Oxide

In September 1966 some cylinders of nitrous oxide were contaminated with nitric oxide.[1] Since then much information has accumulated about this matter, and the May issue of the *British Journal of Anaesthesia*[2] is devoted to a series of articles on every aspect of the problem. While much of this material is naturally of specialist interest, certain facts concern anyone who has occasion to use nitrous oxide.

The stringent standards of purity laid down by the *British Pharmacopoeia* are reprinted, and the two manufacturers of nitrous oxide in this country give details of their processes and the steps taken to ensure compliance with these standards. The important contaminant is nitric oxide. If present, it dissolves in the liquid nitrous oxide. The physical properties of these gases are such that, from a full cylinder, most of the dissolved nitric oxide emerges with the first 7% of the nitrous oxide. This fact lends support to one manufacturer's practice of over-filling each cylinder and then "blowing back" the excess into the plant. Methods for the detection and determination of the higher oxides of nitrogen are described, and the practicability of using them in hospitals is discussed. Such testing might be particularly important in pipe-line installations, for here a contaminant could be delivered to several patients before any fault was suspected.

Fortunately until now the number of patients who have inhaled contaminated gases has been very small. There has been little opportunity, therefore, for anaesthetists to become familiar with the clinical picture of acute nitric-oxide poisoning and with the recommended treatment. When nitric oxide is inhaled methaemoglobinaemia, manifested by cyanosis, develops within a few minutes. At the same time intense pulmonary oedema occurs as a result of the nitric oxide dissolving in the pulmonary alveolar fluid to produce nitric and nitrous acids. This causes acute respiratory distress, or, if ventilation is being controlled, progressive difficulty in inflating the lungs. The combination of methaemoglobinaemia and pulmonary oedema results in hypoxia, the severity of which is enhanced by a concomitant acidaemia. Bradycardia is common and there is a rapid and dramatic fall in the blood pressure. The electrocardiograph may show only slight depression of the S-T segment, and any gross changes are usually terminal.

Treatment is aimed at the correction of the physiological disturbances. Oxygen is immediately administered. Intermittent-positive-pressure ventilation is almost certain to be needed. Indeed it may be regarded as mandatory, since absorption atelectasis may develop when pure oxygen is given to patients who are breathing spontaneously. High inflating pressures may be necessary for adequate ventilation, and if the distribution of gas is uneven they may result in alveolar hyperinflation. The methaemoglobinaemia is corrected by intravenous administration of methylene blue, and, since it is important to avoid overdosage, not more than 2 mg./kg. body weight is given initially. This is followed by further doses after laboratory estimation of the amount of methaemoglobin remaining in the blood. At the same time the acidaemia must be corrected by the intravenous administration of sodium bicarbonate. The oedema fluid from the lungs is sucked out and a solution of hydrocortisone and sodium bicarbonate instilled into the respiratory tract.

According to the editorial in the *British Journal of Anaesthesia*, in spite of all the efforts which have been made by the British Oxygen Co. to locate every nitrous-oxide cylinder which could come under suspicion, some have still not been traced and returned to the company's area depots for testing. Such cylinders, issued in the southern region before September 1966, are not marked with a cross on the shoulder. Anyone in this region who has such a nitrous-oxide cylinder in their possession, or who has transported such a cylinder into any other region, should communicate with the firm at once.

That British manufacturers maintain the high standards of purity demanded for medical gases is accepted by everyone using their products, and their excellent record in the past has fully justified such confidence. The prompt and effective action taken by British Oxygen when the contamination was first detected, together with the tightening-up of the precautions which they have taken to prevent and detect contamination, not only at the factory but also at bulk distribution centres, will do much to ensure the profession's confidence that this sort of accident will not happen again.

---

[1] *Brit. med. J.*, 1966, 2, 658.
[2] *Brit. J. Anaesth.*, 1967, 39, 343-448.

B.M.A. at Bristol

Visitors to Bristol very soon realize that its appeal comes from both its geographical setting and its history as a port. The old commercial city by the floating harbour has its original narrow streets and bars where sherry and port can be drunk from the wood, while above hang the Clifton suspension bridge and the Downs, and it was in this elegant setting that the Association's 135th Annual Meeting took place. Three previous Meetings have been held there—in 1833, 1863, and 1894—and if the President, Mr. Robert Cooke, is right in thinking that this will be the only visit the B.M.A. makes to Bristol this century then all who attended the Meeting will join him in regretting it.

Much of the success of the Meeting was due to the generous hospitality of the university and the civic authorities. The welcome reception by the local Branch and Division, the Adjourned Annual General Meeting, and the Degree Ceremony were all held in the University's Great Hall. This, an imposing building with a fine hammer-beam roof, contrasted well with the functional elegance of the new Students' Union, which housed both the Annual Representative Meeting and the Annual Scientific Meeting. The official religious service at Bristol Cathedral was particularly memorable, and this year for the first time was interdenominational —a welcome precedent. Other major occasions included the President's Reception at the City Museum, the Annual Dinner, and the civic reception at the Council House.

The scientific sessions covered a wide range of subjects but shared a theme in concentrating on practical advice which would be of value to doctors treating patients. Problems of everyday occurrence such as headache, diarrhoea, abdominal pain, and pain in the shoulder were discussed by well-known authorities in a down-to-earth way. The symposium on "Prescribing and Adverse Reactions to Drugs" was specially popular. Outstanding among the panel discussions was that on bereavement, and many practitioners will have been helped by it in dealing with this difficult and perennial problem. The plenary session on recreation towards the end of the programme stressed the importance for health of a balanced life. The Scientific and Pharmaceutical Exhibitions were well attended, and the medical films seem to reach higher standards year by year.

The social programme was full and varied. Ballet and light opera at the Theatre Royal and a B.B.C. concert were much enjoyed, and the ladies' programme organized by Mrs. J. Angell James used to full advantage Bristol's fine situation as a touring centre. Visitors will long remember excursions to several lovely mansions in the neighbourhood. The Association is much indebted to all who worked so hard to make the Meeting a success, and particular thanks are due to Professor J. H. Middlemiss, the Science Secretary, Dr. P. B. Bailey, the General Secretary, and to Dr. H. M. Golding, Chairman of the Local Organizing Committee.

The scientific proceedings are reported at p. 227 of this issue of the *B.M.J.*, and the account of the A.R.M. is concluded in the *Supplement* at p. 69.

On 13 July Sir Hedley Atkins was re-elected president of the Royal College of Surgeons of England for the ensuing year.

Papers and Originals

Early Surgery in the Management of Severe Ulcerative Colitis

J. C. GOLIGHER,* CH.M., F.R.C.S.; F. T. DE DOMBAL,* M.B., B.CHIR., F.R.C.P.
N. G. GRAHAM,* F.R.C.S., F.R.A.C.S.; G. WATKINSON,* M.D., F.R.C.P.

Brit. med. J., 1967, 3, 193–195

During the last two decades there has been a substantial improvement in the overall outlook for patients suffering from ulcerative colitis. Nevertheless, many patients continue to experience severe attacks of this disease, and the mortality from these attacks is often very high. Thus Gallagher *et al.* (1962) stated that nearly two-thirds of their patients with "fulminating" attacks of colitis during 1950–8 died; Edwards and Truelove (1963) reported a 26.8% fatality rate in all severe attacks treated during the previous decade; while Demole (1956) noted a 40% fatality rate in *all* acute attacks of colitis.

Recently we also described a large series of cases with severe attacks of ulcerative colitis, the fatality rate of which was considerable, being 9.6% in severe first attacks and 13.7% in severe relapses (de Dombal *et al.*, 1965a). In the care of these patients it had been our practice to submit practically all cases to intensive conventional medical therapy (usually including large doses of corticosteroids), for a period of 10 days or so in the first instance. Only if this regimen failed to secure a remission within that time—or if perforation or massive uncontrollable haemorrhage occurred—was surgical treatment considered.

In view of the disappointing results obtained it seemed to us that a drastic change in our plan of management was justified in the hope of reducing the high mortality. Accordingly we resolved (Watts *et al.*, 1966b) for a trial period to make surgery the sheet-anchor of our therapy in these cases and to invoke surgical aid at a very early stage of severe attacks—within a very few days of the patient entering hospital—*unless there was unequivocal evidence of rapid improvement in his condition on conservative management.*

Since this decision was taken at the end of 1963 some 74 patients have been treated by us for severe attacks of ulcerative colitis; all have been managed according to the plan outlined above. In this paper we report the results obtained and compare them with those previously reported in a similar group of 124 patients managed during 1952–63.

Clinical Material and Methods

Between 1 January 1964 and 30 June 1966 74 patients were admitted to the General Infirmary at Leeds under the care of the professorial surgical unit because they were suffering from severe attacks of ulcerative colitis. Occasionally patients were admitted twice during separate severe attacks, so that the total number of such attacks during 1964–6 was 81. Table I shows the age distribution of the patients at the time of these 81 severe attacks (and, for comparison, the ages of the patients treated for severe attacks of colitis during 1952–63). It will be seen that the composition of the two series of cases is quite similar in this respect.

Assessment of Severity of Attacks.—All attacks of ulcerative colitis were classified as severe according to the criteria of Truelove and Witts (1955), which are: *severe diarrhoea* (six or more motions a day); *macroscopic blood in the stools*; *fever* (mean evening temperature more than 99.5° F. (37.5° C.), *or* a temperature of 100° F. (37.8° C.) or more on at least two days out of four); *tachycardia* (mean pulse rate of more than 90 per minute); *anaemia* (haemoglobin 75% or less, allowance being made for recent transfusion); *E.S.R. much raised* (more than 30 mm. in one hour). Many of these severe attacks would have been labelled by some clinicians as "fulminating," but we have preferred to avoid the use of this somewhat imprecise term in assessing the severity of disease in our patients.

TABLE I.—*Age of Patient at Time of Each Severe Attack of Colitis*

Age	1952–63 (124 Attacks)		1964–6 (81 Attacks)	
	No. of Attacks	% of Total	No. of Attacks	% of Total
0–19 years	34	27·4	12	14·8
20–39 "	44	35·5	35	43·2
40–59 "	28	22·6	25	30·9
60 years and over	18	14·5	9	11·1

Plan of Initial Medical Management.—The patients were all managed according to the following regimen. On their admission to hospital an intensive course of conservative treatment was instituted; the vast majority of patients were treated with large doses of systemic corticosteroids—50 mg. of cortisone by mouth six-hourly or 100 mg. of hydrocortisone intramuscularly twice daily—often with sulphasalazine (Salazopyrin) as well (in a dosage of 1 g. six-hourly). Some of the patients received injections of A.C.T.H. (up to 100 units daily). Intravenous replacement of whole blood, plasma, and electrolytes was carried out as dictated by the needs of each individual patient (see Graham *et al.* (1967) for further details). Under this regimen several outcomes of the attack were possible—*remission* with subsidence of bowel symptoms and constitutional disturbance; *death during medical treatment*; *resort to surgical treatment with subsequent recovery* or *operative death.*

Indications for Surgical Intervention.—These were as follows: (1) persistent massive haemorrhage or the development of abdominal physical signs suggesting the occurrence of perforation of the bowel and peritonitis, particularly if associated with (2); (2) sudden deterioration in the general condition of the patient, which was usually a better guide to the occurrence of a catastrophe like perforation than were local physical signs (de Dombal *et al.*, 1965b); (3) in patients over 60 years of age, failure to show a definite clinical improvement after two to three days of conservative management; and

---

* University Department of Surgery, the General Infirmary at Leeds, Leeds 1.

(4) in younger patients, failure to show a definite clinical improvement after four to five days of intensive conservative treatment. The first two indications called for *emergency* surgical intervention, the patient being brought to operation immediately, or at latest within a few hours of the decision to resort to surgery having been reached. The remaining two indications were regarded as demonstrating the need for *urgent* surgery, the operation usually being performed within the next 24 to 48 hours.

Findings

Outcome of Severe Attacks.—The overall outcome of severe attacks of colitis in the two groups of patients is contrasted in Table II. The remission rate is shown to be slightly lower and the rate of recourse to radical surgery higher in the 1964–6 group. This was inevitable, since occasionally patients were brought to operation who might eventually have gone into remission on more prolonged conservative management, though they more frequently continued to have chronic bowel symptoms (see footnote to Table II). Nevertheless, it is noteworthy that, despite a policy the cornerstone of which was early recourse to surgery, nearly half of the patients seen went rapidly into remission on conservative treatment alone. However, the most striking feature of Table II is the clear reduction in both medical and surgical death rates which has taken place during 1964–6, and which has resulted in a fall in overall mortality from 11.3% during 1952–63 to 1.3% during the period of the present series.

TABLE II.—*Overall Outcome of Severe Attacks of Colitis*

Outcome		1952–63 (124 Attacks)		1964–6 (81 Attacks)	
		Cases	%	Cases	%
Remission		65*	52·4	38	46·9
Resort to surgery		40	32·3	43	53·1
Deaths	Under medical treatment	6	4·8	0	0
	Operative	8	20·0†	1	2·2†
	Total	14	11·3	1	1·3

*Excludes a further 13 patients who were not brought to surgery but continued for over 12 months with chronic symptoms (and hence cannot be classified as remission cases).

† Indicates percentages of patients who came to operation in each group.

Outcome of Severe First Attacks.—The mortality from colitis is always greatest during the first few months of the disease (Hurst, 1935 ; Demole, 1956 ; Edwards and Truelove, 1963). It is therefore particularly gratifying that none of the 19 patients who have been seen by us in severe first attacks during 1964–6 have failed to survive this initial attack (Table III). We have previously shown that it is in first attacks of colitis that the colon is most likely to perforate (de Dombal *et al.*, 1965b), and it is interesting to note that during 1964–6 we did not encounter a single instance of free perforation in an initial severe attack of colitis.

TABLE III.—*Outcome of Severe First Attacks of Colitis*

Outcome		1952–63 (73 Attacks)		1964–6 (19 Attacks)	
		Cases	%	Cases	%
Remission		38*	53·2	10	52·6
Resort to surgery		20	27·4	9	47·4
Deaths	Under medical treatment	2	2·7	0	—
	Operative	5	6·9	0	—
	Total	7	9·6	0	—

* Excludes 13 patients whose symptoms persisted for over 12 months but who did not come to surgery.

Outcome of Severe Attacks in Elderly Patients.—Relatively few of our patients were over 60 years of age, which means that only small groups of cases are available for analysis (see Table IV). Though we were specially ready to resort to surgical treatment in the management of this type of case in the 1964–6 period, in fact no less than half of these older patients in this latter period very rapidly improved on conservative management. Of the remainder who came to early operation none died, compared with 50% during the 1952–63 period.

Operations Performed.—Most patients were submitted to a one-stage total proctocolectomy and ileostomy (Table V). Details concerning the technique of this operation have been presented elsewhere (Goligher, 1954, 1961, 1967), and the question of choice of operative procedure has also been discussed (Watts *et al.*, 1966a). In the present series one young child aged 8 underwent colectomy and ileostomy, with preservation of the rectum. A further patient, a woman aged 29, was admitted with an extremely severe attack of residual proctitis after a previous colectomy and ileorectal anastomosis elsewhere ; she was subjected to excision of the rectum and had an ileostomy established, with uneventful recovery. The patient who had a negative laparotomy merits comment. While under intensive conservative care for a severe attack of colitis he developed tachycardia and pyrexia, together with extreme abdominal rigidity and tenderness. Perforation of the colon was suspected, but at laparotomy no such lesion was found, though the sigmoid colon was clearly the seat of active colitis. The abdomen was therefore closed without removal of the colon or ileostomy for what appeared to be a distal proctocolitis, and the patient subsequently went into remission.

TABLE IV.—*Outcome of Severe Attacks of Colitis in Elderly Patients*

Outcome		1952–63 (16 Attacks)	1964–6 (9 Attacks)
Remission		4	5
Resort to surgery		9	4
Deaths	Under medical treatment	3	0
	Operative	5	0
	Overall	8	0

TABLE V.—*Type of Early Surgery Employed*

	1952–63 (40 Cases)	1964–6 (43 Cases)
Proctocolectomy and ileostomy	32	40
Colectomy and ileostomy	6	1
Rectal excision and ileostomy	—	1
Laparotomy and closure	—	1
Other procedure	2	—

Cause of Operative Death.—There was one operative death, that of a young man of 29 who suffered in addition from cirrhosis of the liver with portal hypertension. At operation a considerable quantity of ascitic fluid was found in the peritoneal cavity. Subsequently ascitic fluid escaped through the main wound, which broke down on the ninth postoperative day and required resuture. Serous fluid continued to pour through the wound for some weeks and the patient eventually died. It is arguable that this man's death was incidental to his colitis, but, in view of the abdominal wound breakdown and of the well-known association between colitis and liver disease, we have classified this as a related death.

Discussion

In assessing the results of treatment of certain disease processes, such as severe attacks of ulcerative colitis or bleeding peptic ulcer, for which the alternatives of medical and surgical management are available, it is essential to remember that, according to the manner of selection of patients for these respective modes of therapy, success with one may be achieved largely at the expense of a high mortality with the other. The important yardstick, therefore, in gauging the value of any change of therapeutic policy is the effect on the *overall mortality*.

Accordingly, in examining the influence of our recent practice of resorting at an earlier stage to surgical treatment in severe attacks of colitis, we have paid special attention to the overall mortality, comparing it with that obtained when a tardier and more restricted use of urgent or emergency operation was in force (Table II). It will be seen that the overall fatality rate of severe attacks since this new regimen has been adopted was only 1.3%, which contrasts with 11.3% previously—a difference that is highly significant. It is also interesting to note that since January 1964 there have been no medical deaths in 81 cases and the operative mortality in the 44 cases coming to urgent or emergency operation has amounted to only one case, or 2.2%. This compares with 6 medical deaths in 124 cases during 1952–63 (a mortality of 4.8%) and a surgical mortality in the 40 cases proceeding to operation during that period of 8 cases (or 20%).

Possible Fallacies

On the face of it, therefore, it might seem that the policy of earlier surgery has achieved its objective of rendering severe attacks of colitis less hazardous; but before reaching this conclusion certain possible fallacies need to be considered.

(*a*) It may be questioned whether there has been any alteration not only in the timing but also in the type of surgical intervention during the second period. However, it will be seen from Table V that the operations employed were very similar during both periods under review and consisted usually of proctocolectomy, or colectomy, and ileostomy. There was indeed a slightly higher proportion of proctocolectomies to subtotal colectomies in 1964–6 than in 1952–63, but it is debatable in which way this might have affected the operative mortality, and inconceivable that it could have been responsible for reducing it to the extent shown in Table II.

(*b*) The possibility that a slight difference in the *form* as well as in the duration of medical treatment in these two periods may have influenced the mortality somewhat requires also to be examined. Though systemic corticosteroid therapy was consistently used in the 1964–6 period, in the first three years of the 1952–63 period corticosteroids were omitted in roughly half the cases during the conduct of the M.R.C. collective controlled trial of corticosteroid preparations in the treatment of ulcerative colitis (Truelove and Witts, 1955). But the total number of patients not receiving corticosteroids amounted to only one-quarter of the 124 in the 1952–63 group, and their mortality (12.5%) was little higher than that of the remainder of the group (11.0%). The medical therapy given to the 1964–6 cases may in general have therefore been marginally more potent than that used for the 1952–63 group; but we find it hard to believe that this slight difference could have played a major part in bringing about the striking reduction in the medical and overall mortalities of the more recent of the two groups of patients. It seems more reasonable to attribute the drop in medical mortality in this group largely to the earlier resort to surgery, and the gratifying thing is that this has been attended also by a striking fall in the surgical mortality.

(*c*) Much more serious is the criticism that the composition of the two groups of cases being contrasted in this study may be dissimilar. The influence of the age of the patient on the risks of a severe attack of colitis has been clearly shown in our previous study (de Dombal *et al.*, 1965a). Analysis of the age of distribution of the patients in our two groups of cases (Table I) shows, however, that they are roughly similar in this respect. It should be emphasized, too, that each of our two series represented nearly *all* the patients with severe attacks of colitis coming to the same hospital centre during the periods under review, the severity of the attacks having in each instance fulfilled certain well-defined criteria (Truelove and Witts, 1955).

It must be admitted that even these criteria allow considerable variation in the severity of attacks, so that there could be a difference in the proportion of particularly ill patients in the two series. Indeed, it has been our clinical impression that the virtually moribund type of case with severe acute colitis has become rather less common in recent years. But, even so, it must be pointed out that some 25 to 30 patients presented during 1964–6 in particularly severe attacks of colitis (with 10 to 15 bowel actions per day, massive rectal blood loss, fever up to 105° F. (40.5° C.), severe electrolyte disturbance, and so on); and *not one of these patients failed to survive the attack,* even though most of them were brought to radical surgery at an early stage.

Therapeutic Trial

Of course the only way to avoid uncertainties of this kind is to plan a properly controlled therapeutic trial, in which the patients are allotted in entirely random fashion to the forms of therapy on trial. Such a trial to compare the efficacy of early surgical intervention against intensive conservative treatment, including corticosteroid therapy for severe attacks of colitis, has already been proposed by us (Goligher, 1956) and by Edwards and Truelove (1963). The results which we now report with early surgery cannot therefore provide a conclusive evaluation; but, like the smaller—also uncontrolled—trial of Gallagher *et al.* (1962), they suggest strongly that in certain centres with extensive experience of colitis surgery this regimen may be the best method of treating severe attacks of this disease.

One objection to the practice of early surgery is that it may occasionally result in some patients with a short history of disease coming to urgent operation, when they might possibly have secured a remission of their severe attack on more prolonged conservative management. This objection is all the more important in view of the radical nature of the surgery involved. However, Table II indicates that the number of such patients who would eventually secure a remission is small (52% versus 46%). Moreover, our own follow-up studies (Watts *et al.*, 1966c) and those of Edwards and Truelove (1963) have shown that a high proportion of those patients who manage to survive a severe attack of colitis on conservative treatment eventually suffer further such attacks, and often end up with radical surgical treatment or succumb to their disease. The conclusion is inescapable that many of them would have fared much better if they had undergone operation at an earlier stage of their illness.

Summary

This paper presents an analysis of the outcome of 81 severe attacks of ulcerative colitis treated during 1964–6. All patients were admitted to hospital, and surgical aid was invoked at an early stage if there was no response to a short course of intensive conservative measures.

Thirty-eight patients underwent remission on conservative treatment and 43 came to operation; there were no medical deaths, but one patient died postoperatively of cirrhosis of the liver. The overall mortality in these severe attacks was thus 1.3%, which is significantly less than the overall mortality of severe attacks of colitis during the previous decade, when operative treatment was resorted to less readily.

These findings strongly suggest that early radical surgical treatment may have considerable advantages for patients with severe attacks of colitis which fail to respond rapidly to intensive medical treatment, but the possible fallacies of conclusions drawn from an incompletely controlled trial are emphasized.

REFERENCES

de Dombal, F. T., Watts, J. McK., Watkinson, G., and Goligher, J. C. (1965a). *Proc. roy. Soc. Med.*, **58**, 711.
—— —— —— —— (1965b). Ibid., **58**, 713.
Demole, M. (1956). *Gastroenterologia (Basel)*, **86**, 608.
Edwards, F. C., and Truelove, S. C. (1963). *Gut*, **4**, 299.
Gallagher, N. D., Goulston, S. J. M., Wyndham, N., and Morrow, W. (1962). Ibid., **3**, 306.
Goligher, J. C. (1954). *Ann. roy. Coll. Surg., Engl.*, **15**, 316.
—— (1956). *Gastroenterologia (Basel)*, **86**, 718.
—— (1961). *Brit. med. J.*, **1**, 151.
—— (1967). *Surgery of the Anus, Rectum, and Colon*, 2nd ed. London.
Graham, N. G., de Dombal, F. T., Watkinson, G., and Goligher, J. C. (1967). In preparation.
Hurst, A. F. (1935). *Lancet*, **2**, 1194.
Truelove, S. C., and Witts, L. J. (1955). *Brit. med. J.*, **2**, 1041.
Watts, J. McK., de Dombal, F. T., and Goligher, J. C. (1966a). *Brit J. Surg.*, **53**, 1005.
—— —— Watkinson, G., and Goligher, J. C. (1966b). *Gut*, **7**, 16.
—— —— —— —— (1966c). *Brit. med. J.*, **1**, 1447.

Acute Metabolic Response to Human Growth Hormone in Different Types of Dwarfism*

K. E. W. MELVIN, M.B., CH.B., B.MED.SC., M.R.C.P., M.R.A.C.P.; A. D. WRIGHT,† M.B., M.R.C.P.
M. HARTOG, D.M., M.R.C.P.; A. C. ANTCLIFF, M.B., B.S.; A. M. COPESTAKE, B.SC.
T. RUSSELL FRASER, M.D., F.R.C.P.

Brit. med. J., 1967, 3, 196–199

The effectiveness of human growth hormone (H.G.H.) in man is now well established from both the acute metabolic response (Beck *et al.*, 1958; Ikkos *et al.*, 1959; Medical Research Council, 1959) and the stimulation of growth after long-term therapy (Raben, 1962). In this paper we report the results of studies of the acute metabolic response to injected H.G.H. in different types of dwarfism and, in some of them, the relation between these responses and the levels of endogenous serum H.G.H. obtained during insulin-tolerance tests. A few of the dwarfed subjects have thereafter received long-term H.G.H. treatment in an attempt to promote growth, and the relation between this growth response and the results of the acute metabolic test has also been examined.

Patients Studied

Twenty-three patients were studied, and some of their details are shown in the Table. Seven had panhypopituitarism due to a variety of causes and 13 were dwarfed for reasons other than primary pituitary disease; the latter included six "idiopathic" dwarfs, three cases of gonadal dysgenesis, one dwarfed patient with Cushing's syndrome, and three patients on chronic corticosteroid therapy for Still's disease or asthma. The growth response of the patient with Still's disease has been reported separately (Ward *et al.*, 1966). We also report the acute response to H.G.H. in three adults suffering from carcinoma of the breast or osteoporosis, who were presumed to have normal pituitary function. The patients with panhypopituitarism were all receiving replacement therapy with cortisone at the time of the study and four were also receiving thyroxine. The only other patients who were receiving hormonal therapy during the tests were those on corticosteroids. The child with Still's disease (Case 17) was receiving 5 mg. of prednisone daily, and the patients with asthma (Cases 18 and 19) were receiving 15 and 12.5 mg. of prednisone daily respectively.

Details of Cases

Category	Case No.	Diagnosis	Sex	Age	Bone Age	Height (cm.)	Weight (kg.)
Panhypo-pituitarism	1	Craniopharyngioma	M	15	9	133	41·5
	2	,,	M	13	8	128	28·0
	3	,,	F	18	10	150	44·0
	4	Idiopathic	M	17	11	126	26·5
	5	^{90}Y implant ..	F	45			
	6	Chromoph. tumour	M	67			81·0
	7	,, ,,	M	45		164	84·0
Idiopathic dwarfs	8	Idiopathic	M	9	6	73·5	8·9
	9	,, ...	M	14	11	146	29·8
	10	,, ...	M	10	12	141	36·4
	11	,, ...	F	16	16	147	44·0
	12	,, ...	F	18	18	141	35·5
	13	,, ...	F	13	16	143	44·0
Gonadal dysgenesis	14	Gonadal dysgenesis	(M)	24	14	141	39·8
	15	,, ,,	(F)	18	16	132	42·5
	16	,, ,,	(F)	16		132	30·5
Chronic cortico-steroid excess	17	Still's disease ..	F	10	4½	113	23·0
	18	Asthma	M	16	11	146	43·0
	19	,, ...	M	15	11	148	58·5
	20	Cushing's syndrome	M	16	6 10/12	151	56·8
Miscel-laneous adults	21	Carcinoma of breast	F	61		169	54·0
	22	,, ,, ,,	F	62		164	55·3
	23	Osteoporosis ..	F	62		164	63·0

Methods

All patients were studied in the metabolic unit. They were given a standard low-calcium diet containing 68 g. of protein, 68 g. of fat, 220 g. of carbohydrate, 200 mg. of calcium, and 1 g. of phosphorus. When necessary this standard diet was altered to meet individual requirements and analysed subsequently. Total calcium intake was standardized to 2 mEq/kg. by means of supplementary calcium tablets. Chromium sesquioxide was given daily (0.5 g. t.d.s.) as a faecal marker, and the faecal analyses were corrected according to their content of this marker (Whitby and Lang, 1960). Urine was collected in 24-hour periods and analysed for nitrogen and calcium. Faeces were collected in three-day pools and were analysed for nitrogen, calcium, and chromium. The blood urea was measured daily. A five-day period for equilibration on the diet and chromium was followed by six days of basal measurements; 10 mg. of H.G.H. (Raben, 1962) was then given intramuscularly at 7 a.m. for three days, and the measurements were continued throughout the period of the injections and for the next three days.

Urine and faecal nitrogen were estimated by the Kjeldahl method (Wootton, 1964). Urine and faecal calcium and faecal chromium were measured by means of a flame spectrophotometer (MacIntyre and Brown, unpublished). The blood urea was measured in an autoanalyser. Specimens collected daily were measured in a batch at the conclusion of the study.

Serum H.G.H. was assayed throughout the course of a standard insulin-tolerance test (0.1 unit/kg.) by an immunoassay method using the double-precipitation technique (Hartog *et al.*, 1964b); the preparation of H.G.H. used as standard was the M.R.C. "A" preparation, and the lower limit of sensitivity of the method was 1–4 mμg./ml. The patients receiving corticosteroids and the boy with Cushing's syndrome were given larger doses of insulin (0.15–0.3 unit/kg.) in view of their expected insulin resistance.

Results

Acute Metabolic Response to H.G.H.

Basal measurements were made over the six days before giving H.G.H. From these a mean value was obtained for each of the measurements, against which the subsequent response to H.G.H. was compared. Though the magnitude of the response was greatest during the three days of hormone administration, the duration of action of H.G.H. was greater in the hypopituitary subjects. A better discrimination between different groups of patients was obtained, therefore, by selecting for comparison the six-day period after the first injection of H.G.H. Thus the response was measured in terms of the

---

* From the Departments of Medicine and of Chemical Pathology, Royal Postgraduate Medical School of London, London W.12.

This work is part of a trial organized by the Human Pituitary Hormones Subcommittee (chairman: Professor Russell Fraser; secretary: Dr. A. Stuart Mason) of the Committee of Clinical Endocrinology of the Medical Research Council.

† M.R.C. Junior Research Fellow

difference between mean basal levels of blood urea, urine nitrogen, and urine calcium, and the mean levels of each during the six days after the first H.G.H. injection (Fig. 1).

In view of the small numbers of subjects in most of the patient categories, the main comparison has been between the hypopituitary subjects and the idiopathic dwarfs.

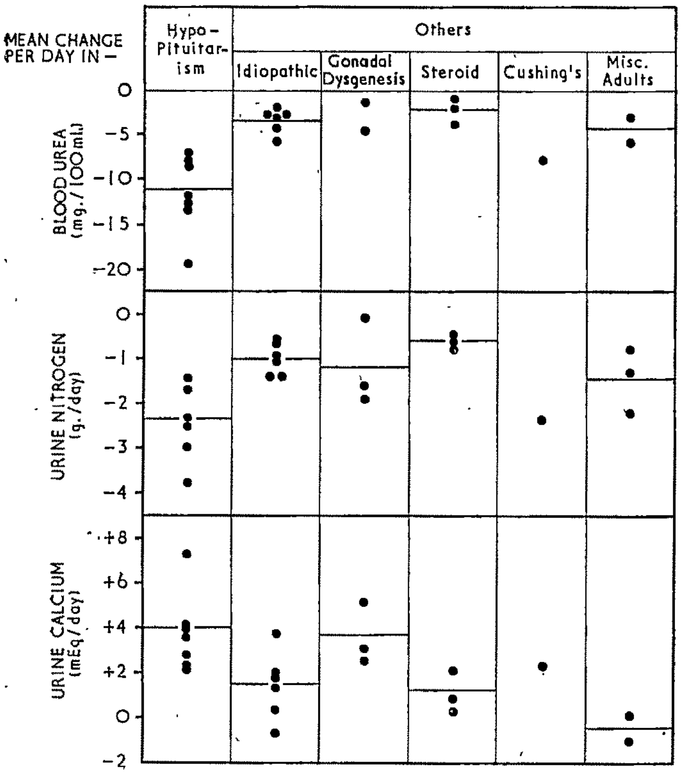


FIG. 1.—Acute metabolic response to H.G.H. (Days 1–6). Mean change per day in blood urea, urine nitrogen, and urine calcium.

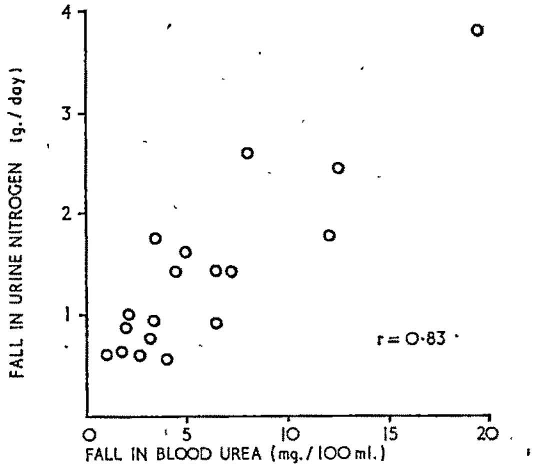


FIG. 2

FIG. 2.—Relation between changes in blood urea and urine nitrogen (Days 1–6).

Blood Urea (Fig. 1).—The fall of blood urea was greater in the patients with hypopituitarism than in the other subjects, with the exception of the boy with Cushing's syndrome. The mean fall in the hypopituitary group (11.3 mg./100 ml.) was greater than that in the group of idiopathic dwarfs (3.6 mg./100 ml.) ($P<0.01$).

Urinary Nitrogen (Fig. 1).—The patients with hypopituitarism also showed a greater fall of urinary nitrogen than did the other groups of subjects, though there was some overlap of individual values. The mean fall of 2.4 g./day in the former group was greater than that of the group of idiopathic dwarfs (1.0 g./day) ($P<0.05$). As shown in Fig. 2, there was a clear correlation between the fall of blood urea in the different subjects and the fall of urinary nitrogen. In Fig. 3 the urine nitrogen response is expressed as a function of body weight. Plotted thus, the distinction between groups of patients is less clear than when plotted in absolute figures.

Nitrogen Balance.—With a single exception, all patients developed a positive nitrogen balance in response to H.G.H. This largely reflected the changes of urinary nitrogen, and little or no change was measured in the relatively small faecal nitrogen values.

Urinary Calcium (Fig. 1).—An increase in the urinary calcium was found in the majority of the subjects. The mean rise was greater in the hypopituitary patients (3.9 mEq/day) than in the group of idiopathic dwarfs (1.4 mEq/day ($P<0.05$), though there was an overlap of individual values in these and the other groups. In particular it was noted that the patients with gonadal dysgenesis showed as large a hypercalciuric effect as did the hypopituitary subjects. A correlation was found between the changes in blood urea and urine calcium (Fig. 4).

Faecal Calcium and Calcium Balance.—No consistent changes were observed in either the faecal calcium or the calcium balance in response to H.G.H.

Relation Between Acute Metabolic Response to H.G.H. and Response of Serum H.G.H. to Hypoglycaemia

Fourteen of the subjects had measurements of serum H.G.H. performed during an insulin-tolerance test. The highest level of serum H.G.H. found during the test has been plotted against the value of the acute metabolic response to H.G.H., which provided the best discrimination between the different groups—namely, the fall of blood urea. It will be seen (Fig. 5) that there was some negative correlation ($r = -0.59$) between these figures. The subjects in whom no measurable rise of serum H.G.H. was found (which included the four hypopituitary subjects tested and the boy with Cushing's syndrome) sustained a fall of blood urea greater than 7 mg./100 ml., while in those in whom clearly measurable rises were found the fall of blood urea was less than 7 mg./100 ml.

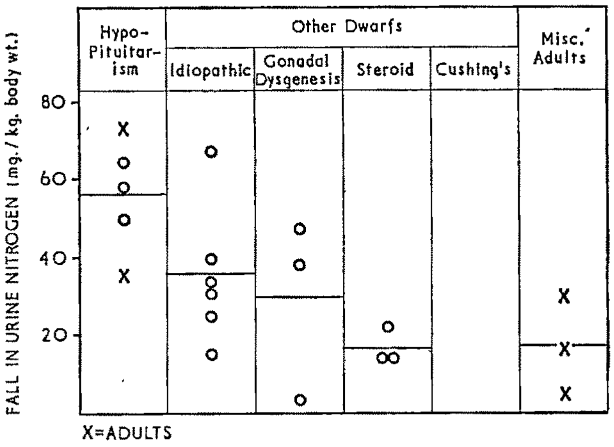


FIG. 3

FIG. 3.—Effect of H.G.H. on urinary nitrogen related to body weight (Days 1–6).

Relation Between Acute Metabolic Response to H.G.H. and Growth Response to Long-term H.G.H. Treatment

Four patients were studied for periods of at least 12 months on treatment with H.G.H. These comprised the patient with Still's disease (Case 17) and three of the hypopituitary dwarfs

(Cases 2, 3, and 4). The relation between the fall of blood urea found during the acute metabolic test on these patients and the long-term growth response is shown in Fig. 6. It will be seen that three of the patients increased their rate of growth by more than 4 cm./year during H.G.H. treatment and that all three had shown a marked fall of blood urea. The fourth patient showed no acceleration of growth with chronic H.G.H. therapy and had sustained a fall of only 4 mg./100 ml. during the acute metabolic test.

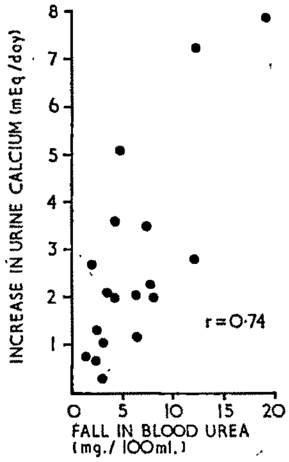


FIG. 4

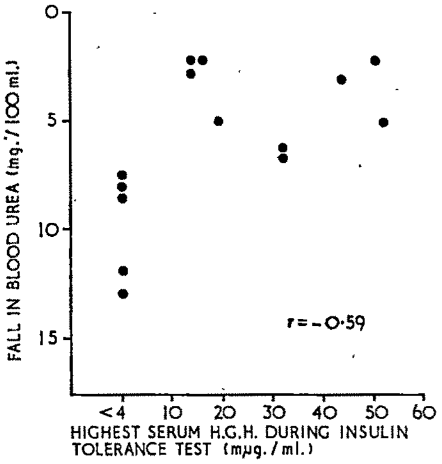


FIG. 5

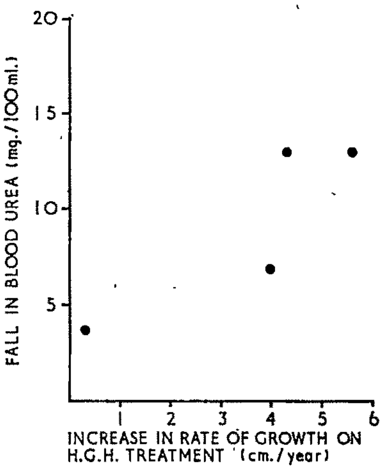


FIG. 6

FIG. 4.—Relation between changes in blood urea and urine calcium (Days 1–6). FIG. 5.—Relation between fall in blood urea (Days 1–6) and highest serum H.G.H. during insulin-tolerance test in 14 patients. FIG. 6.—Relation between fall in blood urea (Days 1–6) and growth response to H.G.H. treatment in four patients.

Discussion

The increased sensitivity of hypopituitary subjects to the metabolic effects of H.G.H. as compared with subjects without hypopituitarism which was found in the present study, agrees with the results of most other investigations (M.R.C., 1959; Daughaday and Parker, 1963; Prader *et al.*, 1964; Soyka *et al.*, 1964; Wright *et al.*, 1965; Hubble, 1966; Scott *et al.*, 1966). The metabolic response which distinguished our patients with hypopituitarism most clearly from the other subjects was their greater fall of blood urea. Nitrogen retention, as measured by the fall of urinary nitrogen, was also most marked in this hypopituitary group; however, the differences were not as great and the results overlapped more than was found with the blood urea responses, possibly because the auto-analyser blood ureas were more accurate. Even when the changes of urinary nitrogen were corrected for body weight this overlap was still present, though Prader *et al.* (1964) found a clear separation in this respect between hypopituitary subjects and controls. The hypercalciuric effect of H.G.H. was also more marked in the hypopituitary group, but again there was overlap of individual results with those of the other groups. We did, however, find a correlation between the fall of blood urea and the rise of the urinary calcium induced by H.G.H., which is contrary to the findings of others (Prader *et al.*, 1964; Wright *et al.*, 1965) and might not be expected if, as has been suggested, the hypercalciuric effect of H.G.H. is a pharmacological one and related to dosage (M.R.C., 1959).

The usefulness of an acute metabolic trial of H.G.H. in distinguishing patients with hypopituitarism from other forms of dwarfism is supported by the relation between the magnitude of the fall of blood urea and the responsiveness of circulating serum H.G.H. to hypoglycaemia. As fasting levels of serum H.G.H. may be too low to be measured, insulin-tolerance tests were performed to assess H.G.H. reserve, since hypoglycaemia is a well-recognized stimulus for growth hormone release (Roth *et al.*, 1963). Patients with serum H.G.H. levels rising above 4 mμg./ml. during insulin hypoglycaemia were found to sustain only a slight reduction of the blood urea in response to injected H.G.H., whereas the patients in whom serum H.G.H. remained undetectable throughout the insulin-tolerance test showed greater falls of blood urea. Scott *et al.* (1966) have reported similar findings. Until more data are available concerning the response of normal children to H.G.H., the significance of our results in those patients without primary pituitary disease remains difficult to assess.

Others have also found idiopathic or primordial dwarfs to be resistant to the nitrogen-retaining effect of H.G.H. (Shepard *et al.*, 1960; Lipsett *et al.*, 1961), and it seems likely that, though this group of dwarfs is probably a heterogenous one, a peripheral resistance to the action of H.G.H. might be a factor in some.

The cause of the growth defect in gonadal dysgenesis is also uncertain. Normal levels of serum H.G.H. have been found by bioassay (Forbes *et al.*, 1962) and by immunoassay (present study), and Daughaday and Parker (1963) found normal serum sulphation factor in 9 of their 12 patients. A peripheral insensitivity to the action of H.G.H. was postulated by Willemse (1962); however, Forbes *et al.* (1962) and Wright *et al.* (1965) measured the metabolic effects of H.G.H. in patients with gonadal dysgenesis and concluded that they were not subnormal. Forbes *et al.* (1962) suggested that there may be an abnormal form of circulating H.G.H. in this condition. We have tested this suggestion by measuring the serum H.G.H. from two patients by the immunoassay technique at different dilutions of serum. The slope of these assay lines was identical with that of the H.G.H. used in the standards, so that these assays failed to provide any evidence of an abnormal form of circulating H.G.H.

Overdosage with cortisone is a well-known cause of arrested growth, and two mechanisms may be involved in this. A peripheral antagonism between the actions of growth hormone and A.C.T.H. or corticosteroids has been shown both in animals (Becks *et al.*, 1944) and in man (Soyka *et al.*, 1964), and high doses of corticosteroid have been shown to suppress the release of H.G.H. from the pituitary (Hartog *et al.*, 1964a; Frantz and Rabkin, 1964). It was therefore of interest that the three patients receiving moderate doses of corticosteroids, in whom clearly measurable levels of serum H.G.H. were found, showed a smaller metabolic response to H.G.H. than that found in the hypopituitary subjects. In contrast, the patient with severe Cushing's syndrome, in whom no circulating H.G.H. could be detected, showed a response similar to that of the hypopituitary group. Hennemann *et al.* (1964) have also reported marked nitrogen retention after the administration of H.G.H. to a patient with Cushing's syndrome.

There are conflicting reports on the usefulness of measuring the metabolic response to H.G.H. in predicting the growth response to long-term H.G.H. therapy. Prader *et al.* (1964), using a dose of 2 mg./sq. m. body surface area daily (Raben preparation), found that four primordial dwarfs sustained only slight nitrogen retention with H.G.H. and failed to respond to long-term therapy, while six out of nine hypopituitary dwarfs who all sustained marked nitrogen retention showed a satisfactory acceleration of growth with long-term H.G.H. therapy. The three exceptions were patients who developed high titres of antibody to H.G.H. in the course of treatment. We have followed the growth response of only four patients, but it did appear that, in them, the degree of nitrogen retention was related to their subsequent course. Wright *et al.* (1965), using a Wilhelmi preparation 5 mg. daily, however, were unable to find any parameter in the metabolic response which was of use in predicting subsequent growth response, with the possible exception of minimal nitrogen retention, which was associated with failure of acceleration of growth with chronic H.G.H. therapy.

Summary

The acute metabolic response to injected human growth hormone (H.G.H.) has been compared in seven patients with panhypopituitarism, six cases of idiopathic dwarfism, three cases of gonadal dysgenesis, three patients dwarfed as a result of chronic corticosteroid treatment, one case of Cushing's syndrome, and three adults without pituitary disease. Change in blood urea appeared to be the most sensitive factor.

The acute metabolic response was greater in patients with hypopituitarism than in those without primary pituitary disease.

Measurements of endogenous H.G.H. in response to insulin hypoglycaemia were made in 15 subjects. The acute metabolic response to injected H.G.H. was greatest in those with no measurable serum H.G.H. in response to insulin.

The relevance of the acute metabolic response to the linear growth response was examined in four patients who received long-term treatment with H.G.H. Growth was accelerated only in the three patients showing marked nitrogen retention during the acute metabolic test.

Under the Human Pituitary Subcommittee of the Committee of Clinical Endocrinology of the M.R.C. the H.G.H. was prepared by Dr. Anne Hartree, Department of Biochemistry, University of Cambridge, and ampouled, assayed, and tested for sterility and pyrogens by Drs. D. R. Bangham, P. M. Cotes, M. P. Stack-Dunne, and G. W. Bissett, Division of Biological Standards, Medical Research Council. Growth measurements were made by Professor J. M. Tanner and Mr. R. H. Whitehouse at the Institute of Child Health, University of London.

We would like to thank the M.R.C. for a grant for technical assistance for the assay of H.G.H. We also thank the physicians who referred the patients, and the dietitians and nursing and technical staff of the metabolic unit, for all their help in these studies.

REFERENCES

Beck, J. C., McGarry, E. E., Dyrenfurth, I., and Venning, E. H. (1958). *Ann. intern. Med.*, **49**, 1090.
Becks, H., Simpson, M. E., Marx, W., Li, C. H., and Evans, H. M. (1944). *Endocrinology*, **34**, 311.
Daughaday, W. H., and Parker, M. L. (1963). *J. clin. Endocr.*, **23**, 638.
Forbes, A. P., Jacobsen, J. G., Carroll, E. L., and Pechet, M. M. (1962). *Metabolism*, **11**, 56.
Frantz, A. G., and Rabkin, M. T. (1964). *New Engl. J. Med.*, **271**, 1375.
Hartog, M., Gaafar, M. A., and Fraser, R. (1964a). *Lancet*, **2**, 376.
—— —— Meisser, B., and Fraser, R. (1964b). *Brit. med. J.*, **2**, 1229.
Henneman, P. H., Avioli, L. V., McDonald, J. E., and Melby, T. C. (1964). *Proceedings of the Second International Congress of Endocrinology*, London, p. 1013.
Hubble, D. (1966). *Arch. Dis. Childh.*, **41**, 17.
Ikkos, D., Luft, R., and Gemzell, C. A. (1959). *Acta endocr. (Kbh.)*, **32**, 341.
Lipsett, M. B., Bergenstal, D. M., and Dhyse, F. G. (1961). *J. clin. Endocr.*, **21**, 119.
Medical Research Council (1959). *Lancet*, **1**, 7.
Prader, A., Illig, R., Széky, J., and Wagner, H. (1964). *Arch. Dis. Childh.*, **39**, 535.
Raben, M. S. (1962). *New Engl. J. Med.*, **266**, 82.
Roth, J., Glick, S. M., Yalow, R. S., and Berson, S. A. (1963). *Science*, **140**, 987.
Scott, D. J., Ibbertson, H. K., Farrelly, R. O., Cameron, S., and Harper, P. (1966). *N.Z. med. J.*, **65**, 398.
Shepard, T. H., Waxman, S., Bernstein, N., and Ferrier, P. (1960). *J. Pediat.*, **57**, 363.
Soyka, L. F., Ziskind, A., and Crawford, J. D. (1964). *New Engl. J. Med.*, **271**, 754.
Ward, D. J., Hartog, M., and Ansell, B. M. (1966). *Ann. rheum. Dis.*, **25**, 416.
Whitby, L. G., and Lang, D. (1960). *J. clin. Invest.*, **39**, 854.
Willemse, C. H. (1962). *Acta endocr. (Kbh.)*, **39**, 204.
Wootton, I. D. P. (1964). *Micro-analysis in Medical Biochemistry*, 4th ed. London.
Wright, J. C., *et al.* (1965). *Amer. J. Med.*, **38**, 499.

Chronic Intestinal Ischaemia

J. KENNEDY WATT,* CH.M., B.SC., F.R.C.S., F.R.C.S.GLASG.; W. C. WATSON,† M.D., PH.D., F.R.C.P.GLASG., M.R.C.P.
S. HAASE,‡ M.A., M.B., CH.B., D.M.R.D.

[WITH SPECIAL PLATE]

Brit. med. J., 1967, **3**, 199–202

When thrombosis of the superior mesenteric artery occurs with acute infarction of bowel the mortality rate approaches 100% in untreated cases and is over 90% in those treated surgically (Mavor *et al.*, 1963). The acute episode is preceded by prodromal symptoms of intestinal ischaemia in approximately 50% of cases (Dunphy, 1936). If these symptoms can be recognized, direct arterial surgery may avert the inevitable arterial occlusion and save life (Morris *et al.*, 1962). The provisional diagnosis of mesenteric ischaemia may be confirmed by lateral aortography of the abdominal aorta, but the principal difficulty in diagnosis is a failure to suspect that the presenting symptom pattern may be due to ischaemia of small bowel.

In most cases of chronic intestinal ischaemia due to atherosclerosis at least two of the three principal arteries to the alimentary tract must be stenosed or occluded before symptoms result (Morris *et al.*, 1962), but Morris *et al.* (1966) reported 6 out of 31 cases in which a lesion of the coeliac axis alone was the cause of symptoms. Marable *et al.* (1966) reported three cases of stenosis of the coeliac axis caused by constricting bands without superior or inferior mesenteric abnormality. This was the cause of ischaemic foregut symptoms in one of our cases.

* Consultant Surgeon, Glasgow Royal Infirmary and Peripheral Vascular Unit, Belvidere Hospital, Glasgow E.1.
† Senior Lecturer in Medicine, Glasgow Royal Infirmary, Glasgow C.4.
‡ Radiologist-in-Charge, Stobhill Hospital, Glasgow N.1.

We also report three cases of superior mesenteric occlusion and one case in which all three vessels were severely affected by atherosclerosis.

Case 1

A man aged 56 attended in October 1962 complaining of epigastric pain of one year's duration relieved by defaecation. He had occasional diarrhoea with yellow stools, and had lost 21 lb. (9.5 kg.) in weight. He had had coronary artery thrombosis in 1951 and 1954. Examination showed a thin, poorly nourished man with no specific findings, and a provisional diagnosis of malabsorption or alimentary carcinoma was made.

The principal laboratory investigations are listed in the Table. Test for faecal occult blood was negative, and barium-meal examination showed a malabsorption flocculation pattern on one film. Steatorrhoea was demonstrated, and jejunal biopsy by the peroral technique, using a Crosby capsule, showed changes in the jejunum corresponding to the group 4 lesion of Watson *et al.* (1965); that is, definitely abnormal but less severe than the changes found in adult coeliac disease.

A provisional diagnosis of mild adult coeliac disease was made, and after dismissal he improved slightly on a gluten-free diet. However, he became anaemic and was readmitted on 7 March 1963 for further investigation. One week later he had a mild cerebral attack with paresis but recovered rapidly. Faecal occult blood was present on two occasions, and radioactive chromium studies showed a daily alimentary blood loss of 5–6 ml.

At this point intestinal ischaemia or carcinoma was suspected, and at laparotomy on 1 April the small intestine was cyanotic and without detectable mesenteric pulsation. The ileocolic artery was exposed and divided, and the proximal end dilated by forcible saline injection to a calibre of about 4 mm. and anastomosed end-to-side to the right common iliac artery. On removal of the clamps mesenteric pulsation appeared and the previously cyanotic bowel became red and contractile.

His subsequent recovery was satisfactory, with relief of symptoms and gain in weight, and repeat jejunal biopsy 29 days after operation showed normal tissue. Three months after operation (Special Plate, Fig. 1) retrograde Seldinger catheterization of the right common iliac artery and injection of Urografin visualized the terminal mesenteric vessels. He thereafter remained well until December 1963, when he died from a coronary artery thrombosis.

Case 2

A man aged 54 presented on 26 February 1965 with loss of weight of two years' duration, loss of appetite for 10 months, and a tendency to constipation. He had been treated in 1961 for intermittent claudication due to bilateral femoropopliteal occlusions.

Principal Laboratory and Other Investigations

	Case 1	Case 2	Case 3	Case 4	Case 5
Age in years ..	56	54	54	51	40
Height	4 ft. 11 in. (150 cm.)	5 ft. 3 in. (160 cm.)	5 ft. 3 in. (160 cm.)	5 ft. 2 in. (157 cm.)	5 ft. 5 in. (165 cm.)
E.S.R. (mm./hr.) ..	51	50	24	12	6
Hb (g./100 ml.) ..	10·7	13·2	15	15·5	14·7
Film ..	Anisocytosis	Anisocytosis	Anisocytosis	Normal	Normal
Albumin (g./100 ml.)	2·7	3·5	3·5	3·4	4·0
Globulin „ ..	4·9	2·7	2·6	2·8	2·5
Thymol turbidity (units) ..	0·2	6·3	0·8	1·8	0·6
Bromsulphalein excretion (% dye remaining at)					
25 minutes ..	—	—	25	23	15
45 minutes ..	—	—	15	22	8·5
Ca (mEq/l.) ..	4·5	—	4·7	4·6	4·7
P (mg./100 ml.) ..	3·0	—	3·0	3·8	—
Alkaline phosphatase (K.A. units) ..	14·5	9·8	22·0	15·5	11·5
Faecal fat (g./day) ..	9·8	—	19·7	5·2	9·2
Jejunal biopsy:					
Histology* ..	4	—	4	4	2
Maltase†	—	—	1·5	24·5	11·1
Sucrase† ..	—	—	0·3	5·1	2·9
Lactase†	—	—	0·1	0·9	0·8
Lactose tolerance test	—	—	Flat curve	—	Flat curve
E.C.G.	Normal	Normal	Normal	Posterior ischaemia	Normal
Chest x-ray film ..	„	Aortic calcification	Apical fibrosis, right	Normal	

* Histological grading used by Watson *et al.* (1965).

† Lower limit of normal: maltase = 13·6; sucrase = 3·5; lactase = 1·7 units (Paton *et al.*, 1966).

Examination confirmed the severe weight loss, the liver was just palpable, and the colon was palpable in the left iliac fossa. A provisional diagnosis of alimentary carcinoma or mesenteric ischaemia was made, and he was admitted for investigation (see Table).

Barium enema was negative, and a barium-meal examination report stated: "Irritability of the duodenal cap and coarsening of its mucosa. An ulcer crater at the base of the cap cannot be entirely excluded." Faecal occult blood test was negative.

At operation on 7 April the abdominal aorta showed severe atherosclerosis, and there was no palpable arterial pulsation throughout the alimentary tract, in the viscera supplied by the coeliac axis and superior and inferior mesenteric arteries. Revascularization was not thought feasible and the abdomen was closed. He died suddenly three days later from coronary artery thrombosis.

Case 3

A man aged 54 was investigated in February 1965. He complained of abdominal pain of three months' duration, loss of 1 stone (6.4 kg.) in weight, occasional diarrhoea, and claudication of the left thigh and calf. Barium-meal examination showed a flocculation pattern suggesting malabsorption, and florid liver palms suggested liver disease (see Table).

Lateral aortography (Special Plate, Fig. 2) showed occlusion of the superior mesenteric artery and stenosis of the common iliac arteries. At operation on 25 April 1966 there was no pulsation in the branches of the coeliac axis and superior mesenteric artery. The latter was exposed at the root of the mesentery (where it was patent), divided, and reimplanted into the aorta at a convenient level. Vigorous pulsation was restored to the mesenteric vessels and the small bowel became red and contractible.

Postoperatively he developed diarrhoea (four stools daily), which persisted for several weeks but responded to Lomotil, and he began to gain weight.

Repeat jejunal biopsy showed regression of abnormal histological changes and intestinal disaccharidase levels improved but faecal fat remained high at 10 g./day. Repeat lateral aortography showed revascularization of the small intestine.

Case 4

A man aged 51 had a coronary artery thrombosis in 1961. In 1963 he developed claudication of the left calf, and an aortogram in 1965 showed narrowing of the left common femoral artery and a left superficial femoral occlusion. At operation on 15 March 1965 a large plaque was removed from the common femoral artery and a bypass vein graft inserted from this to the popliteal artery with complete relief of claudication.

Nine months later he developed a right femoropopliteal occlusion and also complained of poor appetite and loss of weight. Barium-meal examination showed some deformity of the duodenal cap and he was put on an ulcer regimen.

In March 1966 claudication recurred in the left leg with absence of the left femoral pulse, and aortography (Special Plate, Figs. 3 and 4) showed occlusion of the left external iliac artery, the vein graft remaining patent. The inferior mesenteric artery was hypertrophied and gave origin to a large marginal artery which supplied the colon and ileum. The marginal artery was larger than in the aortogram of 1965, and a provisional diagnosis of superior mesenteric occlusion or stenosis was made.

At this time he complained of persistent postprandial pain with flatulence, and abdominal distension and early liver palms were present (see Table).

At laparotomy on 27 June there was no detectable pulsation in the stomach and small-intestinal vessels, the small intestine was cyanotic, and the inferior mesenteric and marginal arteries were hypertrophied.

After splenectomy and mobilization of the pancreas the superior mesenteric artery was found to be obliterated at its origin, owing to atherosclerosis, and pulsation in the coeliac axis was poor. The superior mesenteric artery was exposed at the root of the mesentery

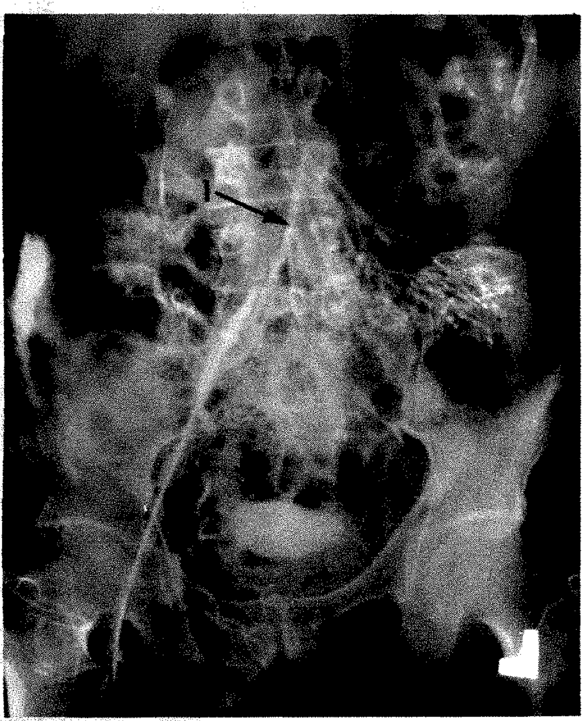


FIG. 1.—Case 1. Seldinger catheter lies in right common iliac artery and injection of dye at this site has visualized the right iliac arteries. At the same time the terminal mesenteric vessels (1) can be seen, indicating that these have filled through a patent ileocolic to common iliac anastomosis. This film was taken three months after operation.

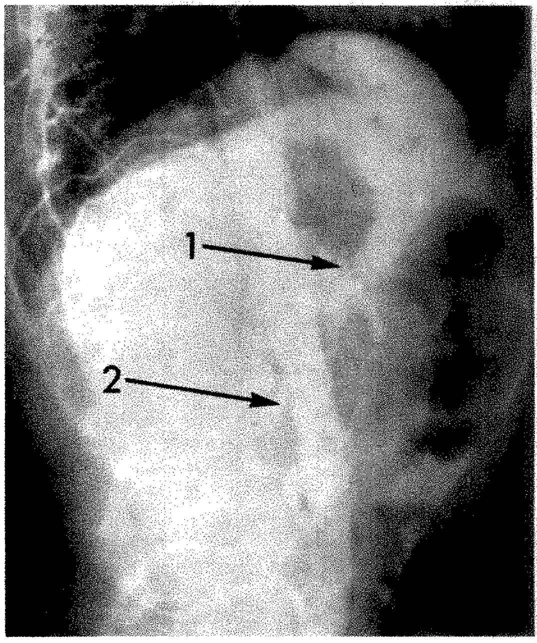


FIG. 2.—Case 3. Lateral aortogram showing dye in coeliac (1) and renal (2) arteries. Superior mesenteric artery is not visualized.

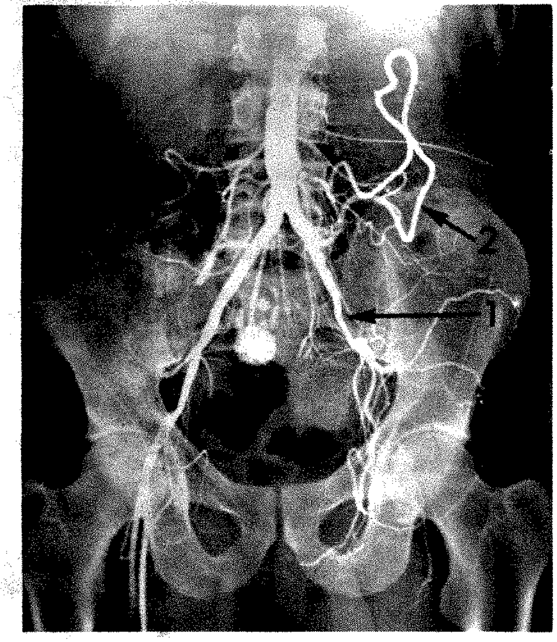


FIG. 3

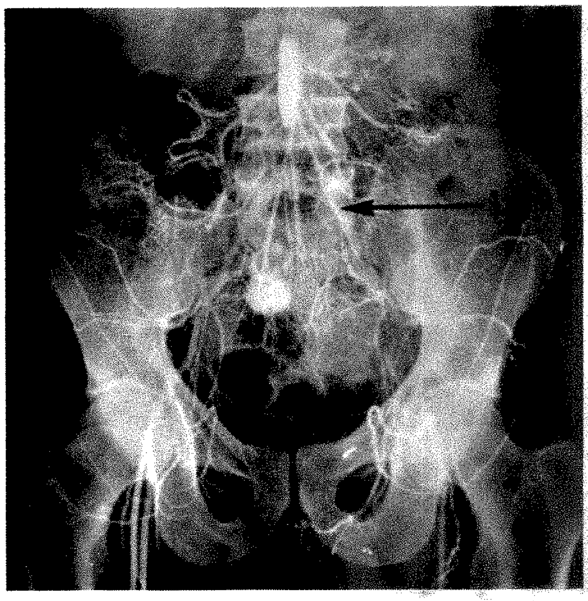


FIG. 4

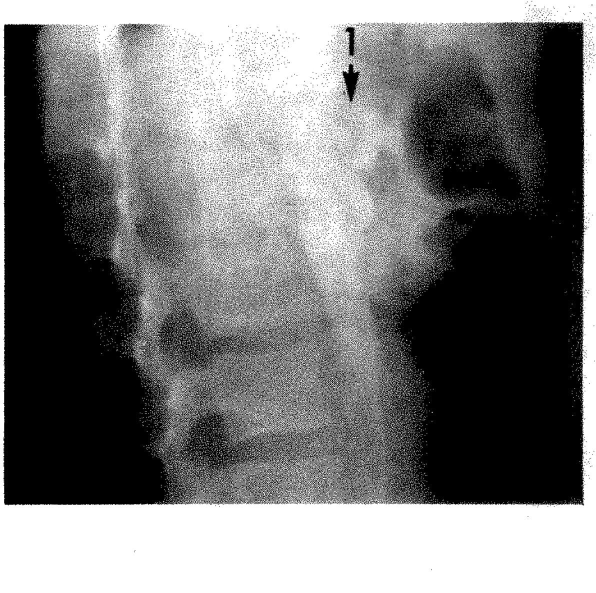


FIG. 5

FIG. 3.—Case 4. Translumbar aortogram showing occlusion of left external iliac artery (1). The inferior mesenteric artery is hypertrophied and gives origin to a large marginal artery (2).

FIG. 4.—Case 4. Late film after the injection of dye illustrated in Fig. 3. Terminal branches to small bowel (1) derived from the superior mesenteric artery can be seen. As the level of aortic injection was well below the origin of the superior mesenteric artery, the terminal mesenteric arteries must have filled from the large marginal artery and superior mesenteric occlusion can be assumed.

FIG. 5.—Case 5. Early film of lateral aortogram showing dye in proximal portions of coeliac axis and superior mesenteric artery. There is a deep notch in upper border of coeliac axis (1) without evidence of atherosclerosis of aorta.

A. E. A. RIDGWAY: SOLAR RETINOPATHY

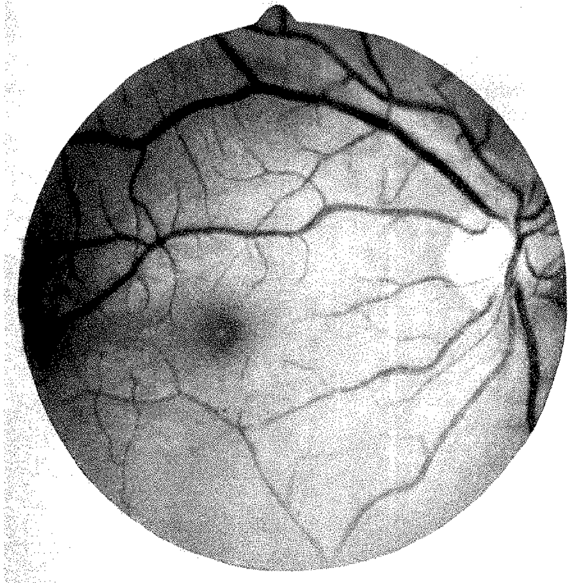


FIG. 1.—Case 3. Photograph taken on 24 May. Kodachrome II. Kowa fundus camera.

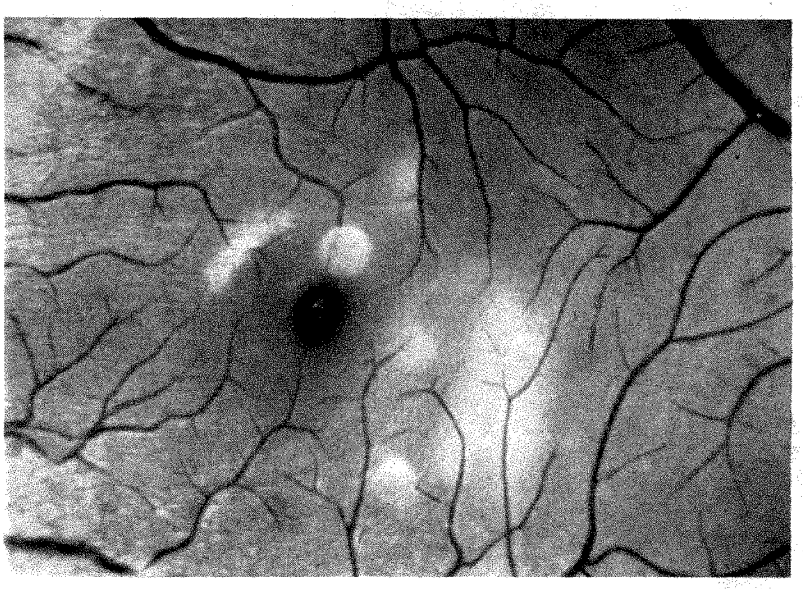


FIG. 2.—Case 5. Photograph taken on 3 June. Kodachrome II. Nordensen fundus camera.

P. D. GULATI *ET AL.*: ENGLEMANN'S DISEASE

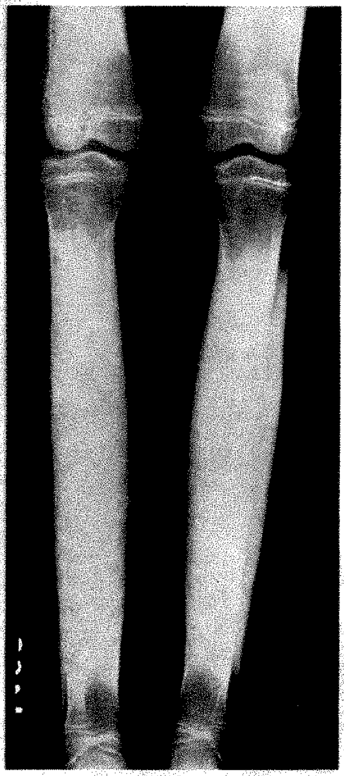


FIG. 1

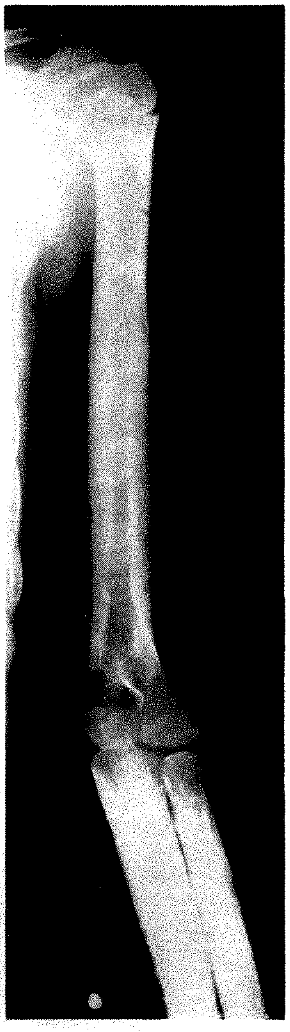


FIG. 2

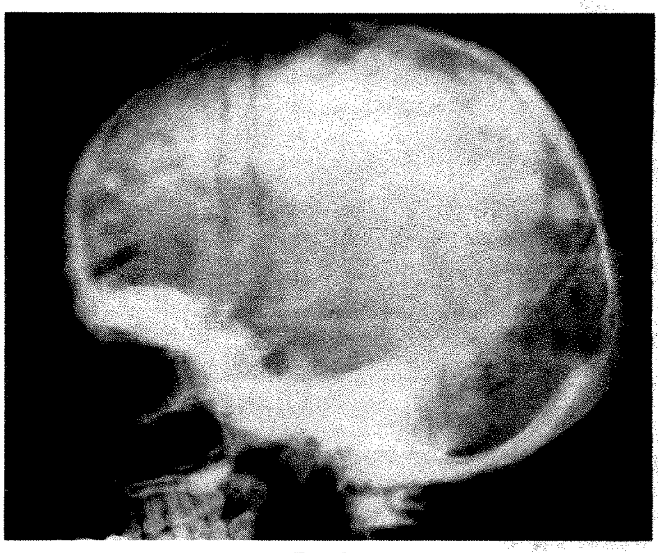


FIG. 3

FIG. 1.—Radiograph showing increased density of the diaphysis of long bones of the lower extremity. Epiphysial and metaphysial zones show normal density.

FIG. 2.—Radiograph showing increased density of the diaphysial zones of long bones of the upper extremity.

FIG. 3.—Radiograph of skull showing osteosclerosis of base of skull as well as bones of calvarium.

and the distal normal artery reimplanted into the aorta with return of colour and pulsation in the small intestine.

Postoperatively he experienced diarrhoea for several weeks. Thereafter he was symptom-free and gained weight.

Case 5

A man aged 40 had had occasional abdominal pain for nine years, and for two and a half years had constant dull periumbilical pain with three motions daily. The pain was not related to meals but was relieved by defaecation and associated with abdominal distension. There was no loss of weight. He had previously been a heavy drinker.

Serum amylase was normal. Other investigations are listed in the Table. Lateral aortography showed narrowing of the coeliac axis (Special Plate, Fig. 5).

At operation on 31 May 1966 there was reduced pulsation in the stomach arteries and no hypertrophy of the pancreatico-duodenal anastomosis. Numerous adhesions were present round the left lobe of the liver, and the coeliac axis appeared to be compressed by the median arcuate ligament and by fibrosis around the coeliac plexus. The ligament was divided, giving normal arterial pulsation. Biopsy of the liver showed a mild inflammatory infiltration round the portal tracts with lymphocytes and occasional eosinophils.

After a smooth convalescence he continued to complain of some mild abdominal pain, but faecal fat was 1 g./day and bromsulphalein clearance 10 days after operation was normal (1.5% dye remaining at 45 minutes).

Discussion

The characteristic presentation of persistent postprandial pain in an undernourished male patient who tends to eat small meals and who may be known to have atherosclerosis constitutes a syndrome which should be readily recognizable as due to ischaemia of the midgut. Dardik *et al.* (1965) collected accounts of only 18 cases successfully treated surgically (including cases reported by Morris *et al.* in 1962), but since then Morris *et al.* (1966) have reported 31 cases treated surgically without mortality, and Rob (1965) has reported 18 cases. This relatively small number of cases, most of which were treated in large centres, suggests either that the condition is rare or that recognition of the symptom pattern is difficult. Our own experience of five cases of chronic intestinal ischaemia operated on within three years (four successfully) suggests that it is not necessarily rare.

Difficulty in diagnosis is due to lack of awareness on the part of the clinician, who fails to include intestinal ischaemia in his differential diagnosis when a patient presents with atypical abdominal pain. Fry and Kraft (1963) analysed the prodromal symptoms of 20 patients who had died from acute infarction of bowel and stated that each had experienced abdominal pain and loss of weight but that the symptom pattern was not "stereotyped."

This is certainly true, and the middle-aged patient who presents with abdominal pain and severe loss of weight may be suspected of having an alimentary carcinoma. This diagnosis was thought to be a possibility in Cases 1 and 2, but barium studies were negative. From our experience we would strongly recommend that any patient with abdominal pain and loss of weight suggestive of carcinoma, in whom barium investigations prove negative, should be suspected of having chronic intestinal ischaemia. Evidence of athersclerosis elsewhere enhances this suspicion and is an indication for lateral aortography.

Barium-meal examination showed minor abnormalities of the duodenal cap suggestive of ulcer in Cases 2 and 4, and ulcer was confirmed in Case 4 at operation. Such findings in patients with chronic intestinal ischaemia may lead to an erroneous diagnosis of duodenal ulcer and delay effective treatment. This sequence of events was observed in a patient who presented with an acute infarction of bowel, having attended elsewhere with his "ulcer" for six months.

Malabsorption is a common occurrence in visceral ischaemia. It occurred in Cases 1, 3, 4, and 5 and might have been discovered in Case 2 if the appropriate investigations had been carried out. Heard *et al.* (1963), who reported one case and reviewed 18 others from the literature, found that malabsorption was a feature in five (26%). Most of the case reports in the literature are poorly documented in this respect (Dardik *et al.*, 1965), and our experience suggests that malabsorption is commoner than the figures of Heard *et al.* indicate.

Small-bowel disease was demonstrated by steatorrhoea (Cases 1, 3, and 5), abnormal histology (Cases 1, 3, and 4), and low intestinal disaccharidase activity (Cases 3, 4, and 5). Abnormality of liver function was shown by impaired bromsulphalein excretion in Cases 3 and 4, though routine liver-function tests in these patients were normal.

Chronic ischaemia has therefore a functional effect on small intestine and liver. It may even cause abnormalities of pancreatic secretion, though we have no evidence to offer on this point. In addition to the loss of weight in these five patients, it was noteworthy that all were small, measuring from 4 ft. 11 in. to 5 ft. 5 in. (150 to 165 cm.) in height.

When mesenteric pulsation is found to be reduced or absent at operation, a variety of surgical procedures may be employed. Morris *et al.* (1966) prefer bypass Dacron graft, but employed endarterectomy in five cases. They performed single artery revascularization in 14 cases and revascularization of two arteries in 17 cases, but point out that full restoration of normal blood flow is not necessary for a good result, unlike revascularization in renal artery stenosis. Long-term survival of bypass grafts seemed good, and one had been successful for eight years.

Bypass saphenous-vein grafting (Fry and Kraft, 1963) and homografts (Mavor and Lyall, 1962; Heard *et al.*, 1963) have also proved successful.

Thromboendarterectomy is a logical procedure where the lesion is confined to the first centimetre or two of the main trunk, and this method was successfully employed in two cases by Shaw and Maynard (1958). Exposure of the origin of the coeliac axis and superior mesenteric artery from the aorta was easily achieved in Cases 4 and 5, without opening the chest, by mobilization of the splenic flexure of colon, splenectomy, mobilization of pancreas, and retraction of stomach and pancreas to the right. Occasionally stenosis may affect a longer segment of artery (Fry and Kraft, 1963—2 cases in 20) and this technique cannot be employed.

The possibility of direct arterial anastomosis between the aorta and the mesenteric vessels is illustrated by the successful result obtained by Ranger and Spence (1962) when a functioning side-to-side anastomosis was made between the aorta and ileocolic artery and by the successful result obtained in our first case by end-to-side anastomosis of the distended ileocolic artery to the right common iliac artery.

Mikkelsen (1957) advocated reimplantation of the distal portion of the superior mesenteric artery into the aorta. Experience of the satisfactory function of a reimplanted artery in cases of renal artery stenosis led to the reimplantation of the superior mesenteric artery in Cases 3 and 4. Brolin and Hansson (1964) have also reported the use of this method. The lumen of the anastomosis is not as large as that of a healthy superior mesenteric artery, but the efficiency of revascularization appears superior to that achieved by bypass grafting.

The assessment of the relative values of operative procedures to relieve chronic intestinal ischaemia will be possible only when sufficient cases become available for operation, and this requires the greater use of lateral aortography as a diagnostic procedure in suspected cases.

The prohibitive mortality of acute infarction emphasizes the necessity for early diagnosis at the stage of chronic ischaemia. Mavor and Lyall (1962) suggest that the period of prodromal symptoms is not necessarily prolonged, and in the collected series of 19 cases of Heard *et al.* (1963) the mean duration of symptoms was four to five months. This suggests that prolonged investigation and indecision are undesirable in the management of these cases.

Summary

Five cases of visceral ischaemia are presented. Successful operative and clinical results were obtained in three of the four cases of chronic intestinal ischaemia and in one case of coeliac axis stenosis.

Malabsorption was a feature of four cases. Abnormalities of faecal fat, jejunal histology, disaccharidase activity, and bromsulphalein excretion were present, and improvement or reversion to normal followed successful operation.

Chronic intestinal ischaemia should be strongly suspected in middle-aged patients with atypical abdominal pain and loss of weight, especially when alimentary carcinoma is suspected and barium studies are negative. Successful revascularization of the abdominal viscera can be achieved when the diagnosis has been proved by lateral aortography.

We wish to thank Mr. C. J. Longland for permission to include Case 2 in this report and Dr. D. Murray for the histological examination of the intestinal biopsies.

References

Brolin, I., and Hansson, L. O. (1960). *Acta chir. scand.*, **128**, 261.
Dardik, H., Seidenberg, B., Parker, J. G., and Hurwitt, E. S. (1965). *J. Amer. med. Ass.*, **194**, 1206.
Dunphy, J. E. (1936). *Amer. J. med. Sci.*, **192**, 109.
Fry, W. J., and Kraft, R. O. (1963). *Surg. Gynec. Obstet.*, **117**, 417.
Heard, G., Jefferies, J. D., and Peters, D. K. (1963). *Lancet*, **2**, 975.
Marable, S. A., Molnar, W., and Beman, F. M. (1966). *Amer. J. Surg.*, **111**, 493.
Mavor, G. E., and Lyall, A. D. (1962). *Lancet*, **2**, 1143.
—— —— Chrystal, K. M. R., and Tsapogas, M. (1963). *Brit. J. Surg.*, **50**, 219.
Mikkelsen, W. P. (1957). *Amer. J. Surg.*, **94**, 262.
Morris, G. C., jun., Crawford, E. S., Cooley, D. A., and DeBakey, M. E. (1962). *Arch. Surg.*, **84**, 95
—— DeBakey, M. E., and Bernhard, V. (1966). *Surg. Clin. N. Amer.*, **46**, 919.
Paton, E., Murray, E., and Watson, W. C. (1966). *Brit. med. J.*, **1**, 459.
Ranger, I., and Spence, M. P. (1962). Ibid., **2**, 95.
Rob, C. (1965). *Bibl. gastroent. (Basel)*, **8**, 149.
Shaw, R. S., and Maynard, E. P. (1958). *New Engl. J. Med.*, **258**, 874.
Watson, W. C., Paton, E., and Murray, D. (1965). *Lancet*, **2**, 47.

Controlled Trials of a Sulphonamide Given Weekly to Prevent Exacerbations of Chronic Bronchitis

A. PINES,* M.D., M.R.C.P.ED.

Brit. med. J., 1967, 3, 202–204

Purulent exacerbations are difficult to prevent in patients with chronic bronchitis. Trials of antibiotics administered continuously for long periods have given variable and often negative results (Elmes, 1962). Most of these studies have been in outpatients, in whom regular treatment and exact assessment are notoriously difficult (Porter, 1966). I present the results of a controlled trial of a new sulphonamide given weekly to hospital inpatients with chronic bronchitis.

Sulphormethoxine (Fanasil) is a sulphonamide with a half-life in the body of 100 to 200 hours, so that it is effective if given once weekly. In a preliminary study in this hospital it was found to have some effect in mild exacerbations of chronic bronchitis, especially when given in a 2-g. dose weekly. A weekly dose over long periods is so convenient that it seemed worth assessing the value of the drug in preventing purulent exacerbations of chronic bronchitis.

First Trial

Many of the patients in this hospital stay for long periods because of medical or social reasons, or both. Patients who suffered from chronic bronchitis were eligible for the trial if (1) they were going to stay for long periods ; (2) had a history of at least one acute exacerbation during the previous 12 months as defined by hospital admission, treatment by antibiotics, or confinement to bed at home ; and (3) had purulent sputum at the time of admission.

Plan of Trial.—In all patients the initial purulence of the sputum was cleared with courses of antibiotics. They were then divided into two groups by random selection, in a proportion of two treated to one control. Cards with treatment or control written on them were placed in sealed envelopes at random and taken in strict order of entry into the trial. As it was anticipated that many of the controls would relapse, this ratio would allow more patients to be treated. The treated patients were given sulphormethoxine 2 g. once weekly. The control patients were given symptomatic treatment only. Because sulphormethoxine is a relatively new drug in this country, a double-blind trial with a placebo as well was not thought advisable, so that a close watch could be kept for any toxicity. No antibiotics were given to patients in either group unless a purulent exacerbation occurred. The patients were admitted to the trial from January 1964 until October 1964.

Patients.—All the patients were men. Most were aged from 40 to 70 (Table I). All had had symptoms of bronchitis for at least five years. Both groups were comparable in age (Table I) and in initial distribution of quantity of sputum (Table II). The method of allocation ensured that patients entered the trial in balanced proportions during each month of the year. Those

TABLE I.—*Ages of Patients in First Trial*

Age	Treated Patients	Control Patients
40–60 years	10	4
61–70 "	18	8
71–75 "	4	4
Total	32	16

TABLE II.—*Results According to Initial Quantity of Sputum in First Trial*

Sputum Quantity	Treated Patients		Control Patients	
	Success	Failed	Success	Failed
Less than 30 ml. daily	17	3	3	9
30 ml. or more daily	4	8	1	3
Total	21	11	4	12

---

* Ware Park Hospital, Ware, Herts.

patients who did not relapse were observed for at least four months and some for up to eight months.

Daily Observation.—A 24-hour specimen of sputum was examined for purulence and quantity. Sputum purulence was graded into three categories—mucoid, with at the most a trace of pus ; grade 1 purulence when up to 50% of the specimen was purulent ; and grade 2 purulence when over 50% was purulent. This was assessed daily by an independent observer, an experienced charge nurse who was completely unaware of whether patients were being treated or not. An exacerbation was diagnosed when the sputum became purulent, either grade 1 or grade 2, for three successive days, whether accompanied by fever or other manifestations or not. Most patients did in fact feel ill and had fever. They were then withdrawn from the trial and the exacerbation treated with an antibiotic. *Only the independent and " blind " assessment of the sputum was taken into consideration.*

The sputum was tested routinely at monthly intervals or at the time of an exacerbation for pathogenic bacteria, though these were not tested for sensitivity to sulphormethoxine. The haemoglobin, white count, and urine were tested monthly and a blood urea was taken initially. The assessments of respiratory function and additional biochemical data were regarded as unimportant in this trial and were not carried out routinely.

Results.—There were no withdrawals except where an exacerbation occurred. Of the 16 control patients exacerbations took place in 12 (75%). Of the 32 patients treated with sulphormethoxine exacerbations occurred in 11 (35%). There were no exacerbations in 4 (25%) of the 16 controls and in 21 (66%) of the 32 treated patients. The difference in the percentage of exacerbations is 40%, which is three times the standard error of 13.68%. The 95% confidence interval for the true difference is 14–68%. Sulphormethoxine seemed more successful in those patients who expectorated less than 30 ml. of sputum daily at the beginning of treatment (Table II).

Second Trial

Because of the success of sulphormethoxine and its lack of toxicity, a further trial was carried out during the winter of 1965–6. This was " double-blind " in a group of 60 patients similar to those in the first trial, again with independent assessment of the purulence of the daily 24-hour specimen of sputum. Four tablets of placebo or of sulphormethoxine (2 g.) were given weekly for a period of 10 weeks, whether relapse occurred or not.

Ten weeks' supply of tablets for each patient had been placed in a bottle by Roche Products Ltd. and numbered. The order in which either placebo or sulphormethoxine was issued was determined at random (Fisher and Yates) in a proportion of two treated to one placebo. The key to the trial was kept in a sealed envelope and not opened until both the trial and the final assessments of all patients had been completed. Though it would have been preferable for patients to continue throughout the winter in the trial, few would have stayed long enough in hospital to allow this assessment.

Patients.—Four had to be withdrawn from the trial, leaving 56 patients. Most were aged between 40 and 70 (Table III). All had had symptoms of bronchitis for at least five years (Table IV). In many patients an initial maximal peak flow reading had been obtained (Table V), and almost all showed a severe ventilatory defect. The placebo-treated patients tended to be younger, to have a shorter history of disease, to have less sputum (Table VI), and, in those tested, to have a higher range of maximal peak flow.

Results.—Three sulphormethoxine-treated patients were withdrawn (one discharged himself, cultures were positive for *Mycobacterium tuberculosis* in the second, and in the third an eosinophilia of 15% was present in the sputum). One control patient was withdrawn (eosinophilia in the sputum, 10%). In the placebo group exacerbations occurred in 13 (68%) out of 19 patients, and in the sulphormethoxine group in 14 (38%) out of 37. There were no relapses in 6 (32%) placebo-treated patients and in 23 (62%) sulphormethoxine-treated patients. The difference in the proportion of exacerbations is 30%, which is more than twice the standard error of 13.35%. The 95% confidence interval for the true difference is 3–51%. More exacerbations occurred among those patients who had over 30 ml. of sputum daily, both those treated and the controls. In those patients who had exacerbations there was a mean of 2.1 illnesses in 10 weeks among those sulphormethoxine-treated and of 1.5 among the controls. This may be related to the milder bronchitis which predominated among the latter.

TABLE III.—*Age of Patients in Second Trial*

Age	Treated Patients	Control Patients
40–60 years	6	7
61–70 "	23	10
71–75 "	8	2
Total	37	19

TABLE IV.—*Duration of Symptoms in Second Trial*

Duration	Treated Patients	Control Patients
5–10 years	16	12
11–20 "	12	3
21+ "	9	4
Total	37	19

TABLE V.—*Initial Maximal Peak Flow Rates in Second Trial*

Rate	Treated Patients	Control Patients
Less than 100 l./min. ..	5	0
100–200 " ..	14	7
Over 200 " ..	3	1
Total	22	8

TABLE VI.—*Results According to Initial Quantity of Sputum in Second Trial*

Sputum Quantity	Treated Patients		Control Patients	
	Success	Failed	Success	Failed
Less than 30 ml. daily ..	16	5	5	7
30 ml. or more daily ..	7	9	1	6
Total	23	14	6	13

Comment

When the results of both trials are combined the difference in the proportion of exacerbations is 35% and the standard error 9.603. The 95% confidence interval for the true difference lies between 16 and 54%.

Toxicity.—No toxicity or intolerance was found among any of the patients in either trial.

Bacteriology.—In both trials sputum was tested monthly as a routine. In the first trial *Haemophilus influenzae* was found at some time in 12 out of 48 patients and *Streptococcus pneumoniae* in five. In the second trial *H. influenzae* was found in eight and *Str. pneumoniae* in three. These results are too scanty to merit further analysis.

Discussion

The sulphonamides are generally held to be effective in vitro against *Str. pneumoniae* and *H. influenzae :* sulphormethoxine is equally effective in vitro (E. Bohni, personal communication, 1966). With 2 g. once weekly of sulphormethoxine plasma levels of free sulphonamide lie between 15 and 20 mg./100 ml. throughout the week, which may be comparable to that found with daily sulphadimidine by Newbould and Kilpatrick (1960). The mean half-life is 180 hours. Sulphormethoxine 1 g. weekly gives slightly lower levels (Clarke, 1964).

In previous work on the prophylaxis of chronic bronchitis sulphonamides have not been shown to be effective (Kilpatrick and Oldham, 1954; Edwards *et al.*, 1957; Francis *et al.*, 1964). However, Clarke (1964), Aguirre and Casado (1964), and Frank (1964) were impressed with sulphormethoxine in preliminary studies. With sulphormethoxine the results I have described show a definite prophylactic effect in hospital inpatients. The number of exacerbations was significantly reduced. The initiation of many relapses must often be outside the control of ordinary chemotherapy (Scadding, 1966). Nevertheless, these results are better than in most other studies utilizing antibiotics, which have usually shown no reduction in the number of acute exacerbations (Scadding, 1966). These studies with antibiotics have shown reduction in the length of the acute illness (Scadding, 1966), but this was not so with sulphormethoxine. Naturally, inpatient conditions are more sheltered; an outpatient investigation on the effect of sulphormethoxine would be necessary on a larger scale and for longer than is possible in hospital before advocating its widespread use.

Perhaps sulphormethoxine is more effective than other long-acting sulphonamides: the percentage of protein-binding is less than with sulphadimethoxine (Madribon), especially in higher levels, so that more diffusible and active sulphonamide is available. The effect of protein-binding on activity is sometimes uncertain and paradoxical (*Brit. med. J.*, 1966). The steady effect throughout the week is likely to suppress the growth of *H. influenzae* and *Str. pneumoniae* once the major proportion of the infecting population has been eradicated by the more powerful antibiotics. Sulphonamides are said to be inactivated in the presence of pus, so that it is important to clear this from the bronchi so far as is possible *before* starting chemoprophylaxis. This may explain why sulphormethoxine was not very effective in treating an actual exacerbation in the preliminary study, or in reducing the duration of each acute illness during the trials. It may be a reason why others have obtained poor results with sulphonamides alone when treating patients in whom varying amounts of pus may often have been present in the sputum at the beginning of treatment.

The tolerability of sulphormethoxine and its ease of administration once weekly are important advantages over the antibiotics used in the prophylaxis of purulent exacerbations of bronchitis. During the course of much experience with sulphormethoxine side-effects have occurred in about 2% of patients. These consisted mainly of headache, nausea, and vomiting, but very occasional cases have been described of allergic skin rashes and leucopenia, all ending in recovery. The incidence of these effects is certainly no higher than with other sulphonamides, and appears insignificant compared with the seriousness of repeated purulent exacerbations of chronic bronchitis. Theoretically the time that sulphormethoxine remains in the body may prolong sensitivity reactions. Nevertheless, experience has shown that reactions last for no longer than with short-acting sulphonamides.

Summary

Sulphormethoxine (Fanasil) is a sulphonamide which if administered once weekly gives effective levels over the whole week. Two such trials are described in hospital long-stay inpatients suffering from chronic bronchitis and in whom the initial purulence of the sputum had been cleared with antibiotics. Assessment was by " blind " independent evaluation of the daily, 24-hour sputum for purulence.

In the first trial 11 (34%) out of 32 treated patients relapsed, as did 12 (75%) out of 16 given symptomatic treatment only (95% confidence interval 14–68%). In the second trial there were relapses in 14 (38%) out of 37 treated patients and in 13 (68%) out of 19 given a placebo only (95% confidence interval 3–57%). If the results of both trials are combined the 95% confidence interval is 16–54%.

There were no side-effects.

Sulphormethoxine shows significant prophylactic benefit in patients with chronic bronchitis and should be assessed on a larger scale in outpatients.

I wish to thank the medical, nursing, and secretarial staff of Ware Park Hospital for their help; the physicians who sent me their patients; Dr. D. Linsell and Dr. P. D. Griffiths and their staff, of the Pathological Laboratory, Hertford County Hospital, for the pathological investigations; Mr. M. Hills, London School of Hygiene and Tropical Medicine, for his statistical advice; Dr. I. Lenox-Smith, Roche Products Ltd., for supplies of sulphormethoxine, for criticism, and for the unpublished information about this drug which I have quoted; and Professor J. W. Crofton, University of Edinburgh, for criticism.

A short version of this paper was given at the Fourth International Congress for Infectious Diseases, Munich, April, 1966.

ADDENDUM.—Recent but as yet unpublished experience on a very large scale during an outbreak of meningococcal meningitis, in which sulphormethoxine was used prophylactically in very high and repeated doses, has shown that the drug can occasionally produce skin reactions. These usually occurred in children, were mild, and followed a benign course. In some cases, however, they were generalized, more severe, and showed features of Lyell's syndrome.

REFERENCES

Aguirre, M., and Casado, J. (1964). *3rd International Congress of Chemotherapy*, Stuttgart, 1963, edited by H. P. Kuemmerie, and P. Preziosi, vol. 1, p. 672.
Brit. med. J., 1966, **1**, 1059.
Clarke, G. B. M. (1964). *3rd International Congress of Chemotherapy*, Stuttgart, 1963, edited by H. Kuemmerie and P. Preziosi, vol. 1, p. 680.
Edwards, G., Buckley, A. R., Fear, E. C., Williamson, G. M., and Zinnemann, K. (1957). *Brit. med. J.*, **2**, 259.
Elmes, P. (1962). *Irish J. med. Sci.*, 6th Series, p. 243.
Francis, R. S., May, J. R., and Spicer, C. C. (1964). *Brit. med. J.*, **1**, 728.
Frank, A. (1964). *Wien. klin. Wschr.*, **76**, 668.
Kilpatrick, G. S., and Oldham, P. D. (1954). *Brit. med. J.*, **2**, 385.
Newbould, B. B., and Kilpatrick, R. (1960). *Lancet*, **1**, 887.
Porter, A. M. W. (1966). *Brit. med. J.*, **1**, 1301.
Scadding, J. G. (1966). Ibid., **1**, 1281.

Comparison of Methods of Expressing the Results of Augmented Histamine Tests

R. J. ABERNETHY,* F.R.C.S.ED.; R. M. ROSS,* F.R.C.S.ED.; A. G. COX,*† M.D., F.R.C.S.ED.
A. W. KAY, M.D., CH.M., F.R.C.S.; I. E. GILLESPIE,* M.D., F.R.C.S.

Brit. med. J., 1967, 3, 205–206

The augmented histamine test (Kay, 1953) has been widely used as a reliable means of measuring maximal acid secretion by the stomach. There is general agreement that the dose of histamine (0.04 mg./kg. body weight) recommended by Kay evokes a maximal or near-maximal acid response. However, the period during which the response is greatest is the subject of dispute, and workers have used the acid output in different periods to report their results. Most have used the response in the 30-minute period from 15 to 45 minutes after the histamine injection, as originally suggested by Kay. Baron (1963) showed that the maximal response did not always coincide with this period and suggested that the greatest half-hour response (the "peak half-hour") should be used whenever it occurred. Other workers have referred to the secretion during the whole 60-minute period after histamine as the maximal histamine response (Bruce *et al.*, 1959).

If the results of augmented histamine tests are expressed in different ways the conclusions may also differ. In this paper we present a detailed analysis of the effect of reporting the results in these different ways. The data are taken from acid tests in a consecutive series of 100 patients with duodenal ulcer studied before and after vagotomy with a simple drainage procedure.

Materials and Methods

Each patient had an augmented histamine test and a "medical vagotomy" test (Gillespie and Kay, 1961) before operation, and an augmented histamine test and an insulin test approximately 8 to 10 days after operation. Each test was carried out after a 12-hour fast. Before operation a radio-opaque nasogastric tube was passed under fluoroscopic control. In the postoperative tests use was made of a gastrostomy tube placed in the stomach at operation. Gastric secretions were collected by continuous suction by electric pump, with occasional interruption to ensure patency.

In the augmented histamine test four basal specimens were aspirated at 15-minute intervals after removal of the fasting juice. Mepyramine maleate, 50 mg., was injected intramuscularly, and 30 minutes later histamine acid phosphate, 0.04 mg./kg. of body weight, was given by subcutaneous injection. Thereafter 15-minute aspirates were collected for one hour.

In the medical vagotomy test a combination of hexamethonium bromide, 50 mg., and atropine sulphate, 0.325 mg., was given as a single deep intramuscular injection one and a half hours before the injection of histamine. The details of antihistamine and histamine dosage and timing were otherwise the same as in the augmented histamine test.

In the insulin test 20 units of soluble insulin was given intravenously after collection of two 15-minute basal specimens. Blood sugar concentration fell to below 35 mg./100 ml. in all cases. Fifteen-minute aspirates were collected for two hours after the insulin injection.

The volume of each 15-minute specimen was measured. After filtration acid concentration was measured by titration against 0.1 normal sodium hydroxide with phenol red as indicator (end-point *p*H 6.8–8.4). Acid outputs were obtained by multiplication of volume and concentration values and expressed as mEq.

The response to the insulin test was classified as positive if the criteria of Hollander (1951) were satisfied at any time within the two hours of collection of specimens after the insulin injection. A positive response was denoted by an increase in acid concentration of more than 20 mEq/l. over basal concentration or by an increase in concentration of more than 10 mEq/l. in the presence of basal anacidity.

Analysis of Results

For the purposes of this analysis the results of all augmented histamine tests were expressed in three different ways: (1) "mid-half-hour," acid output in the 15- to 45-minute period after histamine; (2) "peak half-hour," acid output in the 30-minute period giving the greatest response after histamine; and (3) "whole hour," acid output in the 60 minutes after histamine. Each of these methods of reporting the results was compared with each of the others by calculating the correlation coefficient between each possible pair.

Table I shows the exceptionally high degree of correlation between each pair of measurements in (*a*) the preoperative augmented histamine response, (*b*) the medical vagotomy modification, and (*c*) the postoperative augmented histamine response. Similarly, as shown in Table II, there was good correlation between the three pairs of measurements when the effects of medical and surgical vagotomy were expressed as percentage reductions of the preoperative augmented histamine response. These correlations were not so close to unity, because each point represents the results of four tests. Despite this, all correlation coefficients were statistically significant.

Within the series of 100 patients there were subgroups which differed significantly one from the other with regard to

TABLE I.—*Correlation Coefficients Between Results of the Augmented Histamine Response Expressed in Three Different Ways* (100 *Cases*)

	Peak Half-hour v. Mid-half-hour	Mid-half-hour v. One Hour	One Hour v. Peak Half-hour
Preoperative augmented histamine response	0·925	0·909	0·942
Medical vagotomy response ..	0 909	0·949	0·961
Postoperative augmented histamine response	0·927	0·948	0·977

All correlation coefficients are statistically significant (P < 0·001).

TABLE II.—*Correlation Coefficients Between Reduction of Augmented Histamine Response by Medical and Surgical Vagotomy Expressing the Results in Three Ways*

Percentage Reduction of Augmented Histamine Test by:	Peak Half-hour v. Mid-half-hour	Mid-half-hour v. One Hour	One Hour v. Peak Half-hour
Medical vagotomy	87 cases 0·752	89 cases 0·777	89 cases 0·820
Surgical vagotomy	99 cases 0·881	98 cases 0·885	98 cases 0·948

All correlation coefficients are statistically significant (P < 0·001).

---

* University Department of Surgery, Western Infirmary, Glasgow W.1.
† Present address: Department of Surgery, Royal Postgraduate Medical School, London W.12.

augmented histamine response. A notable example was the difference between the two sexes, the males secreting more acid than the females. It was of interest to see whether this difference was quantitatively the same with each of the different methods of expressing the augmented histamine response. Table III shows that the male/female ratios for all three methods were virtually identical, as were the Student's *t* test values for each.

TABLE III.—*Comparison of Differences Between Male and Female Preoperative Augmented Histamine Responses with the Three Methods of Expression (Standard Deviations in Parentheses)*

	Mean Values of Test		Ratio of Male/Female (Mean Values)	*t*	P
	Males (83)	Females (17)			
Mid-half-hour secretion	19·9 (±8·0)	13·3 (±5·3)	1·50	3·284	<0·01
Peak half-hour secretion	22·0 (±8·0)	15·2 (±6·2)	1·45	3·319	<0·01
One hour secretion ..	33·8 (±13·8)	22·8 (±10·3)	1·48	3·123	<0·01

Finally, the effect of taking the three different estimates of augmented histamine response was observed in comparing two subgroups whose responses differed by a much smaller amount. These were the group with a negative response to insulin and the group with a small positive response occurring late in the two-hour collection period after the insulin injection. Though the classification of this late type of insulin response was made on an arbitrary basis, it had previously been found that the reduction in augmented histamine response due to vagotomy in patients comprising this subgroup was greater than the reduction in those with large and early positive insulin responses, and only slightly less than the reduction seen in those with completely negative insulin responses (Ross and Kay, 1964). Table IV shows that the relation between the two insulin groups is virtually the same regardless of the method used to express the augmented histamine responses.

TABLE IV.—*Comparison of Percentage Reduction in Augmented Histamine Response in Patients with a Negative Insulin Test, and Those with a "Late Positive" Insulin Test After Vagotomy and Drainage (Standard Deviations in Parentheses)*

	Percentage Reduction of Augmented Histamine Response		Ratio of % Reductions: Negative/Positive	*t*	P
	Insulin Negative (69 cases)	Insulin "Late Positive" (27 cases)			
Mid-half-hour output	75% (±18·3)	56% (±19·3)	1·34	4·551	<0·01
Peak half-hour output	69% (±17·5)	54% (±20·8)	1·28	3·579	<0·01
One hour output..	73% (±18·9)	58% (±20·4)	1·26	3·377	<0·01

Conclusions and Summary

It can be seen from Tables I and II that there was a highly significant degree of correlation between the three methods of expressing the results. Tables III and IV show that when differences exist between the results of subgroups of patients within the series these differences are of the same magnitude, regardless of the way in which the results are expressed.

We therefore conclude that variations in the method of expressing the results of the augmented histamine test are unlikely to alter the conclusions derived from a particular series of such tests. It is likely, therefore, that conclusions in studies using different ways of expressing the test responses can be directly related one with another.

REFERENCES

Baron, J. H. (1963). *Gut*, 4, 136.

Bruce, J., Card, W. I., Marks, I. N., and Sircus, W. (1959). *J. roy. Coll. Surg. Edinb.*, 4, 85.

Gillespie, I. E., and Kay, A. W. (1961). *Brit. med. J.*, 1, 1557.

Hollander, F. (1951). *Meth. med. Res.*, 4, 166.

Kay, A. W. (1953). *Brit. med. J.*, 2, 77.

Ross, B., and Kay, A. W. (1964). *Gastroenterology*, 46, 379.

Late Changes in Peripheral Blood after Thorotrast Administration

A. O. LANGLANDS,* M.B., CH.B., B.SC., D.M.R.T., F.F.R.; E. R. D. WILLIAMSON,* M.B., B.CH.

Brit. med. J., 1967, 3, 206–208

From its introduction in 1930 a stabilized colloidal suspension of ^{232}thorium dioxide (Thorotrast) was extensively used either to outline body cavities, such as the renal pelvis or the paranasal sinuses after direct injection, or as a contrast medium in angiography, and, after deposition, for visualization of the liver and spleen. Its use was largely discontinued in 1947 after the report of MacMahon *et al.* (1947) on the first malignancy due to Thorotrast. Horta *et al.* (1965) reported a follow-up study of some 1,100 persons who had received Thorotrast. In addition to malignancies arising at sites of Thorotrast deposition 16 deaths out of a total of 699 were due to leukaemia, aplastic anaemia, or purpura.

We have recently undertaken a study of patients who had received intra-arterial Thorotrast, in an attempt to obtain information on the morbidity and haematological and cytogenetic changes due to Thorotrast. The purpose of this communication is to report the findings on examination of peripheral blood from these patients.

Material and Methods

Between 1930 and 1947, during investigation in the department of surgical neurology, Edinburgh, 137 patients received intra-arterial Thorotrast. In 1966 there were 37 survivors still residing in Edinburgh or near by. A venous blood sample was obtained from 35, comprising 18 men and 17 women. With one exception all had received Thorotrast before 1947.

The details of Thorotrast administration in these patients are summarized in Table I.

Packed cell volumes were determined according to the method described by Dacie and Lewis (1963) ; haemoglobin was esti-

TABLE I

	Age (years)		Dose Thorotrast (ml.)		Latent Period (years)	
	Range	Mean	Range	Mean	Range	Mean
18 men	37–71	52·4	12–50	26·2*	19–30	22·7
17 women	33–78	56·6	10–90	24·9	11–31	24·2

* Based on 13 cases. The dose was unrecorded in five.

---

* M.R.C. Clinical Effects of Radiation Research Unit, Western General Hospital, Edinburgh 4.

mated photoelectrically as oxyhaemoglobin; white blood cells and platelets were counted, after bulk dilution, in a new Neubauer counting-chamber. Films made from fresh blood were air-dried, fixed in methanol for 10 minutes, and stained by May–Grunwald–Giemsa.

Absolute values for polymorphonuclear leucocytes, lymphocytes, monocytes, and eosinophils were calculated using the total white cell count and a differential white cell count based on 200 cells.

Results

In all 35 patients the packed cell volume, haemoglobin level, white cell count, and platelet count were within the normal range. A few patients showed a relative lymphocytosis, but the mean values for the differential white cell count did not differ significantly from the normal values given by Dacie and Lewis (1963). The mean values are shown in Table II.

TABLE II

	P.C.V.		Hb (g./100 ml.)		W.B.C. (× 10³/cu. mm.)		Platelets (× 10³/cu. mm.)		Neutrophils		Lymphocytes		Monocytes		Eosinophils	
	Range	Mean	Range	Mean	Range	Mean	Range	Mean	× 10³/ cu. mm.	%	× 10³/ cu. mm.	%	/cu. mm.	%	/cu. mm.	%
18 men ..	41·0–52·0	45·6	11·2–16·4	14·3	5·0 –13·6	6·6	174–262	219	3·38	51	2·58	39	440	6·6	200	3·0
17 women	35·5–48·0	40·9	10·5–14·9	12·7	4·85– 9·05	6·7	140–358	220	3·44	51	2·58	38	410	6·1	250	3·7

The most striking feature on examination of peripheral blood films was a disturbance of red cell morphology. There was a varying degree of anisocytosis, with occasional well-filled macrocytes, and, in addition, numerous burr cells and occasional target cells and stipple cells were present. Giant platelets were a common finding. Howell–Jolly bodies were present in 34 out of 35 films, the exception being that of a woman of 55 who, 23 years previously, had received 40 ml. of Thorotrast during right carotid angiography. On examination of her neck a hard mass was found at the site of injection. *X*-ray films showed this to be a dense aggregation of Thorotrast. Virtually no Thorotrast was visible in the spleen on abdominal *x*-ray examination.

In each of eight patients 1,000 red cells were counted, the percentages of abnormal cells being recorded in Table III. Fig. 1 shows a field from a peripheral blood film which illustrates these findings.

TABLE III

Case No.	Sex and Age	Thorotrast (ml.)	Latent Period (years)	Burr Cells	Target Cells	Stipple Cells	H.J. Bodies	Giant Platelets
				Per 100 Red Blood Cells				
1	F 61	18	11	7	5	1	0·8	+
2	F 42	45	30	7	1	1	0·9	+
3	F 51	90	21	2	1	1	0·9	+
4	F 40	20	23	7	1	1	0·5	+
5	M 60	26	24	12	2	1	2·6	+
6	M 54	38	25	8	2	1	1·5	+
7	M 55	36	20	6	2	1	0·5	+
8	M 56	14	25	2	1	1	0·5	+

Discussion

The presence of Howell–Jolly bodies in erythrocytes is classically associated with removal of the spleen but also occurs in congenital absence of the spleen (Bush and Ainger, 1955), in the splenic atrophy which is occasionally associated with steatorrhoea (Boveri, 1942; Fraser *et al.*, 1966), and in a variety of dyshaemopoietic states such as megaloblastic anaemia and leukaemia (de Gruchy, 1964). Nevertheless, the finding of Howell–Jolly bodies in erythrocytes is a rare event in the absence of a history of splenectomy. Boveri reviewed all the haematological reports for a five-year period at Guy's Hospital and could find only seven cases, in addition to the two he described in detail, in which Howell–Jolly bodies were reported in non-splenectomized patients. Of these, three were cases of pernicious anaemia with haemoglobin levels in the region of 60–70%, and one was a case of carcinomatosis with a haemoglobin level of 20%.

The finding of Howell–Jolly bodies in erythrocytes in 34 out of our 35 cases is therefore all the more striking in view of the otherwise normal haematological findings in these patients (Table II).

Howell–Jolly bodies have been demonstrated in the later erythroblasts in cases of vitamin-B_{12} or folic-acid deficiency (Hutchison and Ferguson-Smith, 1959; Dawson and Bury, 1961; Fraser *et al.*, 1966). The last-mentioned authors, in contrast to Hutchison and Ferguson-Smith, also demonstrated Howell–Jolly bodies in erythroblasts after splenectomy. We have been able to examine only two marrow preparations from Thorotrast patients, both of whom had Howell–Jolly bodies in erythrocytes. In neither case were Howell–Jolly bodies seen in marrow erythroblasts.

The presence of burr cells is a less reliable index of a disturbance of splenic function and occurs in other diverse conditions such as glomerulonephritis and gastric carcinoma (Schwartz and Motto, 1949). In microangiopathic haemolytic anaemia

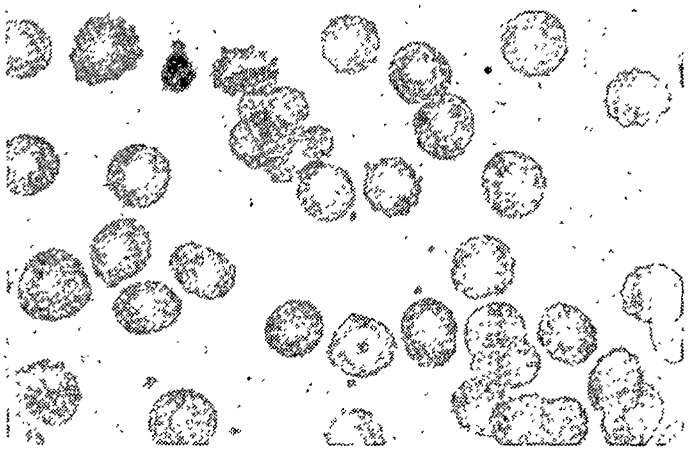


FIG. 1.—Peripheral blood. (×1,110.)

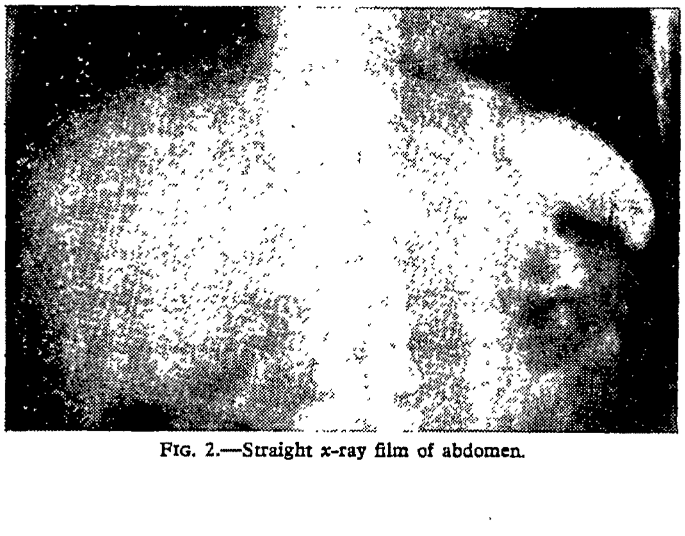


FIG. 2.—Straight *x*-ray film of abdomen.

direct contact between erythrocytes and damaged blood vessels may be a factor in the production of burr cells (Brain *et al.*, 1962). Burr cells were present in all cases that we examined.

The peripheral blood film in our patients is therefore in many ways similar to that seen after removal of the spleen. In two patients the level of Howell–Jolly bodies was greater than that said to occur after splenectomy (0.3% of erythrocytes) and was closer to the higher values (3.9–5.3% of erythrocytes) which Fraser *et al.* reported in three cases of splenic atrophy associated with steatorrhoea.

The significance of these findings, we believe, is twofold. Firstly, the sequelae of Thorotrast characteristically occur after a long latent period—of the order of 20 years or more—and most patients are unaware that the injection has been made. In the absence of a history of splenectomy previous Thorotrast administration may be suspected when the peripheral blood film shows the changes usually associated with removal of the spleen. This is particularly so when haematological examination is otherwise normal.

Secondly, these changes may be indicative of a progressive loss of splenic function in patients exposed to Thorotrast. After intravascular injection the particles of thorium are phagocytosed by reticuloendothelial cells and are deposited mainly in the spleen and liver, and to a lesser extent in the bone marrow. Fig. 2 shows the appearances of heavy deposits of thorium in the spleen of a 33-year-old woman who at the age of 13 had 20 ml. of Thorotrast injected into the left carotid artery.

Attempts to estimate dosage to the spleen from the radioactive material deposited there are for technical reasons extremely difficult, but the dosage has been calculated by Rundo (1955) to be in the region of 1,100–1,300 rep[1] of α-rays and 130–150 rep of β-rays 20 years after an injection of 20 ml. of Thorotrast. As a result of this irradiation, and the interstitial fibrosis which follows the deposition of thorium in tissues, it is not unreasonable to postulate that over the years there will be a progressive loss of splenic function in these patients, and that this will underlie the peripheral blood changes we have described. The careful study and follow-up of such cases may therefore provide useful information regarding the effects of the loss of splenic function and its possible role in some of the sequelae of Thorotrast administration.

Summary

Thirty-five persons who had received intra-arterial Thorotrast 11 or more years previously were examined. A consistent finding in films of peripheral blood was a disturbance of red cell morphology and the presence of Howell–Jolly bodies. In the absence of splenectomy, and when haematological examination is otherwise normal, such findings are extremely rare. It is thought likely that a progressive loss of splenic function has occurred in these patients as a result of irradiation and that this has caused the peripheral blood changes which we have described. More refined studies of splenic function in such patients are indicated.

We are grateful to Professor Norman Dott, Professor John Gillingham, Dr. Kate Herman, and Mr. Jeffrey Maccabe for access to their case records and permission to study patients under their care. Dr. J. T. Boyd, of the M.R.C. Radiation Registry, kindly provided follow-up information. We are also grateful to Miss Zoe Fotheringham for help in tracing patients.

References

Boveri, R. M. (1942). *Guy's Hosp. Rep.*, **91**, 81.
Brain, M. C., Dacie, J. V., and Hourihane, D. O'B. (1962). *Brit. J. Haemat.*, 8, 358.
Bush, J. A., and Ainger, L. E. (1955). *Pediatrics*, **15**, 93.
Dacie, J. V., and Lewis, S. M. (1963). *Practical Haematology*, 3rd ed. London.
Dawson, D. W., and Bury, H. P. R. (1961). *J. clin. Path.*, **14**, 374.
de Gruchy, G. C. (1964). *Clinical Haematology in Medical Practice*, 2nd ed. Oxford.
Fraser, I. D., McCarthy, C. F., and Read, A. E. (1966). *J. clin. Path.*, **19**, 190.
Horta, J. da S., Abbatt, J. D., da Motta, L. C., and Roriz, M. L. (1965). *Lancet*, **2**, 201.
Hutchison, H. E., and Ferguson-Smith, M. A. (1959). *J. clin. Path.*, **12**, 451.
MacMahon, H. E., Murphy, A. S., and Bates, M. I. (1947). *Amer. J. Path.*, 23, 585.
Rundo, J. (1955). *Brit. J. Radiol.*, 28, 615.
Schwartz, S. O., and Motto, S. A. (1949). *Amer. J. med. Sci.*, **218**, 563.

[1] Roentgen equivalent physical.

Association between Digital Ischaemia and Malignant Disease

P. R. HAWLEY,* M.B., B.S., F.R.C.S.; A. W. JOHNSTON,*† M.D., M.R.C.P.; J. T. RANKIN,* B.M., B.CH., F.R.C.S.

Brit. med. J., 1967, 3, 208–212

The association between thrombophlebitis and carcinoma has become well recognized since it was first described by Trousseau in 1865. The following cases suggest that there may be a similar association between digital ischaemia and malignant disease. Digital ischaemia as an early or presenting feature of malignant disease has not been described before.

Case 1

A woman aged 59 was well until December 1958, when severe pain developed in the left side of her face after the extraction of a left upper wisdom tooth. The left nostril was obstructed and discharged pus. After antral washouts these symptoms were to some extent relieved.

In February 1959, after taking a hot bath, she noticed that the index and middle fingers of the left hand had become numb and white. The left middle finger was painful, and there was an area of discoloration at its tip, which later became black. A persistent pain, severe enough to prevent sleep, developed in the finger.

A year before this episode her right foot had become cold and white, and she had felt a pain in her right calf on walking uphill. Tolazoline hydrochloride was given by her doctor, and these symptoms soon disappeared. She habitually smoked 20 cigarettes a day. In 1949 she had had a gastroenterostomy for duodenal ulcer.

The severe pain led to her admission to hospital. On examination her general appearance was of good health, but there was a slight swelling of the left side of her face. The terminal phalanx of the left middle finger was black and dry. Adjacent to this was an area of painful erythema. The remainder of the finger was swollen and fixed in the extended position. There was a small area of discoloration on the pulp of the left index finger (see Fig. 1). Both fingers were colder than the other fingers of the left hand. Her blood pressure was 150/90, and the peripheral pulses, including the brachials and radials, were present and normal. There was no evidence of heart disease. Clinical examination was in all other respects normal.

Investigations.—Hb 67%. W.B.C. 10,200/cu. mm., normal differential count. No L.E. cells. E.S.R. 50 mm./hr. Electro-

---

* University College Hospital, London W.C.1.
† Present address: Aberdeen Royal Infirmary.

phoretic strip normal. Chest *x*-ray normal. *X*-ray examination of the thoracic inlet showed disc degeneration in the lower cervical spine but no cervical rib. E.C.G. normal. Arteriography revealed normally patent left subclavian and brachial arteries. A reactive hyperaemia test resulted in flushing of the whole of the left hand with the exception of the tips of the index and ring fingers and the middle finger distal to the proximal phalanx.

The condition of the left middle finger failed to improve and amputation was performed. Two weeks later left cervical sympathectomy was carried out. At operation two small soft plaques of atheroma were palpable in the subclavian artery but were not causing obstruction. After this operation she again developed pain in the left side of her face. The left nostril was found to be occluded by a friable mass, which on biopsy proved to be anaplastic carcinoma arising from the maxillary antrum.

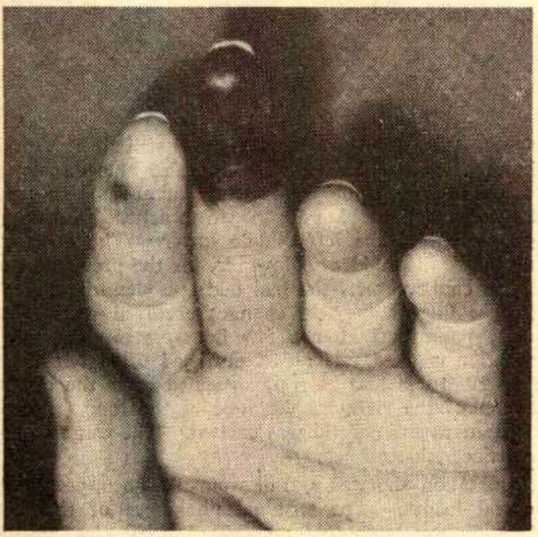


FIG. 1.—Case 1. Necrosis involving the terminal phalanges of the left index and middle fingers.

A course of palliative radiotherapy was soon discontinued, as the growth was not responding and was beginning to invade the orbit. She was discharged home on sedatives and analgesics, and died in June 1959.

Case 2

A woman aged 54 complained of coldness, numbness, and pain in the fingers of three months' duration. She first noticed her symptoms after she had been shopping on a cold winter morning. The distal two phalanges of the right middle finger had become cold, pale, and numb. These changes passed off with massage, but a few days later the tips of the fingers of both hands became painful and black (see Fig. 2). There were no changes in the feet and there was no history of sensitivity to cold or ingestion of drugs.

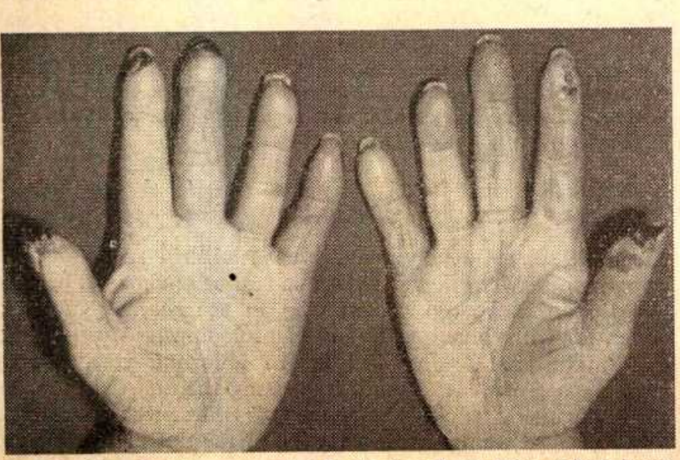


FIG. 2.—Case 2. Necrotic patches at the tips of the digits of both hands.

After admission to hospital for investigation she developed a low-grade fever for which no cause was found. She was then referred to University College Hospital, and while awaiting admission developed a right pleuritic pain and slight dyspnoea. She had had appendicectomy and cholecystectomy seven years previously and an attack of jaundice five years later. Otherwise she had been well. She smoked 10 cigarettes a day.

On examination she looked well. Her fingers were dusky and the skin was thickened. Black necrotic areas were present at the tips of all digits except the left little finger. There were areas of erythema and cyanosis and the fingers felt cold. Radial and ulnar pulses were absent in the right arm but present in the left. Leg pulses were present with the exception of the dorsalis pedis. Fundi were grade 0. B.P. was 140/90. There were no other cardiovascular abnormalities, and clinical findings, including pelvic examination, were otherwise negative.

Investigations.—Hb 92%. E.S.R. 72 mm./hr. Red cells normal. W.B.C. 6,600, with normal differential count. Blood urea 26 mg./100 ml. Plasma albumin 3.7 g., globulin 4.8 g./100 ml. Electrophoretic strip showed moderate increase of gammaglobulin and small increase of alpha-2 globulin. Plasma cholesterol 170 mg./100 ml. No cryoglobulins or excess macroglobulins. Serum cold agglutinins negative. No L.E. cells. Wassermann reaction and Kahn and Reiter protein complement-fixation tests negative. Catheter specimen of urine: red cells 3–5 per one-sixth field; pus cells 1–3 per one-sixth field; otherwise no abnormality. Chest *x*-ray examination: right pleural effusion, no cervical rib. Pleural fluid contained lymphocytes and red cells, but no malignant cells. Culture and guinea-pig inoculation negative. Pleural biopsy and bronchoscopy negative. Blood culture negative. Stool occult blood negative. Barium meal and follow-through normal. E.C.G. normal. A reactive hyperaemia test showed slight delay in the vasodilatation of the digital arteries.

While under investigation she developed a pleural effusion and recurrent fever. After four weeks her condition began to improve. Her right wrist pulses returned and the gangrenous lesions healed. Her pyrexia ceased, though she continued to lose weight. The cause of her condition remained obscure.

In view of her improvement she was discharged home. Within a few weeks she was readmitted in a confused and drowsy state and died shortly afterwards. At postmortem examination the upper two-thirds of the right kidney were replaced by a large hypernephroma. There were multiple brain secondaries but her lungs were clear. A secondary in the wall of the atrial septum and deposits in the right ovary were present.

Case 3

A woman aged 45 had undergone excision of the rectum for carcinoma in 1954. She was then well until September 1964, when a vaginal discharge occurred. Three months later she had an attack in which her fingers became dead-white and later blue. Since that time, on exposure to cold her fingers turned white, then blue, and then became red and tingled. Later her fingers remained persistently discoloured and painful, the symptoms becoming more severe during the course of each day, so that she was unable to use her finger-tips, though gangrene did not appear.

She had always tended to have cold fingers and had suffered from chilblains. Her general health was good. There was no family history of "Raynaud's disease," and she was a non-smoker.

On examination she looked fit and was not anaemic. Her fingers were blue and there were splinter haemorrhages under the nail edges. The peripheral pulses, including radials and ulnars, were palpable and normal. Her pulse was regular, B.P. 180/90, and there was no other cardiovascular abnormality. There was an irregular mass in the left hypochondrium and, per vaginam, the uterus felt bulky and fixed.

Investigations.—Hb 75%. W.B.C. 8,000, normal differential count. E.S.R. 43 mm./hr. Electrophoretic strip showed decrease in albumin and in alpha-1 globulins, but no evidence of cryoglobulins. Chest *x*-ray normal. *X*-ray examination of thoracic inlet showed no abnormality. A reactive hyperaemia test showed normal flushing of the upper limbs with the exception of the distal halves of the fingers of both hands.

Laparotomy was performed. There was a large mobile carcinoma of the splenic flexure. The uterus was bulky and there was a large cystic tumour of the left ovary. There were secondary deposits in the omentum but not in the liver or peritoneum. Partial colectomy and a modified Wertheim hysterectomy were performed. Histology showed a primary carcinoma of the colon with metastases in lymph nodes, omentum, and ovary. The uterine tumour proved to be a primary carcinoma of the body.

She made a good recovery and remained well for some weeks, though the ischaemic changes in her fingers persisted. She was readmitted in July 1965 with carcinomatosis and died three weeks later.

Case 4

A woman aged 45 had been well until May 1957, when in the course of a brief illness, during which she suffered from a sore throat, diarrhoea, and generalized aches, she began to develop symptoms in her hands. Her fingers became numb and felt cold. Her original symptoms resolved but her fingers became painful and blue and then black at their tips. The fingers were slightly swollen and the skin began to flake off. She had had no serious illness and had not been unduly sensitive to cold. She was a non-smoker and there was no family history of "Raynaud's disease."

On examination she looked fit. The tips of the index and middle fingers of both hands were blue, cold, and tender. The changes originally noticed in the other fingers had resolved. All peripheral pulses, including the digitals and radials, were normally palpable. Her pulse was regular, the B.P. 200/125, and there was a soft apical systolic murmur. There was no other abnormality on clinical examination.

Investigations.—Hb 92%. W.B.C. 7,800, normal differential count. E.S.R. 12 mm./hr. Catheter specimen of urine normal. Cold agglutinins negative. No cryoglobulins detected. Electrophoretic strip showed small increase in gammaglobulin. Chest *x*-ray normal. E.C.G. normal.

Her symptoms resolved spontaneously and the cause remained obscure. She was readmitted in October 1957 complaining of a painful swelling in the lower abdomen. A tender mass arising from the pelvis was present. At laparotomy she was found to have a malignant left ovarian cyst. There were secondary deposits in the omentum, aortic glands, and liver, and the tumour was irremovable. Histology was that of a poorly differentiated adenopapillary carcinoma of the ovary. A course of palliative radiotherapy was given. She subsequently developed ascites and died shortly afterwards.

Case 5

A woman of 58 first attended hospital in June 1965, when she complained of attacks of pain, numbness, and pallor in her fingers which had started six months previously. These changes were first noticed in both middle fingers, and the attacks lasted about half an hour. Each attack would end with a tingling sensation in the fingers and a return to their normal colour without intermediate rubor or cyanosis. Gradually all the fingers distal to the proximal interphalangeal joints became affected, but the thumbs were never involved. The attacks, which became increasingly frequent, were usually precipitated by exposure to cold.

Shortly after the onset of these symptoms her sleep began to be disturbed by paraesthesiae over the flexor surfaces of her forearms and wrists and the lateral halves of her palms. Her fingers were not usually affected. These attacks were quite distinct from those brought about by exposure to cold. Her nocturnal symptoms were attributed to bilateral carpal tunnel syndrome. The diagnosis was supported by the finding of grossly abnormal conduction times in the median nerves. There was some response to hydrocortisone injections and splintage, but her digital symptoms continued.

In October 1965 she was admitted to hospital with dyspnoea, abdominal pain, nausea, and diarrhoea of three weeks' duration. She felt rather unwell with a vague abdominal discomfort for about one year. There was no significant family history and she did not smoke.

On examination she looked ill and was found to have a left pleural effusion and ascites. Her hands showed no abnormality and all peripheral pulses were present, including both brachials and radials. Her B.P. was 120/70, the pulse regular, and an apical systolic murmur was present. There was no abnormality in the C.N.S., and clinical examination was otherwise negative.

Investigations.—Hb 100%. E.S.R. 65 mm./hr. W.B.C. 8,000, normal differential count. Midstream specimen of urine normal. Sputum showed no malignant cells. No L.E. cells found. Serum albumin 2.9 g., globulin 3.5 g./100 ml. Empirical liver-function tests normal. No cryoglobulins found. *X*-ray examination showed left pleural effusion and disc degeneration of cervical spine only. Barium-meal examination showed pyloric antrum displaced forwards, suggesting a retroperitoneal mass. Barium enema showed sigmoid diverticular disease. Both pleural and ascitic fluids contained malignant cells suggestive of adenocarcinoma. A reactive hyperaemia test showed normal vasodilatation as far as the proximal interphalangeal joints.

The ascites and pleural effusion were tapped and the fluids replaced by radioactive gold. Some delay in the reaccumulation of fluid was achieved by this means and she was discharged home, where she died in February 1966. Her primary neoplasm was presumed to be pancreatic or ovarian.

Case 6

A woman aged 42 was admitted to hospital in April 1953 complaining of persistent pain, tingling, and blue discoloration of some of her fingers. One week before admission the tip of the left index finger became blue and began to ache. Next day similar changes occurred in the left middle finger. The onset of these symptoms was quite sudden. However, for the previous two years, especially in cold weather, she had had episodes of numbness and pallor in her fingers. These changes occurred without warning and usually passed off after a few hours, sometimes assisted by the application of heat. Her feet also had often felt numb. In September 1950 she had been investigated after the discovery of consolidation of the right middle lobe of the lung. Also at this time a tumour of the parotid was excised. The cause of her chest lesion remained obscure.

On examination she was a frail woman who appeared to be in poor general health. The terminal phalanges of the left index and middle fingers were cold and blue, with a loss of sensation in the involved areas. The radial, ulnar, and digital arteries were all palpable. There was an enlarged gland in the right supraclavicular region and a varicose ulcer on the left leg. The foot pulses were palpable and there was no other cardiovascular abnormality. The signs of consolidation were still present in the right chest and the right kidney was palpable. The affected fingers made a slow recovery to normal colour with the exception of the top of the left middle finger, which became gangrenous. In hospital it was noticed that her other fingers had become transiently cyanosed.

Investigations.—Hb 78%. W.B.C. 12,000, normal differential count. E.S.R. 65 mm./hr. Sputum and gastric washings were negative for malignant cells and acid-fast bacilli.

The supraclavicular gland was excised, and proved to be involved by Hodgkin's disease. Review of the parotid tumour suggested that this also was Hodgkin's disease. She was given a course of radiotherapy to the neck region and mediastinum.

She was readmitted in July 1953 in an emaciated condition with polyarthritis and multiple enlarged glands. On this occasion her serum was found to contain cryoglobulins. Other investigations: W.R. and Kahn test negative; bone marrow normal; plasma protein showed marked rise in alpha-2 globulin and slight reduction in albumin; chest *x*-ray examination revealed persistent right middle lobe collapse.

Her condition did not improve despite treatment with A.C.T.H., cortisone, and nitrogen mustard. She died in November 1954. At post-mortem examination she was found to have widespread Hodgkin's involvement of hilar and aortic lymph nodes and glands in the porta hepatis.

Discussion

A few isolated reports have been published suggesting an association between digital ischaemia and carcinoma. The first was that of a young woman who in the summer of 1866 presented with blue, cold, and painful fingers (Fagge and Pye-Smith, 1891). She died in the following year, and at necropsy a growth was found infiltrating the first dorsal nerve and sympathetic trunk. O'Connor (1884) described the case of a middle-aged woman with gangrene of the tips of her fingers. She subsequently developed a mass of supraclavicular glands on the left side which were thought to be metastases from a carcinoma of the breast. Before the onset of her digital symptoms a lump had been removed from the left breast. Pasteur and Price-Jones (1901) described the case of a man of 61 who in the terminal stages of carcinoma of the stomach developed cold blue extremities said to be like "Raynaud's disease." Hamilton (1920) saw a man of 54 with advanced carcinoma of the oesophagus who developed typical "Raynaud's disease." Bennett and Poulton (1928) reported the case of a man of 61 who developed "Raynaud's disease" the previous summer. He died during the performance of a cervical sympathectomy for severe pain, and necropsy revealed the presence of an occult carcinoma of the stomach. In these reports it is not made clear whether the digital ischaemia was persistent or occurred in attacks.

No further reports were published until Domz and Chapman (1961) described the case of a woman of 56 with digital ischaemia and gangrene of the distal third of the left index finger. She proved to have myelofibrosis, an adenocarcinoma of the lower lobe of the right lung, and cryoglobulinaemia. After resection of the tumour her digital symptoms resolved within a week and separation of the necrotic finger-tip followed within a month. More recently, Nielsen and Petri (1963) have described the case of a woman of 77 with symmetrical gangrene of the fingers. At necropsy she was found to have a malignant neoplasm of the colon with cervical metastases infiltrating the stellate ganglion. The authors thought that the digital necrosis was the result of vasospasm due to sympathetic irritation.

Raynaud's Phenomenon

Impairment of the circulation in the fingers has been well recognized since Maurice Raynaud published his first thesis entitled "Local Asphyxia and Gangrene of the Extremities" in 1862. It is clear that the cases which he described represented a number of different disease processes. Nevertheless the term "Raynaud's disease" gained common usage, and it is hardly surprising that it cannot be defined. Lewis and Pickering (1933–4) suggested that the term "Raynaud's disease" should be abandoned and that "Raynaud's phenomenon" should be retained, defining it as "the active and intermittent closure of small arteries of the order of digital arteries supplying the extremities." They described the changes in colour, temperature, and sensation that characterize the phenomenon. Many people experience the phenomenon without ever showing any evidence of structural change in the vessels, but, in some, structural changes occur and lead to nutritional changes and tissue loss. In addition to those patients with Raynaud's phenomenon in whom no predisposing cause can be found, these changes may occur in association with systemic illness. Recognized as giving rise to secondary forms of Raynaud's phenomenon are obliterative arterial disease, thoracic outlet syndrome, occupational trauma, collagen diseases (especially scleroderma), ergot poisoning, and haematological diseases (particularly where cryoglobulins and cold agglutinins are found) (Gifford, 1963).

Previous to the work of Lewis and Pickering it was widely believed that digital ischaemia occurring in association with malignant disease was due to the involvement of the cervical sympathetic trunk by neoplasm, with resulting peripheral vasoconstriction. Lewis and Pickering showed that the ischaemic changes could not be due to sympathetic overactivity but were attributable to local spasm of the digital arteries, which were shown to be unduly sensitive to cold. The essential feature of the phenomenon is that it is intermittent and the term should not be applied to permanent changes in colour, temperature, and sensation. Lewis and Pickering also described cases of bilateral gangrene of digits, and of particular relevance to the present paper are their two examples of a "curious malady" which "customarily starts without warning, several fingers or toes becoming discoloured within a period of several days. The part attacked is not affected transiently or intermittently, but remains discoloured until, after weeks or months, it recovers colour, usually with loss of tissue at its end by a process of dry gangrene." In their examples there was no evidence of vascular disease proximal to the digital vessels, which they assumed on the basis of their tests to be thrombosed. It is our suggestion that an incident of this sort should alert the physician to the possibility of latent cancer. Lewis and Pickering and others have recognized digital ischaemia as a complication of advanced malignant disease but not as a feature of early or symptomless cancer.

Other Features

In the cases described above a number of features are worthy of mention. All of the patients were women and their digital symptoms were relatively late in onset, the youngest being 42 when first seen. None gave a previous history or family history of Raynaud's phenomenon. Symptoms were bilateral in five cases and affected two fingers on one side only in the other. In all cases the symptoms were sudden in onset and, with the exception of cases 3 and 5, rapidly progressed to gangrene. The site of origin of the primary tumour does not appear to be of significance: primaries were located in the maxillary antrum, kidney, and ovary respectively in three cases; one patient had carcinoma of both the colon and the corpus uteri; and in another case the organ of origin was not established but was probably the ovary or pancreas. In the remaining case the patient suffered from Hodgkin's disease. It is of interest that Case 3 had had a carcinoma of the rectum 10 years previously but at that time did not develop symptoms in her fingers. Three cases presented with digital symptoms; in the other three digital symptoms overshadowed earlier but milder symptoms which in retrospect were related to the underlying neoplasm. In Cases 3 and 5 the attacks of ischaemia were intermittent, but only in the former did the typical triphasic response to cold of Raynaud's phenomenon occur. In all others ischaemia was persistent though showing a tendency to improve.

There is no evidence that any of the predisposing conditions described by Lewis and Pickering were present in our series. Proximal arterial block could be excluded on clinical grounds in five cases, and in Case 1 an arteriogram showed the major vessels to be patent. In four cases reactive hyperaemia tests showed normal vasodilatation down to the proximal interphalangeal joints of the involved fingers. In those in which gangrene occurred, arterial occlusion is likely to have been caused by intense digital artery spasm, and this is supported by the fact that in some cases cold seems to have been a precipitating factor. Alternatively, ischaemia could have been the result of peripheral intravascular thrombosis. Venous thrombosis occurring in some forms of malignant disease is well recognized. Though the cause of this has not been established it seems at least possible that the same factors may operate to produce thrombosis in peripheral arteries in which the circulation has been rendered sluggish by cooling. Even so, it would be surprising if such a predisposition to thrombosis did not also show itself in episodes of phlebothrombosis. None of our patients developed symptoms or signs suggestive of venous thrombosis. It seems more likely that in those cases in which gangrene ensued vascular occlusion was the result of arterial thrombosis superimposed on spasm rather than the outcome of increased coagulability of the blood.

Vascular occlusion by emboli is unlikely in the absence of any discoverable predisposing lesion. In no case was there evidence of large-vessel or cardiac disease which might have given rise to emboli. It would also be difficult to explain the symmetrical and bilateral cases on the basis of embolism. There was no history of ergotism, and none of the patients had received drugs with vasoconstrictor effects such as methysergide.

Cryoglobulinaemia, a rare condition, may lead to intolerance of cold, peripheral gangrene, and allergic phenomena (Mackay *et al.*, 1956). These abnormal globulins can occur in multiple myeloma, lymphoma, and occasionally in other malignant disease. It is of interest that in the case of Domz and Chapman (1961) resection of the tumour led to a fall in the level of circulating cryoglobulins. The level, however, remained high and the cryoglobulinaemia could have been due to the coexisting myelofibrosis. Waldenström (1961) found that in 276 unselected cases of macroglobulinaemia 10 suffered from malignant disease. He concluded that the finding of macroglobulins in any patient should warrant further investigation to exclude neoplasm. Bohrod (1957) thought that cryoglobulinaemia, which can occur together with plasmacytosis and urticaria, represented an immunity reaction between tumour and host. In our cases cryoglobulins were looked for in all patients except Case 1, and in her case the electrophoretic strip was normal. They were found to be present only in Case 6, who suffered from Hodgkin's disease.

On the basis of the six cases described above it is suggested that malignant disease may give rise to digital ischaemia, and this may be the presenting or the only symptom. How this occurs is a matter for speculation. The incidence of "Raynaud's disease" in the older age groups of the general population is not known. It is possible that the occurrence of attacks of blue and numb fingers in association with malignant disease was coincidental in cases 3 and 5. The presentation in the remaining four cases, in which necrosis was an early feature and the onset more or less sudden, is unusual enough to suggest a more than fortuitous relationship. All of these patients with the exception of the case of Hodgkin's disease died within 18 months of the onset of the ischaemic changes. In some the malignancy remained undiagnosed until the patient's death and in others was advanced when eventually discovered. Patients who present with digital ischaemia, often loosely termed "Raynaud's disease," in whom the accepted causes have been excluded, deserve the fullest investigation in an attempt to discover an occult neoplasm.

The variety of neoplasms described in our series would suggest that the search must be wide and may even necessitate laparotomy in certain cases. If thorough investigation proves negative a careful follow-up should be undertaken. In two further cases not described in this series, the patients presented with digital ischaemia and remained undiagnosed despite the fullest investigation. They were well at nine months and three years respectively from the onset of their symptoms. In such cases a careful follow-up should always be undertaken. If the possibility of occult neoplasm as a cause of digital ischaemia is kept in mind diagnosis may be hastened and radical treatment made possible.

Summary

Six cases are described suggesting an association between digital ischaemia and malignant disease. They were a group of middle-aged women who either presented with atypical Raynaud's phenomenon or in whom this was a prominent feature. The symptoms were of sudden onset, bilateral in five cases, and in four rapidly progressed to gangrene. None of the commonly accepted causes of digital ischaemia was present. On investigation three patients were found to have a primary carcinoma of the maxillary antrum, kidney, and ovary, respectively; one patient had primary carcinomata of both the colon and corpus uteri, and in another the origin was not established but was probably the ovary or pancreas; the remaining patient was suffering from Hodgkin's disease. All of the patients with the exception of the last died within 18 months of the onset of the ischaemic changes. In some the malignancy remained undiagnosed until the patient's death and in others was advanced when eventually discovered. It is suggested that malignant disease may give rise to digital ischaemia and that it may be the presenting or only symptom. Patients who suddenly develop "Raynaud's disease" in whom the accepted causes have been excluded deserve the fullest investigation in an attempt to discover an occult neoplasm.

We wish to thank Professor R. S. Pilcher for his advice and encouragement in the preparation of this paper. We are also grateful to Professor Sir Max Rosenheim, Dr. E. E. Pochin, Dr. K. E. Harris, Dr. Matthew Steel, and Mr. D. R. Davies for permission to publish details of those cases which were under their care.

REFERENCES

Bennett, T. I., and Poulton, E. P. (1928). *Amer. J. med. Sci.*, **176**, 654.
Bohrod, M. G. (1957). *J. Amer. med. Ass.*, **164**, 18.
Domz, C. A., and Chapman, C. G. (1961). *Calif. Med.*, **95**, 391.
Fagge, C. H., and Pye-Smith, P. H. (1891). *Text Book of the Principles and Practice of Medicine*, 3rd ed., vol. 2, p. 118. London.
Hamilton, W. F. (1920). *Canad. med. Ass. J.*, **10**, 670.
Gifford, R. W., jun. (1963). *Circulation*, **27**, 970.
—— and Pickering, G. W. (1933–4). *Clin. Sci.*, **1**, 327.
Mackay, I. R., Eriksen, N., Motulsky, A. G., and Volwiler, W. (1956). *Amer. J. Med.*, **20**, 564.
Nielsen, B. L., and Petri, C. (1963). *Nord. Med.*, **69**, 237.
O'Connor, B. (1884). *Brit. med. J.*, **1**, 460.
Pasteur and Price-Jones (1901). *Trans. clin. Soc. Lond.*, **34**, 160.
Trousseau, A. (1865). *Clinique Médicale de l'Hôtel-Dieu de Paris*, 2nd ed. Paris.
Waldenström, J. (1961). *Acta med. scand.*, Suppl. No. 367, p. 110.

Solar Retinopathy

A. E. A. RIDGWAY, M.B., B.CHIR.

[WITH SPECIAL PLATE]

Brit. med. J., 1967, 3, 212–214

Five cases of solar retinopathy presenting in Oxford within three months of the partial eclipse of 20 May 1966 are described.

Pathogenesis

Of the sum of solar radiation reaching the surface of the earth, only the visible and short infrared wavelengths reach the retina, the ultraviolet and longer infrared rays being absorbed in the cornea and lens (Verhoeff *et al.*, 1916; Irvine, 1945). The 60 to 70% of solar energy reaching the retina is absorbed by its pigment epithelium with the liberation of heat. With a meiosis of 2 mm., a 30-second exposure leads to the production of heat at a rate of 70 calories/sq. cm./min., which is more than enough to produce a severe retinopathy experimentally (Verhoeff *et al.*, 1916; Ludvigh and McCarthy, 1938; Eccles and Flynn, 1944).

Exposure of pigmented rabbit retinae to xenon arc photocoagulator light has been shown to produce very similar lesions to human solar retinopathy, but similar exposures of albino rabbit retinae were tolerated without damage, and ten times the dose was needed to produce equivalent burns (Geeraets *et al.*, 1962; Geeraets and Ridgeway, 1963).

Further experimental work with xenon and carbon arc photocoagulators, the emissions of which are close to that of sunlight, has shown that the earliest damage is pyknosis of pigment epithelium cells with loss of fine structure in rods and cones, and local oedema, which may cause bulging of the retina into the vitreous cavity with resolution after a few days (Ham *et al.*, 1958).

The other factors influencing the severity of solar retinopathy are the intensity of the incident light—never less than 60% of full sunlight in the eclipse of 20 May 1966—and the duration of exposure.

Reflex meiosis of the order of 1.6 to 2 mm. (Verhoeff *et al.*, 1916) and refractive error tend to protect against damage. It has been shown that uncorrected myopes, who do not focus the sun's image on the retina, are relatively protected by reason of the lower density of illumination of the exposed areas (Das *et al.*, 1956). Physiological movements of fixation result in the exposure of a crescentic arc of retina on sun-gazing with a central zone always exposed and a peripheral zone intermittently exposed. Lastly, constancy of exposure is of importance in that repeated short exposures at short intervals do not summate in effect because of the good thermal conduction away from the macular area by its excellent blood supply.

Case 1

A 21-year-old labourer looked at the eclipse with both eyes without any protection for "about five minutes." He presented on 22 May 1966 complaining of dazzling when looking into the distance.

On examination the right visual acuity (R.V.A.) was 6/12 unaided, and the left visual acuity (L.V.A.) 6/9 unaided. On refraction both eyes were emmetropic, he had no strabismus, and no scotoma was demonstrable in either visual field. There was slight prominence of both maculae, and he was offered no treatment.

Progress.—His right macula became more prominent over the next three days and then subsided, and by 3 June was thought to be within normal limits. His symptoms improved and on 17 June his visual acuity was 6/4 unaided in both eyes, and his only complaint was that he had to alter fixation to read the middle two letters of the bottom row of the test chart with each eye. It was impossible to demonstrate a scotoma objectively in either eye, but ophthalmoscopically minute yellow spots were visible at both maculae.

Case 2

A 19-year-old male undergraduate reading physics presented on 24 May, having watched the eclipse through a plain glass window for a few seconds, and with sun-glasses for half a minute. He complained of a black spot in his right central field.

On examination the R.V.A. was 6/4 and the L.V.A. 6/9 (parts) uncorrected. On refraction the right eye was emmetropic and the left 0.25 dioptre sphere myopic, with which correction he achieved 6/4. He had no strabismus. Projection campimetry showed a small scotoma across and below fixation to a 3/2000 mm. red object, using a green fixation object and coloured goggles, green before the left and red before the right eye (Gambs *Perimeter Handbook*, p. 10, 1966). He had moderate macular oedema in the right fundus. He was treated with prednisolone 5 mg. three times a day.

Progress.—Over the next two weeks the macular oedema cleared and the prednisolone was tailed off and stopped. On 15 June his black spot was smaller and less dense, he had no visible macular abnormality, and on campimetry the scotoma was minute.

Case 3

A manual worker aged 36 presented on 22 May after watching the eclipse "for a few minutes" with his right eye through the gaps between his fingers. He complained of blurring of central vision.

On examination the R.V.A. was 6/6 (parts) and the L.V.A. 6/4. On refraction the left eye was emmetropic and the right eye had one dioptre sphere of hypermetropia. With this correction his R.V.A. was 6/5. He had no strabismus.

Projection campimetry showed a circular blurred area to 10 degrees from fixation and he had gross perimacular oedema. He was started on prednisolone 10 mg. three times a day by mouth.

Progress.—On 24 May the perimacular oedema was less but there was a swelling at the macula (Special Plate, Fig. 1). On 27 May the oedema had receded further and there was a definite macular cyst. The prednisolone was reduced to 10 mg. twice daily. On 1 June his blurred patch was much smaller but considerably denser and a scotoma of 1 degree diameter was demonstrated at fixation to a 3/2000 mm. red object. The R.V.A. had dropped to 6/9 corrected. The prednisolone was tailed off and stopped over the next seven days. During the next two weeks the macular cyst became smaller, as did his scotoma, and on 17 June he managed R.V.A. 6/5 corrected, scanning the smaller letters.

Case 4

A schoolboy aged 13 presented on 11 August complaining of blurring of vision in the right eye after viewing the eclipse. He had gazed at the sun through two sun-glasses for two to three minutes between classes. Three hours later he noticed green flashes in the right eye and that evening his vision in this eye became very blurred. It had now recovered somewhat.

On examination the R.V.A. was 6/6 (parts) and the L.V.A. 6/4. Both eyes were emmetropic and there was no strabismus. Campimetry showed a small scotoma between one and two degrees, nasal to (binocular) fixation and extending five degrees up from the horizontal meridian. He had a flat lesion below a moderate-sized paramacular hole in the right fundus.

Progress.—In view of the lateness of presentation no treatment was offered, and to allay parental anxiety follow-up has been deferred for six months.

Case 5

An accounting-machine operator aged 25 presented on 3 June. She had been sunbathing without sun-glasses five days previously, and had been "squinting at passers-by against the sun" through her left eye. On awaking the next morning she had noticed a shimmering patch in her left central field, which had become smaller and was now opaque.

For 10 years she had had migraine two to four times a year. This consisted of flashing lights in the right eye spreading to the left, followed by a generalized headache not relieved by aspirin.

On examination the R.V.A. was 6/5 and the L.V.A. 6/36+2. On refraction both eyes were emmetropic and she had no strabismus. Campimetry showed a crescentic scotoma in the upper and lateral macular region and she had much macular and perimacular oedema maximal below a small macular hole (Special Plate, Fig. 2). She was treated with prednisolone 5 mg. four times a day by mouth.

Progress.—On 11 June her field defect had contracted to a 2 by 1 degree scotoma across and above fixation on projection campimetry to a 3/2000 mm. red object, and her L.V.A. had improved to 6/18 unaided. The macular oedema had disappeared and the macular hole was less prominent. Her corticosteroids were tailed off over the next week. On 17 June her L.V.A. had improved to 6/9 part unaided and she was no longer conscious of the field defect, which was unchanged. There was some fine pigmentation around the macular hole.

Discussion

The first four cases demonstrate the damage which may be caused by short exposure of the retina to the sun. In the past, damage caused by watching eclipses has been related to similar changes seen in people who have looked at the sun for other reasons.

Das *et al.* (1956) reported cases among Punjabis who look at the sun for religious reasons. Pittar (1943) reported one case in an anti-aircraft gunner firing at an enemy plane flying out of the sun, and fighter pilots performing the same manœuvre have suffered similar consequences. Irvine (1945) has recalled the case of a seaman "steering into the sun's eye." Bates (1920) advocated prolonged sun-gazing as the treatment of myopia, with disastrous results.

However, solar retinopathy takes on a much more sinister aspect with the presentation of the fifth case. Here a healthy young woman was sunbathing, and it seems probable that as a consequence of this innocent act she sustained a severe macular burn, leaving her with a permanent central field defect in one eye, an anatomical lesion, and possibly the predisposition to macular degeneration in this eye in later life (Corcelle, 1958).

The warnings made by Knudtzon (1948) need repeating, especially as they bear on the false sense of protection afforded by dark glasses, red glass filters, smoked glass, and overexposed negative films. The only safe way of observing the sun, the method used by astronomers, is to project the sun's image on to a screen. For the amateur a pin-hole and sheet of matt paper held in the shade behind it will suffice (Gilkes *et al.*, 1961).

In the case of accidental solar retinopathy it is difficult to suggest any protective measure other than greater public awareness of the dangers involved. Publicity before the eclipse of 20 May 1966 was responsible for much sun-gazing, and no safe protective methods were advocated. In effect, interest was aroused and the dangers were minimized.

Summary

Four cases of eclipse burn and one of solar retinopathy due to sunbathing are presented. The seriousness of an apparently trivial action in terms of visual function is demonstrated and attention is drawn to the possibility of accidental macular burns.

More effective methods of prevention are advocated and it is urged that public awareness of the dangers be aroused.

I wish to record my thanks to Messrs. J. P. F. Lloyd, V. Purvis, and A. C. L. Houlton for permission to report cases under their care, to Mr. T. Ramsell for much critical assistance, and to Mr. E. W. Allen and his staff for the photography.

References

Bates, W. H. (1920). *The Cure of Imperfect Sight by Treatment Without Glasses.* London.
Corcelle, L. (1958). *Arch. Ophthal. (Paris)*, **18**, 555.
Das, T., Nirankari, M. S., and Chaddah, M. R. (1956). *Amer. J. Ophthal.*, **41**, 1048.
Eccles, J. C., and Flynn, A. J. (1944). *Med. J. Aust.*, **1**, 339.
Geeraets, W. J., Everett, W. G., and Guerry, D., III (1962). *Amer. J. Ophthal.*, **54**, 393.
—— and Ridgeway, D. (1963). *Acta ophthal. (Kbh.)*, Suppl. No. 76, p. 109.
Gilkes, M. J., Roberts, D. St. C., Osmond, A. H., and Thorne Thorne, B. (1961). *Lancet*, **1**, 109.
Ham, W. T., jun., *et al.* (1958). *Amer. J. Ophthal.*, **46**, 700.
Irvine, S. R. (1945). Ibid., **28**, 1158.
Knudtzon, K. (1948). *Acta Ophthal. (Kbh.)*, **26**, 469.
Ludvigh, E., and McCarthy, E. F. (1938). *Arch. Ophthal.*, **20**, 37.
Pittar, C. A. (1943). *Brit. J. ophthal.*, **27**, 36.
Verhoeff, F. H., Bell, L., and Walker, C. B. (1916). *Proc. Amer. Acad. Arts Sci.*, **51**, No. 13.

Effect of Oral Contraceptives on Erythrocyte Sedimentation Rate in Healthy Young Women

J. Ll. BURTON,* M.B., CH.B., B.SC., M.R.C.P.

Brit. med. J., 1967, **3**, 214–215

The erythrocyte sedimentation rate (E.S.R.) is a useful non-specific test for a variety of diseases accompanied by inflammation or breakdown of tissue. It is often used as a screening test for occult disease in the absence of physical signs, and it is also useful for assessing progress in chronic or relapsing disease.

A recent reply in the "Any Questions?" column of the *British Medical Journal* (25 March 1967) has implied that the E.S.R. in women taking oral contraceptives is normal. It has long been known that the E.S.R. is raised above the usually accepted limits of normal in pregnancy (Fåhraeus, 1918; Bochner and Wassing, 1925; Dawson, 1960), and since the physiological effects of oral contraceptives are in many ways similar to those of pregnancy it was decided to investigate their effect on the E.S.R. in normal young women.

Methods

Women attending a routine family planning clinic were divided into two groups according to whether they used oral contraceptives[1] or an occlusive pessary. After a medical interview a 2.5-ml. sample of venous blood was obtained for the estimation of haemoglobin, packed cell volume, and E.S.R.

All women included in the final study conformed to the following criteria: (1) they were below 40 years of age; (2) they had been using the same contraceptive method for at least six months previously; (3) they gave no history of previous serious or chronic illness, and had not suffered from overt infection during the previous four weeks; (4) they felt perfectly well on the day of attendance at the clinic; and (5) they had haemoglobin levels and packed cell volumes within normal limits (Hb 11.5–16.4 g./100 ml.; P.C.V. 36–47%).

The relation of the timing of the blood sample to the menstrual period was not determined, since this was a random variant in both groups, and in any case the fluctuation of E.S.R. with menstruation is insignificant (Greisheimer, 1927; Wintrobe, 1961).

Seventy-eight women were included in the study, of whom 42 had been taking oral contraceptives and 36 had been using an occlusive pessary.

The blood samples were transported in polystyrene bottles containing Sequestrene anticoagulant, and the E.S.R. was determined within six hours by the Westergren method, a one-fourth part of 3.8% sodium citrate solution (Dacie and Lewis, 1963) being used. Various authors have given results varying from 7 to 25 mm. in the first hour for the upper limit of the normal E.S.R. in women (Westergren, 1926; Dawson, 1960; Dacie and Lewis, 1963; Hilder and Gunz, 1964; Böttiger and Svedberg, 1967). The normal value used in this laboratory for young women is up to 7 mm. in the first hour (Dacie and Lewis, 1963), and this is also the value proposed by the British Standards Institution Technical Committee on Haematological Equipment and Methods (Lewis, 1965).

---

* Assistant Lecturer, Department of Medicine, the Royal Infirmary, Edinburgh 3.

[1] The oral contraceptives used in this study were: Ovulen (mestranol 0.1 mg. and ethynodiol diacetate 1 mg.), Lyndiol (mestranol 0.15 mg. and lynoestrenol 5 mg.), Lyndiol 2.5 (mestranol 0.075 mg. and lynoestrenol 2.5 mg.), and Gynovlar (ethinyloestradiol 0.05 mg. and norethisterone acetate 3 mg.).

Results

The results are presented in the Table. Of the 42 women taking oral contraceptives 19 (45%) had an E.S.R. above our upper limit of normal, the highest value recorded being 17 mm. in the first hour. None of the patients in the control group had an E.S.R. exceeding 7 mm. The mean value for the E.S.R. in the group taking oral contraceptives was 7.2 mm. in the first hour, compared with 4.0 in the control group, and this difference was statistically significant ($P<0.02$).

Westergren E.S.R. (mm. in First Hour)

Women in Control Group			Women Taking Oral Contraceptives			Student's *t* Test
Mean	Range	S.D.	Mean	Range	S.D.	
4·0	1–7	1·9	7·2	2–17	4·4	$0{\cdot}02>P>0{\cdot}01$

Discussion

The E.S.R. depends on the rate of erythrocyte rouleaux formation, which in turn depends on the plasma concentration of asymmetric macromolecules such as fibrinogen, and to a less extent on α_2- and γ-globulins (Hardwicke and Squire, 1952). Rouleaux formation is probably mediated by a specific plasma protein called "agglomerin," which requires the presence of a supplement of high molecular weight such as fibrinogen for its action (Ruhenstroth-Bauer, 1961). The E.S.R. thus supplies a simple screening test for the presence of raised concentrations of large molecules such as fibrinogen and the larger globulins.

The rise in E.S.R. which accompanies normal pregnancy is attributable to the increased concentration of fibrinogen, which is well documented (Gillman *et al.*, 1959 ; Ratnoff and Holland, 1959 ; Pechet and Alexander, 1961). Similar increases in fibrinogen concentration have been reported in women taking oral contraceptives (Rapaport, 1962 ; Donayre and Pincus, 1965 ; Miller *et al.*, 1965), and this probably accounts for the increased E.S.R. demonstrated in the present study. The effect of hormonal influences on the E.S.R. merits further investigation, however, since Böttiger and Svedberg (1967) have shown that the normal increase in E.S.R. with advancing age is accelerated after the menopause.

These results are reported in order to draw attention to the fact that the E.S.R. may be raised above normal in women taking oral contraceptives and that the isolated finding of a moderately raised E.S.R. is not necessarily an indication for further investigation. Similarly, the assessment of chronic disease by changes in E.S.R. may need to be modified if it is known that the patient is taking oral contraceptives.

Summary

The Westergren erythrocyte sedimentation rate (E.S.R.) was determined in 42 healthy young women taking oral contraceptives. The mean E.S.R. was significantly higher than in a control group of the same age, and 45% of the women taking oral contraceptives had an E.S.R. above the upper normal limit for their age.

The finding of a slightly raised E.S.R. in an otherwise healthy young woman taking oral contraceptives is not an indication for further investigation.

ADDENDUM.—Since the above report was submitted for publication E.S.R.s in the range 17–36 mm./hr. have been discovered in a further five women taking oral contraceptives who conformed to the above criteria.

Thanks are due to Dr. Nancy Loudon and the staff of the Edinburgh Family Planning Centre, and to Dr. S. H. Davies and the Department of Haematology, Royal Infirmary, Edinburgh.

REFERENCES

Bochner, M., and Wassing, W. (1925). *J. Lab. clin. Med.*, **11**, 214.
Böttiger, L. E., and Svedberg, C. A. (1967). *Brit. med. J.*, **2**, 85.
Brit. med. J., 1967, **1**, 742.
Dacie, J. V., and Lewis, S. M. (1963). *Practical Haematology*, 3rd ed., p. 408. London.
Dawson, J. B. (1960). *Brit. med. J.*, **1**, 1697.
Donayre, J., and Pincus, G. (1965). *Metabolism*, **14**, 418.
Fåhraeus, R. (1918). *Biochem. Z.*, **89**, 355.
Gillman, T., Naidoo, S. S., and Hathorn, M. (1959). *Lancet*, **2**, 70.
Greisheimer, E. M. (1927). *Amer. J. med. Sci.*, **174**, 338.
Hardwicke, J., and Squire, J. R. (1952). *Clin. Sci.*, **11**, 333.
Hilder, F. M., and Gunz, F. W. (1964). *J. clin. Path.*, **17**, 292.
Lewis, S. M. (1965). *Brit. med. J.*, **1**, 1614.
Miller, S. P., Lee, S. L., and Ritz, N. (1965). *Metabolism*, **14**, 398.
Pechet, L., and Alexander, B. (1961). *New Engl. J. Med.*, **265**, 1093.
Rapaport, S. I. (1962). *Thrombo-embolic Phenomena in Women*, p. 154. Chicago.
Ratnoff, O. D., and Holland, T. R. (1959). *Ann. N.Y. Acad. Sci.*, **75**, 626.
Ruhenstroth-Bauer, G. (1961). *Brit. med. J.*, **1**, 1804.
Westergren, A. (1926). *Amer. Rev. Tuberc.*, **14**, 94.
Wintrobe, M. M. (1961). *Clinical Haematology*, 5th ed., p. 331. London.

Treatment of Radiation Sickness with Pyridoxine Hydrochloride in Outpatients of a Radiotherapy Unit

H. MATTIE,* M.B. ; E. W. EMERY,† F.F.R. ; I. D. HILL,‡ B.SC. ; D. R. LAURENCE,§ M.D., F.R.C.P.

Brit. med. J., 1967, **3**, 215–216

Since Maxfield *et al.* (1943) reported "most satisfying" results with intravenous pyridoxine hydrochloride in patients with radiation sickness the vitamin has become widely used in this condition, more often administered orally than parenterally (Reeves, 1946 ; Oppenheim and Lih, 1946 ; Wells and Popp, 1947 ; Shorvon, 1949 ; Strahm, 1955 ; Silverman *et al.*, 1956 ; Stoll, 1957 ; Finney, 1961).

However, so far as we know, of the many reports on this treatment only a few are based on properly controlled studies: one study with rather low dosages (Silverman *et al.*, 1956), and another with breast cancer patients only (Finney, 1961). These authors found no difference between pyridoxine and a placebo.

The study reported here was devised in an attempt to reassess the value of pyridoxine.

Design of the Trial

Since radiation sickness manifests itself as a complex of subjective, often vague, complaints, mixed with symptoms due to the original disease or to anxiety, it is obvious that a study of the effect of treatment should be conducted double-blind, and this was done.

---

* Department of Pharmacology, University of Leiden.
† Department of Radiotherapy, University College Hospital, London W.C.1.
‡ Medical Research Council, Statistical Research Unit, London W.C.1.
§ Medical Unit, University College Hospital Medical School, London W.C.1.

Hitherto in the radiotherapy department of University College Hospital patients who complained of anorexia, nausea, and malaise received pyridoxine treatment routinely, 25 mg. t.d.s., direct from the radiotherapist, who distributed it from a central source of supply. If this was insufficient the patients were referred to a physician for further treatment, generally by recognized antiemetics—for example, meclozine, promazine, etc. Our aim was to keep this simple routine intact, and to ask nothing more of the radiotherapist than to keep a record of the patients' complaints and of their drug treatment, for the department is busy and a design interfering with the routine would have been unacceptable. We did not think it proper to use a dummy tablet, as the radiotherapists' general conviction was that pyridoxine was an effective drug. Therefore we used two different dosage levels: 1-mg. and 50-mg. tablets,[1] at first 1 tablet t.d.s., but the radiotherapist could double the dose on her own initiative if the patient did not respond. Thus the maximum daily dose with the low-dosage tablets—that is, 6 mg.—was somewhat more than the biological need, while with the high-dosage tablets it was 300 mg., which is more than had been ordinarily given in the department.

To minimize interference by other drug therapy we included only outpatients in this trial; inpatients tend to be on a larger number of drugs, and patients were excluded afterwards if they did take other drugs or if they did not take pyridoxine regularly. Moreover, patients who were treated for diseases of skin or joints were not included, as they are rarely troubled by radiation sickness, so that nearly all patients were being treated for malignant diseases—for example, cancer of the lung or the breast, Hodgkin's disease, etc.

The duration of the whole trial was 24 weeks, divided into eight three-week periods. During each period the central source of tablets contained either all high-dose tablets or all low-dose. There were four periods of high and four of low in the total of eight periods in the order HLLHLHHL. Patients were supplied with bottles containing 15 tablets at a time. Patients ordinarily attended for radiotherapy five days a week.

Results

Of the 202 patients initially included 19 were excluded, for reasons given above, after radiotherapy was started. Of the remaining patients 94 had symptoms which justified treatment with pyridoxine; 89 patients never needed pyridoxine.

First the effects of high- and low-dose tablets in the dosage of 1 tablet t.d.s. were compared. If the complaints were controlled—that is, it was not thought necessary to give 2 tablets t.d.s.—or remitted on this dosage a "success" was recorded, otherwise a "failure." Twelve patients could not be used in this scheme, as they changed from the high- to the low-dose tablets, or vice versa, between starting and the occurrence of a success or a failure. This was an inevitable consequence of the use of a single central supply source.

The remaining 82 patients are included in the following Table:

	Success	Failure	Total
High dose	36	10	46
Low dose	22	14	36
	58	24	82

The higher success rate with the high dose (78%, against 61% for the low dose) is not statistically significant (P=0.14) at the generally accepted level. If there was no real difference between high and low doses such a result would occur by chance once in seven times.

As the periods in which two tablets were used are inevitably correlated with the preceding periods on 1 tablet t.d.s., we did not think it proper to make any analysis of this dosage. Moreover, the number of failures—that is, when the patient did not improve while taking pyridoxine—was so low that this test would be unlikely to uncover a difference between the two dosages; 31 patients were treated with the double dose and only 7 of these reported failure (3 out of 13 for the high dose and 4 out of 18 for the low dose). This failure rate was much lower than was anticipated from our previous experience (we roughly estimated that half of all patients should need more potent drugs), and we attribute this to the therapeutic enthusiasm of the radiotherapists participating in the trial. As a matter of fact the failure rate was about the same as that in several of the above-mentioned uncontrolled studies (8–12%).

Conclusion and Summary

We think that the practical conclusion should be that treatment of radiation sickness with 1 or 2 mg. of pyridoxine hydrochloride orally t.d.s. by radiotherapists who are convinced of its efficacy gives very good results. Whether the effect of this low dose would differ from a placebo remains to be seen.

The effect of the treatment of radiation sickness with pyridoxine hydrochloride was studied in outpatients of a radiotherapy unit. No significant difference between a very low (1 mg. t.d.s.) and a high dose (50 mg. t.d.s.) was detected. When, in case of failure of these doses, the daily dose was raised to 2 mg. t.d.s. and 100 mg. t.d.s., only a few patients in either group had to be treated with more potent drugs.

We are grateful to Sister Plowman and her staff for their enthusiastic participation; to Miss Kingsbury and her staff; and to Mr. A. R. Williams, pharmacist to the hospital, who provided the tablets.

References

Finney, R. (1961). *Clin. Radiol.*, **12**, 229.
Maxfield, J. R., jun., McIlwain, A. J., and Robertson, J. E. (1943). *Radiology*, **41**, 383.
Oppenheim, A., and Lih, B. (1946). Ibid., **47**, 381.
Reeves, R. J. (1946). *Sth med. J. (Bgham, Ala.)*, **39**, 405.
Shorvon, L. M. (1949). *Brit. J. Radiol.*, **22**, 49.
Silverman, A., Kligerman, M. M., Fertig, J. W., and Ellis, K. (1956). *Radiology*, **66**, 403.
Stoll, B. A. (1957). Ibid., **68**, 380.
Strahm, A. (1955). *Münch. med. Wschr.*, **97**, 855.
Wells, J. J., and Popp, W. C. (1947). *Proc. Mayo Clin.*, **22**, 482.

---

[1] 10 mg. of ascorbic acid and 0.5 mg. of quinine sulphate were added to all tablets to mask the taste of the higher dosage of pyridoxine hydrochloride.

Medical Memoranda

Case of Englemann's Disease

[WITH SPECIAL PLATE]

Brit. med. J., 1967, 3, 217

Englemann's disease is one of the rarest bone dystrophies causing osteosclerosis. The first case was published by Englemann in 1929. A search of the literature has revealed 53 cases reported up to 1964. However, there has hardly been any record of a similar case in the Indian literature. The purpose of this paper is to report a case of Englemann's disease and to review the literature on the subject.

CASE REPORT

A girl aged 14 was admitted to our medical unit of Irwin Hospital, New Delhi, with the object of investigating the cause of her stunted growth. Her father had noticed that her growth had not been up to the mark since the age of 4 years. She had had slight pain in the legs for one year. Her developmental milestones were normal except that she started walking at the age of 2 years. Past and family history were non-contributory. The outstanding features on general examination were a short stature, a waddling gait, and the absence of secondary sex characters. She had not started menstruation and her genitalia appeared infantile. Her height and span were below average for her age and her crown-to-rump and rump-to-heel ratio was 1.2:1. Local examination revealed thickening, tenderness, and venous prominence over both tibial bones. The ulna was irregularly palpable on both sides. Examination of nervous, cardiovascular, respiratory, and gastrointestinal systems showed nothing abnormal.

Investigations.—Haemoglobin was 12.0 g./100 ml., total leucocyte count 7,700/cu. mm. (polymorphs 50%, lymphocytes 49%, eosinophils 1%), erythrocyte sedimentation rate 9 mm. in first hour (Westergren). Urine and stool examinations showed nothing abnormal. Serum alkaline phosphatase was 4.1 K.A. units, serum calcium 11.2 mg., serum phosphorus 3.7 mg., blood urea 23 mg., and serum cholesterol 150 mg./100 ml., glucose-tolerance curve normal. Twenty-four-hour excretion of fat in stool was 3.5 g., and 24-hour excretion of 17-ketosteroids in urine was 5.9 and 3.2 mg./100 ml. Basal metabolic rate was +8. Mantoux test was positive. Buccal smears for sex chromosomes was positive (female type). Radiological changes were seen in the diaphysis of all the long bones as well as in the skull bones. Bones of hands, feet, clavicle, ribs, spine, scapulae, and pelvis did not show any changes. The typical findings were in the form of cylindrical expansion of the whole of the diaphysis due to cortical thickening which reduced the width of the medullary canal (Special Plate, Figs. 1 and 2). The metaphysis and epiphysis were left unaffected. The skull showed gross thickening and sclerosis of the frontal bones, particularly the supraorbital margins, extending towards the forehead as well as to the floor of anterior and middle cranial fossae and backwards to the petrosal ridge. The parietal and frontal bones showed patchy areas of sclerosis (Special Plate, Fig. 3). Biopsy from the affected bone showed moderate thickening of the bony trabeculae with normal laying down of osteoblasts.

COMMENTS

Englemann's disease is characterized by underdevelopment due to fusiform expansion and sclerosis of the diaphysis of long bones. The disease is diagnosable in infancy and may be suspected in any child with feeding problems and delayed walking. The youngest patient reported by Gvozdanovic (1950) was a 3-months-old girl. During childhood aching limbs and a wide-based waddling gait are characteristic features. Delayed puberty associated with or without skeletal deformities and a variable degree of neurological deficit are common in later life (Riley and Shwachman, 1943). The disease, as in the present case, is often discovered accidentally.

A multitude of laboratory tests revealed no abnormality. However, radiological changes are diagnostic. Classical changes start in the diaphysis of long tubular bones with spindle-shaped sclerotic thickening, and as the age advances osteosclerosis extends lengthwise but the metaphysial and epiphysial zones are usually not affected, though Clawson and Loop (1964) described an unusual case showing widening and osteoporosis of these areas as well. The characteristic changes have been seen mostly in the long bones of extremities, but others are also involved. However, Lennon *et al.* (1961) in a review of 52 cases described the involvement of the base of the skull in 53%, cervical vertebrae in 9.6%, and metatarsals and metacarpals in 9.6%. Long bones as well as skull bones are involved in our case.

The histological picture is very variable (Neuhauser *et al.*, 1948 ; Bingold, 1950). The changes, whenever present, are confined to the radiologically altered areas of bone and consist mainly of cortical hyperostosis. Histologically, the disease has to be differentiated from infantile cortical hyperostosis, which occurs in infants and where the involvement of bone is asymmetrical and ribs and mandible are invariably involved (Caffey, 1956 ; Stewart and Cole, 1956).

The exact pathogenesis of the condition is not known. Englemann (1929) believed that it was caused by a disturbance of the haemopoietic system, but this belief has not been upheld by subsequent workers (Neuhauser *et al.*, 1948 ; Sear, 1948 ; Bingold, 1950 ; Griffiths, 1956). Some suggestion of pituitary deficiency mainly based on the occurrence of infantilism associated with diminished excretion of 17-ketosteroids in urine has been made by Jammes *et al.* (1953) and Buchem *et al.* (1955). However, in our case urinary 17-ketosteroid excretion was within normal limits. The disease is often reported to be familial, though the genetic basis has not been fully worked out.

P. D. GULATI, M.D.,
Lecturer in Medicine.
O. P. BHARDWAJ, M.B., B.S., D.M.R.&E.,
DIPLOMATE OF AMERICAN BOARD OF RADIOLOGY.
Professor of Radiology.
P. B. VYAS, M.D.,
Senior Visiting Physician.
Maulana Azad Medical College and Irwin Hospital,
New Delhi.

Our thanks are due to the Medical Superintendent, Irwin Hospital, for permission to publish this case.

REFERENCES

Bingold, A. C. (1950). *Brit. J. Surg.*, **37**, 266.
Buchem, F. S. P. van, Hadders, H. N., and Ubbens, R. (1955). *Acta Radiol. (Stockh.)*, **44**, 109.
Caffey, J. P. (1956). *Pediatric X-ray Diagnosis*, 3rd ed., p. 817. Chicago.
Clawson, D. K., and Loop, J. W. (1964). *J. Bone Jt Surg.*, **46A**, 143.
Englemann, G. (1929). *Fortschr. Röntgenstr.*, **39**, 1101. Cited by Lennon *et al.* (1961).
Griffiths, D. Ll. (1956). *J. Bone Jt Surg.*, **38B**, 312.
Gvozdanovic, V. (1950). Cited by Lennon *et al.* (1961).
Jammes, A., Seruz, R., Prouxet, J., and Duclos, A. (1953). Cited by Lennon *et al.* (1961).
Lennon, E. A., Schechter, M. M., and Hornabrook, R. W. (1961). *J. Bone Jt Surg.*, **43B**, 273.
Neuhauser, E. B. D., Shwachman, H., Wittenborg, M., and Cohen, J. (1948). *Radiology*, **51**, 11.
Riley, C. M., and Shwachman, H. (1943). *Amer. J. Dis. Child.*, **66**, 150.
Sear, H. R. (1948). *Brit. J. Radiol.*, **21**, 236.
Stewart, H. B., and Cole, E. R. (1956). *J. Pediat.*, **48**, 482.

Phenindione-induced Neuropathy

Brit. med. J., 1967, 3, 218

Mononeuritis has been well recognized in diabetes, alcoholism, polyarteritis nodosa, carcinomatosis, and leprosy. Traumatic mononeuritis was not uncommon during wars. Of the blood disorders haemophilia, thrombotic thrombocytopenic purpura, porphyria, macroglobulinaemia, and myelomatosis are too well known. Two cases of neuropathy due to anticoagulant therapy are reported.

CASE 1

The patient, an old case of malignant hypertension (for which he had had a sympathectomy 13 years previously, followed by control of blood pressure on hexamethonium), was admitted to hospital on 22 May 1963 with a history of sudden onset of retrosternal pain lasting for 45 minutes. Diagnosis of myocardial infarct was confirmed by E.C.G. He was given analgesics, sedatives, and anticoagulants—heparin 10,000 i.u. stat. and 5,000 i.u. six-hourly for five doses intravenously, along with phenindione 200 mg. stat. and 150 mg. next day. The prothrombin time was 17 seconds with a control of 13 seconds on 23 May ; subsequently it was controlled two to two and a half times the control (prothrombin time ranging from 24 to 32 seconds against a control of 12 to 16 seconds), with varying doses of phenindione ranging from 25 to 50 mg. twice a day. On 8 June he complained of severe pain in his right buttock and thigh. On examination there was evidence of right sciatic nerve palsy with motor and sensory changes. Later strength curves showed denervation. Haemoglobin was 14.4 g./100 ml. ; it dropped to 9 g., but returned gradually to normal. Prothrombin time was 24 seconds, with a control of 16 seconds. Prothrombin activity was raised by vitamin-K injections. Total W.B.C., blood urea, E.S.R., electrolytes, liver-function tests, serum proteins, and cerebrospinal fluid were normal.

He was treated with intensive physiotherapy and electrical stimulation of paralysed muscles. Severe pain continued, though after three months there was a good recovery of his hamstring muscles but little improvement in his leg muscles, and the right-foot drop was well marked. Sensations were impaired on the lateral aspects of the right leg and foot. Physiotherapy was continued along with analgesics and tranquillizers.

He was followed up for a year. He continued having pain similar to that encountered in some cases of brachial plexus palsy, with little recovery of muscles below the knee.

CASE 2

This patient, an old case of recurrent myocardial infarction, had been on long-term anticoagulants (phenindione) since his discharge from hospital on 5 June 1965. He was having 50 mg. of phenindione twice a day. His prothrombin time on 8 August was 32 seconds against the control of 14 seconds. While on holiday on 20 August he started having bruising and pain in his left arm, with tingling and numbness in his fingers. Examination showed the clinical picture of a complete median nerve lesion on the left side with motor and sensory features, though no bruising was seen at the time of examination. The lesion was thought to be in the arm between the origin of the nerve and the site of the first muscular branch in the antecubital fossa. Strength-duration curves showed denervation. Investigations included prothrombin time of 83 seconds against a control of 12, which fell to 17 after phenindione was stopped. Haemoglobin was 15 g./100 ml., total W.B.C. 11,000/cu. mm. Platelet count, bleeding-time, and coagulation-time were normal. Blood urea, electrolytes, liver-function tests, pyruvate metabolism test, serum proteins, electrophoresis, chest *x*-ray picture, and cerebrospinal fluid were within normal limits.

He was put on analgesics, after which he was admitted to hospital for a course of corticosteroid therapy to reduce fibrosis around and within the nerve, and electrical treatment. After six weeks' treatment the power in his left hand had improved, and sensations were impaired over the distal interphalangeal joints of thumb, index, middle, and medial half of the ring finger only. He continued to improve with physiotherapy and electrical treatment. Initially he also had a severe causalgic type of pain in the hand and forearm, but this improved with corticosteroid treatment.

COMMENT

Adverse reactions to phenindione are well known. Perkins (1962) reviewed 133 reported cases and three of his own. The most common complication was a rash (100 cases), fever (34 cases), diarrhoea (20 cases), granulocytopenia (18 cases), stomatitis (14 cases), jaundice (10 cases), and nephropathy (5 cases). Occasional cases had vomiting, misty vision, thrombocytopenia, lymphadenopathy, conjunctivitis, loss of hair, and gangrene of the breast. Devanney and Osher (1952) described a case of spontaneous spinal epidural haemorrhage. Further cases were mentioned by Jacobson *et al.* (1966), who added three of their own.

Haematuria and bruising are the presenting features of phenindione overdose in most of the patients. The above cases are of interest, because there was no history of trauma or subcutaneous haemorrhage formation, and I believe the spontaneous haemorrhage into the nerve sheaths due to an unknown local factor, resulting in ischaemic neuritis of the nerve, caused the palsy in both cases. Persistent pain in Case 1 was presumably due to fibrosis in and around the sciatic nerve. The cases differ in the fact that in Case 1 the anticoagulant control was reasonable, though in Case 2 the prothrombin time was prolonged. There was no history of trauma in either case. It is therefore unlikely that either trauma sensitivity to phenindione or prolonged prothrombin time was the sole factor, and the combination of both factors seems to have been more than likely.

I should like to thank Dr. W. A. Elliott, consultant physician, and Mr. R. H. Sewell, consultant orthopaedic surgeon, for allowing me to publish these cases, and for their necessary advice and guidance.

T. N. MEHROTRA, M.D., B.SC., M.R.C.P.ED.,
Medical Registrar, St. Alfege's Hospital, London S.E.10.

REFERENCES

Devanney, J. W., and Osher, D. (1952). *Dis. nerv. Syst.*, **13**, 53.
Jacobson, I., MacCabe, J. J., Harris, P., and Dott, N. M. (1966). *Brit. med. J.*, **1**, 522.
Perkins, J. (1962). *Lancet*, **1**, 127.

Current Practice

MEDICINE TODAY

Recognition of Heart Failure

"Medicine Today" is the television series for doctors produced by the B.B.C. Advice in the preparation of the programme is given by the Association for the Study of Medical Education.

The programme on B.B.C. 2 on 18 July was on the subject of heart failure and portable oxygen equipment for use in the home. Printed below is an article prepared with the help of expert contributors to complement the television programme, which will be repeated on B.B.C. 1 on 26 July at about 11.20 p.m.

In "Medicine Today" Dr. C. S. McKendrick discussed the recognition of heart failure and its long-term management. He pointed out that, though failure of both ventricles may occur simultaneously, the individual clinical presentations of right-sided and left-sided failure had their own specific characteristics and that the aetiological factors differed. Failure of the left ventricle tended to be acute and characterized by paroxysmal nocturnal dyspnoea or acute pulmonary oedema. It was commonly the result of ischaemic heart disease, hypertension, or aortic-valve disease. Failure of the right ventricle was associated with an insidious onset and characterized by a raised central venous pressure and later associated with oedema. It was usually due to pulmonary hypertension secondary to chronic respiratory disease or mitral-valve disease. The more insidious onset of right-sided failure was related to the enormous capacity of the systemic vascular bed as compared with that of the pulmonary vascular bed.

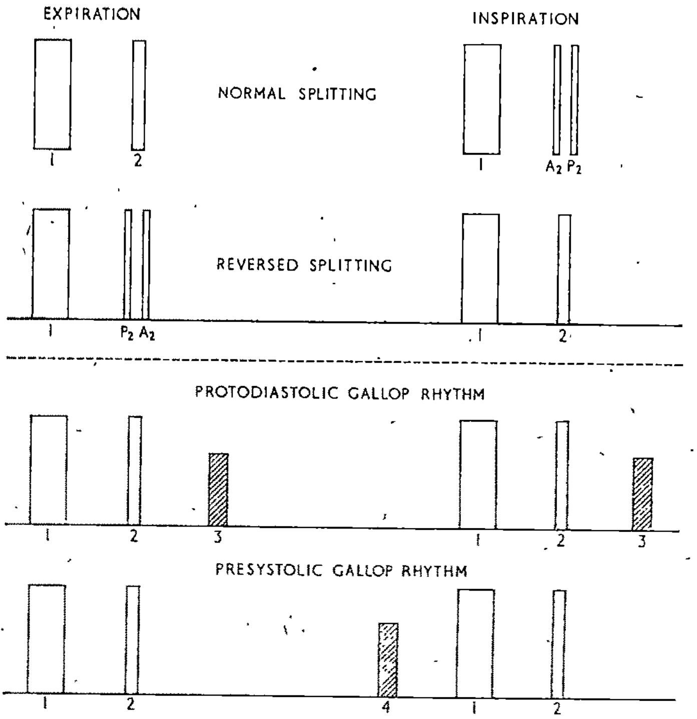
The more dramatic manifestations of heart failure, such as the crepitations of pulmonary oedema and the oedema of congestive cardiac failure, are well known and require no further comment. Moreover, the management of heart failure has frequently been discussed in these columns and will not be considered in this article. Certain points in the diagnosis of heart failure are, however, worthy of further consideration—in particular, gallop cardiac rhythm and the pattern of the jugular venous pulse.

Heart Sounds

The first heart sound is due to the closure of the mitral and tricuspid valves and is loudest at the apex. The second heart sound is due to the closure of the aortic and pulmonary valves and is loudest at the level of the second intercostal space. Splitting of the second heart sound (see Figure) during inspiration into an earlier aortic and a later pulmonary component is normally audible. The delayed closure of the pulmonary valve is due to the intrathoracic pressure falling during inspiration, which causes an increase in the venous return to the right ventricle. As a result of the increased stroke volume the right ventricle takes longer to contract and the pulmonary heart sound is heard after the aortic. Abnormally wide splitting will be heard if there is delay of pulmonary valve closure owing to right bundle-branch block or when the right ventricle ejects more blood than the left, as may occur with atrial septal defects. Sometimes left ventricular contraction is delayed because of left bundle-branch block. The closure of the aortic valve is then delayed and this also results in asynchronous closure of the aortic and pulmonary valves. Here the splitting is reversed and is heard during expiration instead of inspiration. Though split, these two sounds occur very closely together and should not be confused with a third sound, which occurs in mid-diastole.

The sounds of ventricular filling, sometimes called *triple or gallop rhythm,* comprise the atrial sound, the third heart sound, and a summation of the two. These sounds have a peculiarly low pitch, which distinguishes them from other heart sounds. The third heart sound, or *diastolic filling sound,* is due to the sudden stretching of the ventricular walls as the ventricle fills with blood—in much the same way as a noise is produced when the wind fills an empty sail. This sound is commonly heard in normal children and young adults but never in healthy subjects over the age of 40. Though this sound cannot be detected by auscultation in healthy persons of middle age, phonocardiograms demonstrate its presence. When ventricular filling is increased, as in mitral incompetence or in ventricular septal defects, and when constrictive pericarditis limits ventricular filling, the third heart sound becomes audible. More importantly it also becomes audible in ventricular failure when the atrial pressure is increased. In right ventricular failure the third sound is heard best in the tricuspid area over the right ventricle, while in left ventricular failure it is heard at the apex.

The fourth heart sound is caused by atrial contraction and indicates either atrial hypertrophy or enhanced atrial contraction owing to the increased resistance of the failing ventricle. This sound is often easier to feel than to hear.



Upper figure shows splitting of the heart sound. Lower figure shows third and fourth heart sounds.

When the heart rate is rapid the triple rhythm caused by the extra heart sound is called gallop rhythm (see Figure), because of its resemblance to the sound of a horse in canter. If it is due to a third heart sound the gallop rhythm is called *protodiastolic* and if it is due to a fourth heart sound it is called *presystolic*. Nevertheless, when the ventricular rate is very fast the third and fourth heart sounds become superimposed and their differentiation is not possible. The rhythm is then called a *summation gallop*. The real importance of these triple rhythms is that they are evidence of ventricular stress and incipient failure. But, as Dr. McKendrick pointed out, it is rarely necessary to differentiate which sort of triple rhythm is present. The important thing is to look for triple rhythm in anybody who is middle-aged and breathless and recognize it as evidence of ventricular failure. When the triple rhythm disappears it shows that the patient is improving, and if it persists in spite of treatment it is a bad prognostic sign.

The third and fourth heart sounds must be differentiated from another sound called the *opening snap*, which is pathognomonic of mitral stenosis. The snap is clicking in quality and precedes the mitral diastolic murmur characteristic of the valve disorder. It is due to the sudden opening of the anteromedial cusp of the mitral valve.

Raised Venous Pressure

Without depreciating the importance of gallop cardiac rhythm the first recognizable evidence of right ventricular failure is often a raised central venous pressure, and this can be detected long before oedema develops. It is best observed in the internal jugular vein. Because there is no valve between the internal jugular vein and the right atrium this vein accurately reflects pressure in the right atrium. In normal subjects lying down at an angle of 45 degrees the jugular veins are distended to a height of two or three centimetres above the sternal angle. To examine the venous pulse it is essential that the patient is relaxed, as the internal jugular veins lie deep to the sternomastoid muscles. The internal jugular is a better guide to centre venous pressure than the external jugular vein because kinking in the latter may mask the impulse.

A visible pulse in the neck may be arterial or venous, and it is of obvious importance to differentiate them. The carotid pulse is palpable, whereas a venous pulse is not. Furthermore, the carotid pulse has an abrupt onset and is more localized. A venous pulse rises during inspiration and normally has more than one peak. If in doubt pressure on the abdomen will raise a venous pulse but not affect the arterial pulse. Though this hepatojugular reflux has been described as a sign of cardiac failure, it is not reliable as such, for the difference in the normal subject and the patient in heart failure is quantitative and not qualitative.

Two waves may easily be detected in the normal venous pulse. The first is the "a" wave—which is due to atrial systole and occurs immediately before the carotid pulse. The second is the "v" wave of ventricular systole caused by the filling of the right atrium when the tricuspid valve is closed. The "a" wave will be increased when there is atrial hypertrophy, as in tricuspid stenosis, and it will be absent when there is atrial fibrillation. The "v" wave will be increased when there is tricuspid incompetence, whether this is organic from rheumatic heart disease or functional from dilatation of the right ventricle in heart failure.

Inspection of the jugular venous pulse thus not only indicates a raised central venous pressure, which is evidence of right heart failure, but also determines the presence of atrial fibrillation and tricuspid incompetence. It is an important physical sign to seek in patients with acute chest pain. Myocardial infarcts do not occur in the right ventricle, so that if acute chest pain is associated with a raised central venous pressure it is likely to signify pulmonary infarction and not coronary-artery disease.

TODAY'S DRUGS

Hazards of Drug Prescribing in Pregnancy

The common hazards of prescribing any drugs are further complicated in the pregnant woman. Both the embryo or foetus and the parent are susceptible to effects of therapeutic substances which under other circumstances might be expected to be without serious risk. One immediate response to the tragic experience with thalidomide was a reaction towards an attitude of relative therapeutic nihilism during pregnancy. While this, as will be seen, is probably an understandable and proper attitude to adopt towards newly introduced drugs, if followed too blindly it can lead only to discomfort for, or may even be detrimental to, the pregnant woman.

Teratogenic Drugs

The teratogenic capacity of a drug is one—fortunately limited—aspect of the problem. Such effects result from interference with the development of the embryo in early pregnancy. Nevertheless, the drugs *known* to be teratogenic in man are very few. Clearly the prescriber has a responsibility to avoid the use of such drugs in the first twelve weeks of pregnancy, and especially in the period of differentiation from the third to eighth week. Apart from thalidomide, these are drugs mainly used in the treatment of cancer—antimetabolites (such as methotrexate, 6-mercaptopurine, and allopurinol), alkylating agents (such as chlorambucil), and antibiotic substances (such as actinomycin D). Fortunately the conditions for which these particular agents may be indicated are generally unlikely to be associated with pregnancy. Other substances questionably implicated include oral hypoglycaemic agents and adrenocortical hormones. The evidence here is equivocal, and, though some reports link their use with the appearance of foetal abnormalities, the suspicions aroused have not been clearly confirmed.

All these and many other drugs are known to be teratogenic in laboratory animals, usually when given in high doses. The list of such drugs is at first sight alarming, including aspirin, penicillin, streptomycin, sulphonamides, caffeine, and nicotine. "In fact the number of agents shown to be teratogenic in experimental animals is so great that the question arises as to whether all agents might not be teratogenic if applied at the critical time in the appropriate dosage in the right species."[1] Despite the earlier deficiencies in testing for teratogenicity before use in therapy, for none of the compounds in the above list has there been any evidence of such effects in man. "Sometimes we forget that drugs have always been tested for their effect on mammalian development . . . by administering them not to pregnant rodents but to pregnant women."[2]

The acknowledgement that additional tests were needed in animals has only sharpened the realization that the safety of any drug is only as great as it is demonstrated to be in man, and that the use of any new drug must continue to be a most cautiously conducted experiment, particularly in early pregnancy.

Placental Barrier

Apart from truly teratogenic effects, almost any drug given for an effect on the mother during pregnancy may have some effect on the foetus. As A. K. Done[3] has said, "From the pharmacological point of view the 'placental barrier' is largely a myth." The placental barrier may give some protection from effects of drugs taken by the mother, but it is safer to assume that even drugs which are non-lipid-soluble and ionized at tissue *p*H, or whose molecular weight exceeds 600, may be transferred across the placenta. Though such transfer is less likely to occur with these drugs than with those of smaller molecular size and greater lipid-solubility, it is known that red cells may be transferred, and there is the additional factor that the tissues of the foetus may be less able (qualitatively or quantitatively) to handle drugs than those of the mother. Thus even for poorly transferred substances an effective concentration of the drug or a metabolite may be achieved in the foetus. Moreover, in the presence of toxaemia, particularly, any generalization becomes even less valid. Apart from its peculiar liability to hazard from drugs given to the mother early in pregnancy, the foetus may be exposed to other drugs at any time during pregnancy and some of these may have deleterious effects.

While in normal pregnancy there may usually be little need for drug therapy,[4] there are sometimes indications for treatment of directly related symptoms, as well as of complications, including infection. The continuing treatment of a patient who becomes pregnant while already under care for a disease produces further problems.

For the common "morning sickness" simple psychotherapy —perhaps with an antacid or placebo—will often suffice. When these measures fail, and active treatment is required, antihistamine antiemetics such as meclozine may be prescribed ; in such a case the doctor "should not be deterred on account of any danger to the foetus."[2] Metoclopramide (Maxolon), a recently introduced antiemetic, is not recommended for use in early pregnancy—presumably because it is not yet known to be safe. For the rare instance of hyperemesis one of the phenothiazines may be effective ; no good evidence of toxic effects on the foetus has been recorded, but the possibility of their causing liver damage should be remembered. The temporary use of the common antacids or attention to eating habits will usually deal with heartburn. Constipation in pregnancy should be treated, as in most other circumstances, by alteration of diet or by occasional use of a mildly irritant laxative. A standardized preparation of senna taken at night is suitable. Preparations containing aloes should be avoided, but bisacodyl (Dulcolax), given in a suppository, may be used.

Sedatives, Tranquillizers, and Hypnotics

Of the sedative, tranquillizer, and hypnotic group of drugs phenobarbitone and amylobarbitone appear to have been used successfully for relatively long periods of time without apparent harm to the foetus. If given during labour phenobarbitone may have a persistent depressant effect on the newborn baby. A similar effect may be seen with preparations of chloral hydrate, especially in premature infants whose glucuronic-acid-conjugation mechanism is not fully developed. Given earlier in pregnancy, chloral does not seem to be troublesome, presumably because the mother's detoxication processes are of greater importance in removing the drug. Phenothiazines have not been shown to have toxic effects on the foetus, but their unwanted effects will be no less in the pregnant woman than in the non-pregnant.

Experience with newer sedatives and hypnotics has been shorter as to both their possible advantages and disadvantages during pregnancy. In view of their known side-effects in the adult it is not surprising that the giving of these depressant drugs just before delivery has been sometimes associated with less attentiveness, a longer period of disorganized activity, and slow adaptation to breast feeding in infants. Longer-term effects said to occur in rats have not been reported in man. Meprobamate (Equanil), chlordiazepoxide (Librium), oxazepam (Serenid), and nitrazepam (Mogadon) are in this category, and they should not be used without caution during pregnancy.

Though aspirin in large doses is teratogenic in some other species, no such effects have been attributed to it in man. If given late in pregnancy, salicylates, like coumarin and indanedione anticoagulants, may give rise to hypoprothrombinaemia and foetal or neonatal haemorrhage may occur. Suggestions of ill effects of ethyl alcohol during pregnancy have not been positively confirmed. It is known that alcohol rapidly crosses the placenta, but even its use in obstetric analgesia does not seem to be deleterious.

Infections During Pregnancy

Infections arising during pregnancy require appropriate chemotherapy, but here caution is required. A short-acting sulphonamide—such as sulphadimidine—which may be indicated for the early treatment of urinary infection, commonly due to susceptible strains of *Escherichia coli,* is believed to be safe. The sulphonamides with a longer-lasting effect are to a large extent protein-bound and slowly excreted and are known to be undesirable late in pregancy. They may persist in the newborn baby and lead to severe jaundice and possibly kernicterus. Streptomycin, gentamicin, and other antibiotics known to be toxic to the eighth cranial nerve should be avoided if possible, as there is some evidence that they may cause damage to the labyrinth and auditory nerve in the foetus.

Tetracyclines given during pregnancy are now well known to cause staining of the foetal teeth, and, especially in premature infants, cause a reversible impairment of skeletal growth. The antibiotic forms a chelate-complex with calcium, and the period at risk is therefore from about the middle of pregnancy. Not only is the discoloration of the teeth unsightly and permanent, but there is hypoplasia of the enamel with increased susceptibility to dental caries. This effect is probably possessed to some degree by all the tetracyclines. Alternatives should be used whenever possible in the second half of pregnancy. Like other penicillins, ampicillin is not known to have untoward effects on the foetus and is a suitable alternative when the organism is sensitive.

Of the commonly used antituberculous drugs streptomycin, ethionamide, and prothionamide should be used only when this is essential for the control of the disease. Isoniazid does not appear to cause foetal damage, but the toxic potentiality of *para*-aminosalicylate may show up in both mother and foetus. Clearly the chances of foetal damage have to be weighed against the urgent need to continue treatment of the mother with tuberculosis.

Chemotherapy of other diseases during pregnancy may present some difficulties. Evidence on the relative safety during pregnancy of drugs used in malaria is difficult to find, but the abortifacient action of quinine is overrated and other antimalarials have not been reported to cause foetal defects. Where the appropriate drug may have unpleasant effects on the mother, and also a secondary effect on the foetus, this will favour postponement of therapy until after delivery if the condition is not urgent.[4] A recent case of filariasis in a woman 32 weeks pregnant illustrates this situation, for a possible allergic reaction to diethylcarbamazine was a sufficient contra-indication to its use during the pregnancy.

Drugs for Cardiovascular Disease

It is accepted that if the usual therapeutic doses of digitalis glycosides are used in pregnant women no harm comes to the foetus, in spite of clear evidence that they do penetrate to the foetal heart and brain. Drugs which raise the blood pressure as a result of peripheral vasoconstriction may cause foetal asphyxia owing to constriction of the uterine vessels. This situation might arise, especially during labour. Nevertheless, the foetus does appear to be partially shielded from direct effects of catecholamines by the monoamine oxidase present in the placenta.

In severe hypertension it is not clearly known whether the continued use of hypotensive drugs as "the only alternative to termination"[4] carries any additional risk to the foetus beyond that already known to exist in this disease. Ganglion-blocking drugs may produce definite alterations of autonomic activity in the foetus—notably circulatory and intestinal effects. Babies born to mothers given reserpine within two days of delivery show signs of respiratory obstruction associated with nasal stuffiness, owing to transient effects on the nasal mucous membrane.

Thiazide diuretics, though useful in controlling the effects of pre-eclamptic toxaemia, are not without hazard to the foetus. Foetal death, together with liver damage or pancreatitis in the mother, have been reported. The incidence of thrombocytopenia, possibly due to sensitization of the foetus, is uncertain but probably low.

Unless care is taken, iodide or antithyroid drugs given to a pregnant woman may produce enlargement of the foetal thyroid by an analogous mechanism to that which may occur in the mother. If a hyperthyroid woman becomes pregnant drug treatment should be continued with the minimum necessary dosage, though some doctors believe that surgical operation is justified. Symptoms often decrease later in pregnancy. Progressive reduction in the dose of antithyroid drug should aim at stopping treatment by about one month before delivery. If this can be done the likelihood of goitre in the baby is slight. Radioactive iodine is clearly hazardous, because it will be taken up by the foetal thyroid, causing involution and secondary effects.

Treatment of Diabetes

The pregnant diabetic also requires special consideration. Continued use of oral hypoglycaemic agents has been reported to be associated with foetal death, but good evidence on this point does not appear to be available. Control of dosage is likely to be more difficult, especially with the longer-lasting drugs. Careful control, using insulin in hospital, would appear to be a safe recommendation.

Other hormones, adrenocortical or gonadal, are potentially capable of having effects on the skeletal and sexual characteristics of the foetus and newborn child. Androgens, oestrogens, and progestogens should be avoided in pregnancy. Progestational hormones are not of proved value for the prevention of habitual or threatened abortion. The case against adrenocortical hormones is much less strong and there is no proved causal link between them and the occasional abortion or stillbirth. Although "there is no doubt that women taking a steroid throughout (pregnancy) have both conceived and borne normal babies,"[5] it is wise to avoid high doses, especially in the first trimester.

Drugs Used During or Immediately Before Delivery

Care in the use of drugs is particularly necessary at or near to full-term. The susceptibility of the newborn infant to drugs given to the mother may be adversely affected by several factors—including asphyxia and trauma during birth—as well as deficient mechanisms of detoxification and excretion because of enzymological immaturity and inefficient renal function. F. Moya and V. Thorndike[6] have given a useful comprehensive review of this topic.

The problems associated with the giving of sedatives, analgesics, and anaesthetics to the mother are generally well recognized. The use of morphine and similar substances given for maternal analgesia are known to be sometimes responsible for cyanosis and respiratory depression in the baby. In babies born of addicted mothers pinpoint pupils and withdrawal symptoms have been reported. Pethidine is commonly said to cause less respiratory depression than morphine, but it is probable that respiration in the baby will be at least as depressed as in the mother at the time of birth, whichever analgesic is used.

Other potential dangers arise from the infant's inability to metabolize drugs with efficiency equal to that of the adult. In laboratory animals oxidative pathways appear to be the most deficient at birth, but in newborn children conjugation processes for chloramphenicol, paracetamol, salicylate, and bilirubin have been reported to be less efficient. Toxic effects of chloramphenicol in neonates have been reported even after greatly reduced dosage schedules. It is clearly wise particularly to avoid giving this drug to the mother at this time.

Several drugs may produce an exaggeration of the normal hyperbilirubinaemia of babies if given to the mother just before delivery. The conjugation of bilirubin is already relatively inefficient in the neonate. Hence drugs which use the same conjugation mechanism may cause an increase in the concentration of "free" unconjugated bilirubin. Excess of this can result in brain damage—namely, kernicterus.

Protein-bound Drugs

In addition, drugs which are to a large extent protein-bound may compete with bilirubin for protein-binding sites and thus have a similar effect. Thus, as already mentioned, long-acting sulphonamides given to the mother have been reported to cause hyperbilirubinaemia in the baby. The following drugs have been reported to have high in-vitro activity of this kind—though clinical confirmation is fortunately so far lacking—novobiocin, indomethacin, salicylates, and tolbutamide.

Neonates also have a greatly increased sensitivity to drug-induced methaemoglobinaemia, probably because of deficient enzyme activities in the erythrocyte. Phenacetin, local anaesthetics, nitrites, and sulphonamides are dangerous in this respect. Once again there is little evidence to implicate the administration of these drugs to the mother with toxicity in the baby. Nevertheless, it would be wise to use any of them with understanding caution. Haemorrhage—sometimes fatal in the foetus or baby—after giving anticoagulants (or large doses of salicylates) to the mother has already been referred to. This may arise even when the maternal prothrombin level is not excessively depressed.

This brief review seems to have left few classes of drug available for unquestioned use during pregnancy. The risk of giving a drug to a pregnant woman is not confined to the developing embryo in the first trimester, and (as with all treatment) the decision to prescribe must be taken after a careful assessment of the relevant factors. Each prescription should represent a calculated risk. The continuing uncertainty of the extent to which some drugs can be used in pregnancy with relative safety is mainly caused by a lack of adequate knowledge of the clinical pharmacology of both new and not so new drugs. It still remains true for drugs which are used frequently that "where there is lack of positive information it is suggestive that the drugs concerned are at least of no lasting harm to the foetus when given to the mother in the usual therapeutic doses."[7]

Conclusions

(1) In normal pregancy there is little need for drug therapy.

(2) Prescribe drugs for pregnant women only when there is a clear indication and then for as short a period as possible.

(3) Keep a record of the dosage and timing of all drugs given during pregnancy.

(4) Since pregnancy may occur in any woman of child-bearing age, this possibility should act as an additional restraint on unnecessary prescribing of potentially hazardous drugs.

REFERENCES

[1] Wilson, J. G., *Amer. J. Obstet. Gynec.*, 1964, **90**, 1181.
[2] *Brit. med. J.*, 1964, **1**, 195.
[3] Done, A. K., *Ann. Rev. Pharmacol.*, 1966, **6**, 189.
[4] Barr, W., *Prescriber's J.*, 1963, **3**, 41.
[5] Laurence, D. R., *Clinical Pharmacology*, 3rd ed., 1966. London.
[6] Moya, F., and Thorndike, V., *Clin. Pharmacol. Therap.*, 1963, **4**, 628.
[7] Baker, J. B. E., *Pharmacol. Rev.*, 1960, **12**, 37.

ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Cyclandelate and Cerebral Circulation

Q.—*Is there any evidence that cyclandelate significantly improves cerebral circulation?*

A.—There have been a number of recent reports suggesting that cyclandelate can increase cerebral blood flow. It is difficult to evaluate the results of these studies, because different methods of measuring cerebral circulation have been used in them all.

Eichhorn[1] employed a technique injecting a radioactive isotope intravenously and measuring the cerebral circulation by surface counting over the torcular Herophili. He studied 40 patients with cerebrovascular disease and found that cyclandelate in an oral dose of 800 mg. daily for a period of three weeks significantly raised the blood volume and reduced the pathologically increased circulation time in patients with mild to moderate cerebrovascular insufficiency. Luisada and his colleagues[2] used impedance plethysmography, and demonstrated that cyclandelate in a similar dose caused consistent vasodilatation of the arteries of the skull and brain. Their subjects were 26 elderly inmates of a home for the aged.

Kuhn[3] did angiography with high speed film changing on 25 patients with focal cerebral ischaemia. The first angiograph was done within two weeks of the onset of symptoms and the second 12 weeks later, the patients having been given cyclandelate 400 mg. four times daily over this period. He claims that 19 patients were clinically improved, 11 markedly so, and that the repeat angiographs showed an increased velocity of blood flow.

O'Brien and Veall[4] measured cortical blood flow by the clearance of Xe-133 in nine patients with cerebrovascular disease whose clinical condition was stable. The patients acted as their own controls. Observations were made on two occasions, after a placebo and after an oral dose of 1 g. of cyclandelate. Analysis of the results showed that there was a significant increase in blood flow after cyclandelate.

These results must still be regarded as preliminary observations. The number of patients is small, and, except for O'Brien and Veall's study,[4] the investigations have not been as well controlled as one would wish. None the less, it is suggestive that all the observers using different techniques have demonstrated an increase in cerebral blood flow. If the findings are confirmed it will be of great importance, because none of the other commonly used vasodilator drugs has been shown to have a consistent effect upon the cerebral circulation.[5]

REFERENCES

[1] Eichhorn. O., *Vasc. Dis.*, 1965, 2, 305.
[2] Luisada, A. A., Jacobs, R., Bruce, D., Bernstein, J., and MacCanon, D. M., ibid., 1966, 3, 201.
[3] Kuhn, R. A., *Angiology*, 1966, 17, 422.
[4] O'Brien, M. D., and Veall, N., *Lancet*, 1966, 2, 729.
[5] Gottstein, U., *Acta neurol. scand.*, 1965, 41, Suppl. No. 14, p. 136.

Pain in the Back

Q.—*What is the best answer to give to a woman who wishes to know why she has pain in the back of long duration after it has been explained to her that organic disease has been excluded and no abnormality in the back can be found?*

A.—This all too familiar problem can be answered in two ways. Firstly, assuming that the given facts are completely accurate and that there is no organic cause for the patient's pain, the cause of the pain must be psychogenic. If the psychological causes or stresses are reasonably clear these should be dealt with on conventional lines—reassurance, superficial psychotherapy, and mild sedation. Diazepam 6 mg. daily in divided dosage is often very helpful. A small proportion of women with chronic backache for which no organic or other cause can be found are in fact suffering from a depressive illness with somatic conversion symptoms. The response in two to three weeks to imipramine 25 mg. eight-hourly is often dramatic and revealing.

Secondly, there remains a large group of patients who have backache of a few years' duration, often dating from a pregnancy or minor trauma. Physical and radiological examination reveals no abnormality other than tenderness, either diffuse or local, in the lower lumbar and sacral region. The classification of this type of lesion is a matter of considerable controversy. Thus "sacro-iliac strain," "multifidus triangle syndrome," "chronic lumbar strain," "chronic disc prolapse," "postural back strain"—the list is endless. Because no lesion is directly demonstrable, one pays one's money and takes one's choice, and the choice is wide.

The treatment of choice should be the safest and the cheapest. I would suggest a course of postural and back-strengthening exercises, together with exercises to improve abdominal muscle tone, and, when appropriate, a weight-reducing regimen. The general increase in fitness and well-being induced by a regimen of this type can do only good, and after instruction it can be carried out at home. The very few remaining patients who do not respond to these treatments are best managed by a programme of optimistic support and encouragement.

Notes and Comments

Chilblains.—Professor J. T. INGRAM (Leighton Buzzard, Beds) writes: The information provided by your expert ("Any Questions?" 24 June, p. 818) towards the understanding and management of chilblains might with advantage be expanded. The increased susceptibility of young women and the absence of chilblains in certain climates and where central heating and air-conditioning are effectively employed must be significant. Occupational factors and the importance of posture were emphasized by Winner.[1] It might have been explained that an adequate reaction to ultraviolet irradiation causes prolonged relaxation of the spasm of arterioles in the skin—an important factor in the mechanism—as shown by Holti.[2] The brief reference to clothes might have included praise for the fashion of trousers and tights for women and those decorative, long-legged woollen knickers.

Internal measures are admittedly disappointing in the treatment of chilblains of the legs, but chilblains occur elsewhere and there is still a place for small doses of thyroid for chilblains of the digits.

OUR EXPERT replies: While I am sure Professor Ingram's gallant support for decorative woollen knickers will be appreciated in the right quarters, I must now amplify my remarks on therapy. Discussion of the "mechanism" of action of ultraviolet irradiation would best be postponed until such an action is proved, and in this respect the observations of Holti and Ingram[3] were uncontrolled. Finally, the place for small doses of thyroid in the treatment of digital chilblains is in the clouds of dermatological mythology rather than the rocks of practical therapy.

REFERENCES

[1] Winner, A. L., and Cooper-Willis, E. S., *Lancet*, 1946, 2, 663.
[2] Holti, G., *Clin. Sci.*, 1955, **14**, 137.
[3] —— and Ingram, J. T., *Lancet*, 1963, **1**, 141.

Book Reviews

Profitable Reading

Clinical Surgery: Abdomen and Rectum and Anus. Edited by Charles Rob, M.C., M.Chir., F.R.C.S., Rodney Smith, M.S., F.R.C.S., and Sir Clifford Naunton Morgan, M.S., F.R.C.S., F.R.C.O.G., F.A.C.S.(Hon.). (Pp. 645+xiii; illustrated. £7 15s., £4 10s. per vol. in complete set.) 1966.

A good book has been defined as one "which is opened with expectation and closed with profit." This is my experience after a complete perusal of this book where forty-one authors give us the present-day look of abdominal and rectal surgery. Graduates are bound to study it in detail and use it for reference work. It enhances the already established reputation of this valuable system of *Clinical Surgery*.

The division of surgery into component parts, historical, clinical, operative, and experimental, creates certain difficulties for editors and authors in deciding where to "draw the line"; what should be excluded in specific texts? In this book the editors' objective is to give a review of the clinical aspects of the subject and of the investigations required in diagnosis; they have achieved this objective in an admirable manner. Some detail and diagrams of operative technique have, however, been included in certain chapters which could be pruned in view of the availability of the appropriate volume of *Operative Surgery*, and the space given to other material. Each author has made good use of the space allotted to him for complete coverage of his subject, and helpful references for further reading are provided. The present position of a number of subjects will not remain static; the authors demonstrate how much surgical research is still required to understand and manage many abdominal affections. For example, we know little about the aetiology of peptic ulceration, gallstones, and pancreatitis, or the role of degeneration in Auerbach's plexus, a common factor in achalasia of the cardia and Hirschprung's disease. It is fortunate for patients with achalasia that Heller's operation is so satisfactory, although the condition carries the risk of many complications, and the association with oesophageal carcinoma must now be stressed. The number of operations performed for Hirschprung's disease and rectal prolapse witnesses to all the treatment problems awaiting solution. For the latter condition recto-sigmoidectomy must now pass into history. The author calls attention to the experimental evidence for the carcinogenicity of buried thick Ivalon sheets. Mention should be made of the value of perineorrhaphy and sphincter reconstruction for rectal prolapse with anal incontinence.

Although the aetiology of peptic ulceration in the stomach and duodenum still eludes us, the surgical treatment required has been clarified with emphasis on the value of Billroth I gastrectomy for a chronic gastric ulcer and selective vagotomy with a drainage operation for a chronic duodenal ulcer. The treatment of a chronic gastric ulcer is really a surgical problem, for confusion with a carcinoma is not uncommon, and is it wise to leave the ulcer by performing vagotomy and pyloroplasty? The mortality and relapse-rate following present operations for perforated peptic ulcers are still too high; perhaps vagotomy with suture of perforated duodenal ulcers will improve this position. Surgery is wisely advised for asymptomatic cholecystitis and cholelithiasis in the absence of a contraindication, and the patient has a life expectancy of up to 15 years. The arguments are summarized for the surgical or conservative treatment of acute cholecystitis; but I wanted to know the author's opinion! The physiology and clinical evaluation of abdominal pain is helpfully considered and good advice given on abdominal emergencies with a full description of radiology of the acute abdomen. Cancer of the stomach remains a frequent and dangerous tumour, although a little gloom has been dispersed by radical surgery, but this is not entirely satisfactory, for too many patients have lymph node metastases, with consequently a poor prognosis, when this is done. We must now make progress with preventive treatment and early detection methods using newer screening techniques, including cytology and gastrophotography as well as radiology.

A number of useful investigations in abdominal surgery are described, including those relating to the liver. The relationship of the liver with so many abdominal lesions enhances the importance of such studies, including biopsy. The value of the latter when cholecystectomy is done might be mentioned, for sometimes unsuspected biliary cirrhosis is thereby discovered. The rectum and anus have received full attention, including excellent coverage of cancer in these organs, but why is such an important subject as cancer of the colon omitted, except in connexion with intestinal obstruction? Other notable omissions in the book are colonic diverticular disease and ulcerative colitis; both are attracting considerable attention today. It was pleasurable to read Sir Zachary Cope's account of abdominal actinomycosis. Fortunately this is rare in our country today.

I would like to review each chapter, but this is impossible for lack of space; each author has made a valuable contribution and the editors have welded them into a very readable book. This volume deserves to be widely studied.

RONALD W. RAVEN.

Flood of Patients

Psychiatric Illness in General Practice. By Michael Shepherd, Brian Cooper, A. C. Brown, and G. W. Kalton. (Pp. 220+xvii. 45s.) London, New York, and Toronto: Oxford University Press. 1966.

It is generally accepted that a large proportion of medical illness is functional rather than organic. The figures vary considerably, from less than 4% to over 60%, and it is obvious that the populations, or the investigators, or the criteria differ. What is common to most of the published work is that the writers base their opinions on conjecture and clinical impressions, which are notoriously misleading. In this, as in other psychiatric fields, there is a plethora of speculation and a paucity of data.

This book is an attempt to provide data, but it is more concerned with methods than results. It can be divided into three main parts—firstly, a review of the existing state of knowledge in this field; secondly, a description of the methods of investigation; and thirdly, the results.

Briefly, a random sample of the patients seen by 76 doctors in 46 practices was analysed over a period of a year. The results suggest that about 14% of patients seen in general practice are suffering mainly from psychiatric disorders in a proportion of two women to one man. The majority of these are minor cases and only 4% were psychotic. There was, however, considerable variation between individual doctors' reporting. It is also of interest that only about one-tenth of the cases were referred to psychiatrists, and this survey suggests that the reservoir of cases is such that ten times as many patients could be referred to psychiatrists as are at present. If such patients were referred, the psychiatric services would break down, and it is obvious that general practitioners must continue to carry the main burden of psychiatric care even though the treatment of minor psychiatric disorders in general practice is often inadequate and haphazard. The authors conclude that the cardial requirement for the improvement of the mental health services is not an expansion of the psychiatric agencies but a strengthening of the family doctor. This is a process which must start in the medical school, followed by a reduced patient load in general practice and better ancillary services.

This book is of value to general practitioners and sociologists and also to psychiatrists, who may become more sympathetic to the problems of their colleagues in general practice—and grateful to them for the flood of patients they are keeping away.

A. W. BEARD.

Neuroanatomy

The Essentials of Neuroanatomy. By G. A. G. Mitchell. (Pp. 111; illustrated. 15s.) Edinburgh and London: E. & S. Livingstone. 1966.

This modest little volume makes more generally available Professor Mitchell's introduction to the study of the central nervous system, which first appeared as a private publication some sixteen years ago. As is to be expected from the author, it is a completely reliable account of many of the essentials of neuroanatomy and will doubtless provide help to students entering upon the study of the structure of the human nervous system. It is a pity that the opportunity provided by the reproduction of the little volume was not exploited to include some of the considerable developments in our basic knowledge of the structure of the nervous system established in the past few years. In particular some reference to the very considerable contributions to this knowledge made by electron microscopy could have been intercalated to advantage. Indeed, the structure of the nerve fibre itself, and the important relationships between nerve cells and glial elements in the central nervous system, can be reasonably presented only in the light of ultrastructural observations. In the reviewer's opinion some reference to the results of the application of histochemistry to the study of nervous tissues would have been stimulating, showing, as they can, the links between anatomy on the one hand and physiology and biochemistry on the other. An analysis of the nerve supply to a muscle and more detailed accounts of fibres of different calibre in the spinal nerves could also have been expected, and would be helpful to the neophyte. But these are perhaps suggestions for the next edition of this introductory volume; they are not meant to be carping criticisms of a useful book.

J. D. BOYD.

Working and Reproduction of a Cell

Growth, Function, and Regulation in Bacterial Cells. By A. C. R. Dean and Sir Cyril Hinshelwood. (Pp. 439+xii; illustrated. 84s.) London: Clarendon Press. Oxford University Press. 1966.

Despite its title, this book has little in common with others on the subject, and the reader expecting a balanced discussion of chromosomal replication, enzyme induction, and the like will be sadly disappointed. This is a highly idiosyncratic statement of a general model for cell growth and metabolism, accompanied by experimental results similar to those of Hinshelwood's *Chemical Kinetics of the Bacterial Cell* (1946).[1] The heart of the model is the principle of "total integration" which states that the "working and reproduction of a cell demands the harmonious gearing of all its parts." This finds formal expression in the "network theorem" which presupposes that the "growth of living matter depends upon closed cycles of mutually dependent interactions" and yields general relations involving quantities like cell numbers or duration of lag but not specific macromolecules or enzyme pathways.

Considering the model in isolation, most readers would probably agree that cells might conceivably work in this way. Doubts immediately arise from one of the main assumptions—that each cell component increases exponentially as time passes. This can be true for populations of asynchronously dividing cells but is certainly untrue of an individual cell, the subject of the model, in which the number of copies of a given gene or the amount of a given enzyme is known to double abruptly during the growth cycle. On the face of it, assumption and observation appear irreconcilable.

Apart from questions of detail, the principle of total integration leads to a considerable difficulty. While most workers would probably regard the principle almost as a truism, they also believe that integration is not so complete that the study of single enzyme systems or other isolated phenomena is likely to yield meaningless results. The authors, on the other hand, appear to hold that current interpretations of such experiments may well be fallacious because, if integration is indeed "total," then any change in conditions necessarily alters the cell as a whole, so that any response may be due to processes other than that which the experimenter believes he is studying. Thus, any conventional explanation can be countered by a hypothetical alternative justified by the principle. The difficulty of this position is that, granted cells to be complex, the counter hypotheses may be correspondingly complex and hence untestable. There is one notable exception. Certain instances of drug resistance are ascribed to purely non-genetic events, but genetic change has not been excluded by using any of the well-known methods of gene transfer in bacteria.

The authors' model may or may not be correct, but until it is tested more directly it seems unlikely to shift modern biology from its present course.

G. G. MEYNELL.

REFERENCE

[1] Hinshelwood, C., *Chemical Kinetics of the Bacterial Cell*, 1946. Clarendon Press, Oxford.

Textbook of Bacteriology

An Outline of Bacteriology and Immunity. 3rd edition. By Ronald Hare, M.D. (Pp. 472+xii; illustrated. 50s.) London: Longmans. 1967.

The interval between editions of this book has been reduced from seven to four years, a clear indication of growing popularity. The principal change in this edition is an expansion of the section on viruses, the previous single chapter being subdivided into no fewer than nine on a generic basis; that on adenoviruses occupies only one page and some others only two. Might not some of the chapters on bacteria benefit from similar if perhaps less drastic treatment? That on Gram-negative bacilli embraces 15 genera, and even so seems less heterogeneous than its Gram-positive counterpart, which includes the *Mycobacteria*, surely distinctive and important enough to deserve a place of their own, and *Bacteroides*, most of which are in fact unequivocally Gram-negative. *Listeria* and *Erysipelothrix*, which might also have been included, appear in a chapter on filamentous organisms, in which there is also a new description of *Mycoplasma*. Infectious drug resistance is now briefly described, but in this connexion the statement that "ampicillin is the drug of choice" for treating *Salmonella* infections must be contested. This drug is still chloramphenicol, and the main apprehension in connexion with transferable resistance relates to it.

This is a most attractive book, profusely and beautifully illustrated and dealing admirably with principles and the general aspects of its subject—immunity and epidemiology in its widest sense. The largest and perhaps best chapter, on the sources and transmission of infection, embodies much of the author's own original work, and can be read with profit by anyone. In contrast to these the few chapters describing individual bacteria seem in places rather terse and elementary and might fail to provide the more interested student with all the information for which he hopes. In an ever more crowded curriculum the teaching of practical bacteriology may have to be curtailed, but a real and abiding interest in the subject can come only from first-hand bench experience. It is to be hoped that a trend to more theoretical teaching will not deprive the profession of bacteriology of its future recruits.

L. P. GARROD.

Recent Work in Paediatrics

Advances in Pediatrics. Vol. 14. Edited by S. Z. Levine. (Pp. 307. 87s.) London: Lloyd-Luke. 1966.

The fourteenth volume in this series contains the customary six monographs. The subjects covered are: ulcerative colitis, poisonings, haemoglobinopathies, attenuated live virus vaccines, hereditary renal glomerular diseases, and physiological and biochemical determinants of development.

Two of these articles are of practical importance to family doctors as well as to paediatricians. "Poisonings," contributed by the late Dr. H. Jacobziner, Assistant Commissioner, Department of Health, New York, is an excellent exposition, starting with an epidemiological survey, continuing with the commonest specific poisonings, their clinical aspects and treatment, and concluding with control and preventive measures. Particularly important are the nine main contributory factors which he enumerates, and his timely warning that "the universal antidote is neither universal nor specific." The second "practical" article is on the current status of live attenuated virus vaccines by Drs. D. T. Karzon and D. A. Henderson, from New York and Atlanta respectively. This is the longest contribution, occupying 79 pages. Consideration is given to smallpox, rabies, poliomyelitis, measles, yellow fever, and rubella. The information is up to date and includes the use of intradermal injections by jet, the best technique available today.

Three of the articles will appeal particularly to the specialist: those on ulcerative colitis, the haemoglobinopathies, and determinants of development. The first, by Drs. O. Brobergen and R. Lagercrantz, of Stockholm, is an excellent account of the condition, and stress is rightly laid on the extracolonic and systemic manifestations. This article will also be of interest to surgeons. There is an addendum to this chapter which brings the report up to 1966. Erythema nodosum is cited as one of the extracolonic signs and is noted in the index, where the reader is advised to "see under skin conditions"; but unfortunately there is no such heading in the index. The second contribution is from Professor J. H. P. Jonxis, of Groningen, an acknowledged expert in the field of abnormal haemoglobins, and he has given a masterly account; his references even include two from *Nature* in 1966. The third of these articles is a scholarly exposition of recent discoveries in biochemical genetics by Drs. N. Kretchmer and R. E. Greenberg, of California.

The last article is by Drs. W. W. McCrory, M. Shibuya, and H. G. Worthen, of New York, on hereditary renal glomerular diseases. Here are considered chronic glomerulonephritis, nephrosis, nephronophthisis, and Fabry's disease. This is an extremely interesting chapter.

The standard of production of the book achieves the same level as its predecessors, and once again Dr. Levine is to be congratulated on his selection of authors. One of the features is the bibliography supplied by all the writers, more than 900 references being quoted. There are nine plates, nine tables, and 27 figures and there are both author and subject indexes.

WILFRID GAISFORD.

Plants in Pharmacology

Plant Drugs that Changed the World. By Norman Taylor. (Pp. 275+viii. 30s.) London: Allen & Unwin. 1966.

The author of this book is described on the dust-cover as "one of the outstanding authorities in the English-speaking world on plants and flowers. . . ." He has here applied his extensive knowledge to writing a series of essays on the historical background and the economic significance of a number of drugs that are derived from plants. *Plant Drugs that Changed the World*—as becomes a book with such a resounding title—makes interesting reading, but the author falls between two stools. His material is rather too technical for readers other than botanists, pharmacists, and physicians; on the other hand, the literary style—approximating to that of the popular press—will often exasperate the serious student.

Nevertheless, Mr. Taylor shows considerable skill in combining a popular presentation of pharmacology with thumbnail biography. Readers on Tyneside will be surprised to learn that Dr. Thomas Addison, of Guy's, was "a Scottish physician." There is a useful bibliography.

STANLEY ALSTEAD.

Nutrition Review

World Review of Nutrition and Dietetics. Vol. 7. Edited by Geoffrey H. Bourne. (Pp. 255+viii. £7.) London: Pitman. 1967.

The seventh volume in this useful series justifies its global title by including three contributions from the U.S.A., and one each from Canada, England, Holland, and Scotland. L. Cesal, L. Blakeslee, and E. O. Heady, of Iowa, have written the first article on "The World Food Situation." On the maximum basis of a rapid increase in population, combined with greatly improved nutrition, A.D. 2000 may see the world's population more than doubled, and the requirements of animal protein more than trebled. To all but the middle-aged the prospect must be alarming. The authors' final words that the "world food situation will be a subject for close scrutiny from many points of view in the years to come" seem an understatement. S. E. Johnson, of the U.S. Department of Agriculture, deals with "Economic Implications of Food Aid." The supply of free food to a backward country may sometimes help economic development, by giving the inhabitants the bodily strength necessary to get on with their own agricultural activities, or may sometimes hinder, by making the inhabitants complacent and lazy. As in many documents discussing international relationships the verbiage in this article is expansive rather than simple. For example, "food aid" is equated with the food itself as a thing which needs to be transported and stored.

M. C. Latham, of Boston, U.S.A., assisted by F. J. Stare, reports on "Nutritional Studies in Tanzania." The great diversity in both the ecology and the inhabitants in this large country makes it difficult to generalize about either the diet or the nutritional status. Protein-calorie deficiency, nutritional anaemias, vitamin-A deficiency, and ariboflavinosis occur in many areas. The possible danger of liver disease arising from the consumption of groundnuts contaminated with *Aspergillus flavus* urgently requires investigation. A. B. Morrison and M. N. Rao, of Ottawa, discuss "Some Relationships Between Proteins and Calories," emphasizing the point that protein cannot be used efficiently when the diet is deficient in calories. G. A. Garton, of Aberdeen, reviews "The Digestion and Absorption of Lipids in Ruminant Animals," mentioning that some minor components among the fatty acids in foods of animal origin, such as butter, originate in microbial synthesis in the rumen.

For the rest about half the space in this volume is taken up by two long contributions which will appeal especially to dental readers. L. M. Dalderup, of Wagenigen, citing about 500 references, has written on "Nutrition and Caries." The presence in the diet of sugar, or of other forms of refined carbohydrates, tends to produce caries, whereas dietary fluoride protects. Besides the carbohydrate content of the diet its consistency (stickiness) is an important cariogenic factor, as also is the habit of eating at too frequent intervals. G. N. Jenkins, of Newcastle upon Tyne, discusses "Fluoride," with the citation of about 200 references. He endorses the fluoridation of water supplies as a public health measure. In wishing success to this series, which deserves inclusion in all libraries concerned with medicine, nutrition, or food processing, we may hope for a return of the photographic illustrations which are an attractive feature in some of the earlier volumes.

T. MOORE.

Books Received

Review is not precluded by notice here of books recently received.

Play and the Sick Child. By Eva Noble. (Pp. 165; illustrated. 22s. 6d.) London: Faber & Faber. 1967.

Planning Guide for Radiologic Installations. 2nd. edition. Edited by Wendell G. Scott. (Pp. 297+xiv; illustrated. 76s.) Edinburgh and London: E. & S. Livingstone. 1967.

Gruppenpsychotherapie in Klinik und Praxis. Edited by Dr. Kurt Höck. (Pp. 224. £1 7s. 7d.) Jena: Gustav Fischer. 1967.

Die Klinische Anwendung der Strahlen in der Heilkunde. By Professor Ivan Kövesligethy. (Pp. 168; illustrated. 180 Austrian marks.) Vienna: Wilhelm Maudrich. 1967.

Lehbuch der Gerichtlichen Medizin. Für Mediziner und Juristen. Edited by Professor Albert Ponsold. (Pp. 645+xii; illustrated. D.M.89.) Stuttgart: Georg Thieme. 1967.

Lehrbuch der Tropenkrankheiten. Edited by Professor E. G. Nauck. (Pp. 471+xi; illustrated. D.M.69.) Stuttgart: Georg Thieme. 1967.

Nierenkrankheiten. By Dr. Hans Sarre. (Pp. 551+xv; illustrated. DM.90.) Stuttgart: Georg Thieme. 1967.

Advances in Ophthalmology. Vol. 18. Edited by M. J. Roper-Hall, H. Sautter, and E. B. Streiff. (Pp. 248; illustrated. sFr./DM.68.) New York and Basel: S. Karger. 1967.

The Predicament of the Family. A Psycho-Analytical Symposium. Edited by Peter Lomas. (Pp. 219. 36s.) London: Hogarth Press. 1967.

Handbook of Paediatrics. 7th edition. By Henry K. Silver, M.D., C. Henry Kempe, M. D., and Henry B. Bruyn, M.D. (Pp. 648. 42s.) Oxford: Blackwell. 1967.

Sans Everything. A Case to Answer. Presented by Barbara Robb on behalf of AEGIS. Pp. 148+xvi. 18s.) London: Thomas Nelson. 1967.

Lyle and Jackson's. Practical Orthoptics in the Treatment of Squint. (And Other Anomalies of Binocular Vision). 5th edition. By T. Keith Lyle and Kenneth C. Wybar. (Pp. 636+xvi; illustrated. £6 6s.) London: H. K. Lewis. 1967.

The Feminine Mind and Body. The Psychosexual and Psychosomatic Reactions of Women. By J. Dudley Chapman, D.O. (Pp. 325. 60s.) London: Vision Press. 1967.

Documentary History of Psychiatry. A Source Book on Historical Principles. By Charles E. Goshen, M.D. (Pp. 904+x. 84s.) London: Vision Press. 1967.

A Manual of Closed Reduction of Closed Fractures and Dislocations. By Robert Mazet, jun., M.D. (Pp. 131+ix; illustrated. $10.50.) Springfield, Illinois: Charles C. Thomas. 1967.

Introduction to Scientific Psychiatry. A Behavioristic Approach to Diagnosis and Treatment. By H. A. Storrow, M.D. (Pp. 256+xvii. $6.95.) New York: Appleton-Century-Crofts. 1967.

Middle Articles

British Medical Association

Annual Scientific Meeting, Bristol, 10-14 July

The Association's 135th Annual Meeting was held in Bristol from 6 to 14 July. The Annual Scientific Meeting was held in the University Students' Union building from 10 to 14 July. The programme comprised symposia on the Management of Breast Carcinoma, Prescribing and Adverse Reactions to Drugs, Problems of Accident and Emergency Services, Diarrhoea, and Cardiac Emergencies; Modern Trends lectures on Shoulder Pain, Resuscitation in the Newborn, Diabetes—the Present Situation, Cytotoxic Drugs in the Treatment of Malignant Disease, the Natural History of Enuresis, Urinary Incontinence in the Aged, and Rheumatoid Arthritis—Conservative and Surgical Management; Panel Discussions on Vocational Training for General Practice, Bereavement, the Place of Surgery in Acquired Cardiac Disease, Headache, On Withholding Antibiotics, and Maternity Service; and Plenary Sessions on Diagnostic Pitfalls in General Practice—the Abdomen, and Recreation. In addition there was a programme of medical films, and the customary Scientific Exhibition and the Annual Exhibition of Pharmaceutical Products, Instruments, Appliances and Medical Publications were all held in the same building. A report of the scientific sessions is given below and will be concluded next week.

Management of Breast Carcinoma

Monday, 10 July

The symposium on the management of carcinoma of the breast, with Professor Sir HEDLEY ATKINS (P.R.C.S.) in the chair, was opened by Sir STANFORD CADE (Westminster Hospital, London), who discussed the relative value of different forms of treatment. Sir Stanford emphasized that choice of management should depend on clinical and pathological assessment rather than on the philosophy of the clinician. When assessing five-year survival rates it should be remembered that the average survival without treatment at all was three years and eight months. The response to treatment depended on the biological type of the tumour, which could be graded histologically. The stage at which the cancer was seen was not an indication of its malignancy. Reviewing the 4,000 cases of breast cancer he had seen in the last half-century, Sir Stanford had concluded that surgery was the most effective form of treatment and had applications in each stage. However, of 20,000 patients dying annually of breast cancer only 6,000 could benefit from surgery, whereas three times as many could benefit from radiotherapy. Furthermore, the results of radiotherapy were still improving, whereas those of surgery were not. Hormone therapy had been shown to control breast cancer, and ablation of endocrine glands often gave longer remissions than administration of hormones; but this was unpredictable. Chemotherapy was the treatment of last resort. It had never cured patients with this condition, and the least toxic agents were the least effective. The use of 5-fluorouracil intra-arterially was perhaps the most promising method.

Radiotherapy

Professor Sir BRIAN WINDEYER (Middlesex Hospital) presented the radiotherapist's point of view. There were now many radiotherapeutic techniques available for the many presentations and situations arising in breast carcinoma. Results of five-year and 20-year survival studies, respectively 12% and 6% in 1934–5, had improved to 31% and 16% in 1950–4, and to 34% five-year survival in 1955–8. These figures reflected increasing clinical skill and experience and technical advances, but still did not draw attention to the social importance of improved palliative treatment. In outlining his current policy for each stage, Sir Brian emphasized that postoperative radiotherapy had not improved the results of radical mastectomy in stage 1 carcinoma. However, radiotherapy was applicable if examination of the internal mammary or apical axillary lymph glands showed tumour cells.

In stage 2 cases the ideal plan was to take a biopsy of the internal mammary glands in the upper two intercostal spaces before deciding between surgery and radiotherapy. It was usual to give radiotherapy prior to biopsy. This did not affect the histological appearances, but there was no evidence to show that the chances of dissemination were reduced. Finally, radiotherapy was the sheet anchor of treatment for individual metastases.

Hypophysectomy

Mr. J. ANGELL JAMES (Bristol) discussed the role of hypophysectomy in the management of carcinoma of the breast. This operation had proved better in producing remissions than combined oophorectomy and adrenalectomy, probably because other active hormones such as growth hormone and prolactin were also removed. It was important to do the operation as soon as it was clear that other forms of treatment had not been successful, as the chances of success diminished as the patient's condition deteriorated. The best results had been obtained in patients aged between 60 and 70, with deposits in bone, skin, and lymph glands. Chest, brain, and liver metastases had proved less responsive. The transethmosphenoidal operation had the advantages of short operating time, good vision with an operating microscope, minimal pain, and rapid convalescence. It was contraindicated in the presence of nasal or sinus infection. Leakage of cerebrospinal fluid could now be prevented. Some degree of diabetes insipidus always occurred but was easily controlled, and a watch had to be kept for early signs of myxoedema. In a personal series of 326 cases Mr. Angell James reported an operative mortality of 1.3%. Only 7.2% had died in the first three weeks (5.9% died of advanced cancer), and remissions at one month had been 64%, at six months 29%, at 12 months 17%, and at five years 1%. Pain had usually been relieved in 24 hours, and many bedridden patients had been remobilized.

General Practitioner's View

Dr. I. R. MCWHINNEY (Stratford-on-Avon) gave the general practitioner's point of view. He emphasized the personal co-operation needed between surgeon, radiotherapist, and family doctor to obtain not only the best technical results but also the best emotional and social result for the individual patient. The tumour could be palpable before the patient noticed it, and practitioners should take every opportunity of examining breasts. Patients sometimes concealed their tumours for months. When a breast lump was found, Dr. McWhinney's practice was to explain the likely diagnosis and treatment to the patient without evasion, and to obtain surgical consultation as soon as possible to relieve anxiety as much as to arrest the tumour. Later he made sure that the best prosthesis was offered to the patient if mastectomy was performed. Dr. McWhinney was opposed to automatic long-term follow-up in uncomplicated patients except for definite research purposes, and felt that regular careful examination and attention to complaints by the general practitioner gave better clinical and social results than intermittent follow-up by a series of doctors at the surgical clinic.

This last point excited considerable discussion. Sir HEDLEY ATKINS thought that it should not be left to the patient to report merely when she had new symptoms, and that, for example, any pain in the back should be treated as metastatic irrespective of the radiological appearance of the spine. Sir BRIAN WINDEYER said that asking specific questions would elicit evidence of metastasis earlier.

Shoulder Pain

The modern trends lecture on "Shoulder Pain," under the chairmanship of Dr. F. S. COOKSEY (King's College Hospital, London), was devoted to both medical and surgical aspects of the problem. Speaking from the physician's viewpoint, Dr. FRANCIS T. PAGE (Bristol) emphasized the importance of differentiating shoulder pain of local musculoskeletal origin, which was aggravated by movement, from that due to brachial neuritis, which was usually unaffected by movement of the shoulder. Although brachial neuritis due to disc lesions or cervical spondylitis was the commonest "medical" cause of shoulder pain, the presence of radiographic abnormalities in the cervical spine did not necessarily mean that these were responsible for the patient's symptoms. Other criteria were therefore required. Neuritic pain was likely to radiate down the arm, was often sharply worse on coughing, sneezing, and straining, and could be brought on by downwards pressure of the head towards the affected side. There was a tendency for brachial neuritis to settle down spontaneously, and it was best treated by analgesics, a simple collar, and a sling to take the weight of the arm off the shoulder. Physiotherapy was not indicated.

Shoulder Girdle Syndrome

Turning to other nonsurgical causes of shoulder pain, Dr. Page described the shoulder girdle syndrome (myalgic amyotrophy), thought to be due to a neurotropic virus infection, and frozen shoulder, which was common after injury and in those confined to bed. Sometimes frozen shoulder had no apparent cause, but most resolved slowly. Physiotherapy had little place in treatment, since manipulation could be harmful, and less strenuous measures did little good. Polymyalgia rheumatica, malignant disease, the carpal tunnel syndrome, angina, and myocardial infarction were further possible causes of pain in the shoulder region.

Degenerative Lesions

Mr. A. L. EYRE-BROOK (Bristol) described traumatic and degenerative lesions of the shoulder joint and outlined the indications for surgical treatment. Rupture of the rotator cuff—a common cause of shoulder pain—could be either traumatic or pathological in origin. The former was curable by operation, but pathological rupture was due to degenerative changes and was not usually amenable to surgery. Degenerative lesions of the shoulder joint were sometimes associated with calcification, which in the case of "Codman's shoulder" extended through the rotator cuff and ruptured into the subdeltoid bursa. These calcified lesions limited movement and required surgical removal.

Frozen shoulder could be associated with changes in the rotator cuff, said Mr. Eyre-Brook, who then outlined the characteristic features—progressively restricted movement, and pain both in the joint and over the deltoid insertion. The patient experienced pain when he lowered the arm, but this did not occur when the doctor lowered it passively. Suspected rupture of the rotator cuff could be confirmed by intra-articular injection of radio-opaque dye, which would escape through the rupture when the joint was manipulated. Mr. Eyre-Brook concluded by describing some other surgical causes of shoulder pain. These included posterior dislocation, which sometimes occurred during fits and was easily missed, osteoarthritis of the acromio-clavicular joint, neoplasms, haemoglobinopathies, and caisson disease.

In the discussion Dr. G. D. KERSLEY (Bath) was in favour of manipulation of the neck for cervical spondylitis in the treatment of brachial neuritis, and other speakers also supported active measures in the treatment of this condition and frozen shoulder.

Resuscitation in the Newborn

Opening a modern trends discussion on resuscitation in the newborn, with Professor N. R. BUTLER (Bristol) in the chair, Dr. G. JACKSON REES (Liverpool) explained how advances in knowledge of the respiratory physiology had led to the development of scientific methods of resuscitation for infants born in apnoea. Early in intrauterine life rhythmic respiratory movements occurred. Later they stopped until a stimulus, such as cold cutaneous stimulation or clamping of the umbilical cord, reactivated them. At birth the newborn baby had to adapt its respiratory and cardiovascular physiology to extra-uterine life within a matter of minutes. If the infant failed to breathe within four minutes of birth brain damage would occur.

In resuscitation it was essential to maintain an effective circulation as well as to induce respiratory movements. Studies on asphyxiated newborn monkeys had shown that acidosis inhibited rhythmic respiratory activity. Resuscitation should be started as soon as possible if the infant did not breathe, as asphyxia led to a rise in the levels of lactic and pyruvic acids, which in turn further depressed respiration. Brain damage was less likely to occur in the asphyxiated newborn infant if the acidosis was treated with an alkali and fructose or glucose, which should be given in addition to ventilation with oxygen and external cardiac massage. Cooling the infant did not increase its chance of survival, and respiratory stimulants were usually useless. Dr. Rees said that he had found artificial ventilation by intermittent positive pressure to be more effective in resuscitating the newborn than the use of hyperbaric oxygen.

Role of Acidosis

Dr. BERYL D. CORNER (Bristol) said that of 11,000 deliveries in Bristol only 4% of the newborn infants had needed active resuscitation. The incidence of neonatal asphyxia was much greater in premature infants (13.6%). Permanent brain damage, with lesions in the brain stem and thalamus, could occur in newborn animals if asphyxia lasted for more than seven minutes. Intraventricular and subdural haemorrhage and thrombosis were frequently seen in asphyxiated premature infants, owing to changes in cerebral blood flow. Acidosis, due to a rise in the levels of pyruvic and lactic acids and in Pco_2, damaged cell membranes. This damage impaired the action of the "sodium pump" and led to retention of sodium and the escape of potassium, so producing oedema of the brain cells.

The acidosis could be treated by infusing 5% sodium bicarbonate solution and 20% fructose solution into the umbilical vein. Dr. Corner confirmed the observation of Dr. Rees that cooling increased the oxygen requirements of newborn infants, whose reaction to environmental temperatures differed from that of adults.

Long-term Follow-up

A long-term follow-up of infants severely asphyxiated at birth showed that brain damage was seldom permanent if active treatment in the form of intermittent positive-pressure respiration and alkali-fructose infusions were given. Of 88 asphyxiated infants followed up over a period of six years only two had developed severe abnormalities. One child had a left spastic hemiplegia and was prone to fits, another was severely deaf, and three had speech defects. Electroencephalography had shown normal patterns in 35 out of 38 children tested.

In reply to a question by Professor BUTLER Dr. REES said that in domiciliary practice resuscitation could be carried out by mouth-to-nose ventilation. Dr. CORNER pointed out that this introduced the risk of infection and pneumothorax. Asked by Dr. G. M. J. SLOT (London) whether midwives should be taught to intubate newborn infants, Dr. CORNER considered this unnecessary, as in domiciliary work asphyxiated babies were rare. Dr. REES doubted whether holding newborn babies up by their feet was of any value in resuscitation.

Prescribing and Adverse Reactions to Drugs

Tuesday, 11 July

The symposium on "Prescribing and Adverse Reactions to Drugs," under the chairmanship of Professor D. R. LAURENCE (University College Hospital), opened with a survey of the work of the Adverse Reactions Subcommittee of the Dunlop Committee, given by its chairman, Professor L. J. WITTS (Oxford). Professor Witts said that his subcommittee's duty was to maintain surveillance over the adverse reactions of drugs already on the market. For this purpose early warning (yellow) cards had been issued for the reporting of all adverse reactions to newly introduced drugs and new or severe reactions to those already established. Over half the yellow cards received came from general practitioners and just over a quarter from hospitals. Information about side-effects was also obtained from death certificates, letters, and published work. Despite this many adverse reactions still went unreported, and in particular there was a tendency not to report reactions familiar to the doctor. Where a patient received several drugs concurrently or had several types of reaction it was important to report all of these, and the system used could record up to five different drugs and five adverse reactions for each patient. About 10% of patients were followed up by personal visits, which had confirmed the reliability of the reports received.

Professor Witts went on to emphasize that the Adverse Reactions Subcommittee intended to use the reports received—and the results of research work in collaboration with other bodies—as more than a statistical repository by feeding back information to prescribers. He concluded by repeating that there were difficulties in precisely defining adverse reactions, and there was still a need for more yellow cards to be sent in.

MacGregor Classification

Developing the theme that responsibility for prescribing rested with the prescriber, Professor A. G. MACGREGOR (University of Aberdeen) said that the empirical approach had done little harm in the past, when most medications had been ineffective and relatively innocuous. With more effective modern drugs there was a need for more precise evaluation, and this was emphasized by estimates that between 10% and 15% of bed occupancy was accounted for by iatrogenic disease. Professor MacGregor continued by outlining the categories of the MacGregor classification, which was designed to help prescribers recognize preparations which were the subject of monographs in the *B.P.*, *B.P.C.*, or *B.N.F.* (category M) or were acceptable alternatives or combinations of drugs (category A). Drugs assigned to category B were considered less effective or more toxic than those in the other categories, or their efficacy was unproved. Some drug combinations were also considered inappropriate. Evaluation of the action of drugs and their side-effects was hindered by several factors, among them the discrepancy (20% in studies from Belfast and Aberdeen) between what the doctor prescribed and what the patient actually took. Concluding, Professor MacGregor stressed the importance of supplying prescribers with adequate information on which to base their decisions.

Teaching Students

Dr. J. E. CATES (Bristol) said that students now learned about existing knowledge of drug side-effects before they began their clinical training. It was important for consultants to build on this theoretical knowledge by teaching on patients in whom ill effects had actually developed, so that students would learn at first hand about the management of the problems created. When patients developed a complication, however minor, the consultant should first check the prescription card for possible causes of the upset. Students should be taught always to warn patients of the possible ill effects of drug treatment. By seeing or taking part in clinical trials students could see something of statistical methods and the placebo effect, as well as adverse reactions. From adverse reactions Dr. Cates turned to the basic principle of treatment—making a diagnosis before prescribing. After qualification doctors were submitted to the "anti-education" of advertisements, which often suggested that this or that drug was effective treatment for hypertension, anxiety, or even tiredness. It was necessary for doctors to be made proof against this.

Difficulties in Assessing Ill Effects

Making the final contribution to the symposium, Dr. M. J. LINNETT (London) described the uncertainties of drug administration, the unreliability of patients' evidence, and the resultant difficulty in assessing side-effects. There was often a contrast between theory and practice—books listed adverse reactions of drugs, but clinicians found the same substances effective and relatively free of ill effects. It was inevitable that new drugs carried some risk, but this could be limited if adequate information was readily available to the prescriber. Dr. Linnett listed suitable sources of information, among them the *B.N.F.*, journals, consultant advice, and drug-house literature, the latter being often surprisingly objective but needing a critical eye for evaluation of the evidence. The *Drug and Therapeutics Bulletin* (Consumers' Association), *Prescriber's Journal*, and the new *Proplist* published by the MacGregor Committee, were other valuable sources. In the future the early warnings sent out by the Dunlop Committee might usefully be expanded into a regular publication on drug side-effects and their frequency. In conclusion, Dr. Linnett made suggestions for safer prescribing. Doctors should use drugs with which they were familiar, find out if the patient had ever shown any drug sensitivity, inform him of the treatment being given and warn him of possible side-effects, and give notice of any that occurred on the Dunlop Committee's yellow cards.

Discussion

Subsequent discussion centred on the responsibility of consultants to ensure that all adverse reactions were reported, on the need for a wider distribution of yellow cards outside the N.H.S.—Professor WITTS said that this had already been arranged—and on means for doctors to find out rapidly whether a patient was already known to be sensitive to a particular drug. Professor MACGREGOR foresaw the time when doctors would be able to get information rapidly from computerized record-linkage systems. Referring to drug trials, Professor WITTS said that anything which purported to be done by human judgement or intuition could be done more efficiently by computer.

The President, Professor Hamid Ali M. Khan, Mr. Robert G. Cooke, Member of Parliament for West Bristol, and Mrs. Cooke at opening of the Scientific Exhibition.

Problems of Accident and Emergency Services

Mr. Norman Capener (Exeter) introduced the symposium on the problems of the accident and emergency services, which were now having to deal with a quarter of a million accidents each year. The total was rising, so it was vital that the services were efficiently organized and that proper rehabilitation was available for the injured.

Mr. H. Osmond-Clarke (London) said that accidents were now third on the list of causes of death in Britain. Last year 17,700 people had died in England and Wales as a result of accidents, and nearly half of these deaths had occurred on the roads. He outlined an organization of services which would include teaching hospitals and specially designed hospitals closely linked with general practitioners. Dr. R. M. McGregor (Hawick) presented his experience of accidents, and analysed the types of accident seen in 2,933 patients in his practice in the last 18 years. Most had been simple, and with beds available in a local hospital not more than 3% of patients had had to be transferred. The type and incidence of accidents varied with age and sex—for example, elderly female patients were more likely to have accidents than were elderly men, though the reverse of this situation was seen in young people.

Some patients were more prone to accidents than others. Important causes of accidents appeared to be overcrowding, lack of parental care in the young, and physical disability at all ages. It was important to investigate the causes of accidents in the home just as much as the cause of accidents on roads.

Rescue Equipment

Some of the appalling accidents on the roads which had occurred in his practice were described by Dr. K. C. Easton (Richmond, Yorks), and he underlined the need for proper provision of equipment to deal with rescue work. Road recovery vehicles with equipment that could free the trapped occupants of vehicles were essential. It was estimated that a quarter of patients involved in road accidents died on their way to hospital. Many lives could be saved if laryngoscopes, airways, and oxygen were available.

Dr. P. J. Roylance (Kingswood, Surrey) emphasized the need for maintenance of the airway by putting the patient on one side with the head down to avoid regurgitation of fluid into the lungs. Many of the patients dying soon after an accident did so from respiratory obstruction and aspiration pneumonia. Essentials such as the control of haemorrhage and the care of the unconscious patient needed to be stressed in the teaching of first-aid.

Mr. L. W. Plewes (Dunstable) showed how many specialist services were required in a modern accident service. To function efficiently these services must not be overburdened by trivia. General practitioners must be encouraged to form part of this service. Mr. H. H. Langston (Winchester) suggested that small inefficient local casualty departments should be closed, because there was not enough junior staff available. Effective consultant supervision was necessary to attract junior staff. Consultant supervision could reduce the burden on these centres by decreasing the number of patients needing repeated attendances or follow-up.

Accidents in Industry

Dr. R. A. Trevethick (Sheffield) said that little was known of the size of the accident problem in industry. Each year 700 people were killed as a result of industrial accidents, yet detailed figures were scarce. For some industries, such as trawler-fishing, no information was available. The figures derived from hospital statistics were misleading. In his own experience lacerations and burns formed the majority of industrial injuries. With adequate care 97% of injured workers were able to return to work within a week. A good standard of care was easy for large firms but very much more difficult for small firms, who would have to be encouraged to share services. He was disturbed at the inadequate planning for services to deal with industrial catastrophes in some areas.

Head Injuries

Mr. Walpole S. Lewin (Cambridge) discussed the problem of head injury. A quarter of a million head injuries occurred each year, of which over 10,000 required admission to hospital. Proper management included a careful assessment of the patient's level of consciousness, the condition of the pupils, the presence or absence of paralysis, and the state of the reflexes. Failure to show steady recovery in these signs must alert practitioners to possible complications. In addition to what had been said about the maintenance of the airway he would add that patients should not be warmed, they should not be given fluids, and should not have drugs—particularly analgesics. Even with the best management some 400 patients each year were unconscious for a month or longer, and this imposed a heavy burden on the medical and nursing staff. Rehabilitation units should not be asked too soon to take patients who had serious head injuries, because some would not benefit. To be suitable, patients need to be physically fit and to have regained their memory. Rehabilitation when used correctly could get some 80% of these patients back to their normal work.

Diabetes—the Present Situation

Current knowledge of diabetes was discussed in the modern trends series, with Dr. C. T. Andrews (Royal Cornwall Hospital) in the chair.

Professor J. Vallance-Owen (Belfast) described his work on plasma synalbumin insulin antagonists using the isolated rat diaphragm as a biological system. Initially he had found such antagonists to be present in plasma from uncontrolled insulin-dependent diabetics but not in that from obese or controlled insulin-dependent diabetics. However, on dilution of the albumin fraction antagonists had become detectable both in obese diabetics and pre-symptomatic (chemical) diabetics but not in normal people or patients with pancreatic diabetes.

Genetic studies had shown the synalbumin antagonist to be inherited as an autosomal dominant. Professor Vallance-Owen believed that patients who became diabetic were in hyperdynamic equilibrium with regard to insulin and synalbumin antagonists from birth, and he reported some studies on cord blood which supported this. He had also found evidence to suggest that ischaemic heart disease was in some cases genetically related to the presence of synalbumin antagonists.

Genetic Factors

Dr. D. L. Crombie (Birmingham) outlined a dynamic model of diabetes derived from studies carried out by a working party of the Royal College of General Practitioners. He thought that hyperglycaemic factors pressed insulin production beyond its limit and led to destruction of islet cells. In established diabetes an episode of hyperglycaemic stress frequently led to additional insulin requirements afterwards. Dr. Crombie regarded genetic factors as important only in patients who developed diabetes under the age of 30. In this group siblings were found already to have diabetes at the time of onset 26 times as often as in normal people, whereas the ratio was only 6 in the age group 30–49, and 1.5 over 70 years. Finally Dr. Crombie drew attention to the infinite variety and reversibility of the biochemical components of the disease, in contrast with the pathological complications such as retinopathy, nephropathy, and often neuropathy, which were progressive and irreversible. He put forward as a speculation the possibility that such complications were all secondary to the vascular effects of autonomic neuropathy.

Management

Dr. J. D. N. Nabarro (Middlesex Hospital, London) summarized the management of diabetes, emphasizing that in the absence of cure doctors must aim to relieve symptoms, maintain as normal a life as possible for the patient, and prevent complications, even though it was not known why these developed. Management was of paramount importance—physiological levels of blood sugar could be maintained by diet alone in 50% of the 2,000 patients he looked after. Where this was unsuccessful a further 15% could be controlled by diet plus tablets, and 35% needed insulin.

Dr. Nabarro then discussed oral hypoglycaemic drugs. The sulphonylureas stimulated the pancreas to produce more insulin. Tolbutamide was gentle and short-acting; chlorpropamide was the most powerful and could produce prolonged hypoglycaemia; glymidine, acetohexamide, and tolazamide were intermediate in potency and of little extra practical value. These drugs were remarkably free from side-effects, but dietary control was important, as patients often gained weight. Additional stress could render the drugs ineffective, and resistance could develop. However, a few months' control on insulin often made it possible to use drugs again. The diguanides (phenformin and metformin) apparently interfered with glucose utilization, so more glucose was used and the blood sugar fell. However, they had undesirable side-effects, and the theoretical loss of weight was seen in only 25% of cases. Nevertheless, combined therapy with chlorpropamide and phenformin had proved useful.

Insulins

Dr. Nabarro next gave an account of insulins. Antibody production was less with pork insulin than beef insulin. The proportions of these varied in different preparations. Dr. Nabarro said he had not been impressed with newer neutral-buffered or delayed-action insulins. Finally he referred to work suggesting that the mitotic rate in the pancreatic islets was increased by the administration of sulphonylureas. As a practical application of this work patients with pre-symptomatic diabetes had been treated with sulphonylureas. Their glucose-tolerance curves had been found to have become normal when repeated after a year. Further evidence supporting these findings might make the search for latent diabetics of great prophylactic value, Dr. Nabarro concluded.

Diagnostic Pitfalls in General Practice—the Abdomen

Opening a plenary session on diagnostic pitfalls in general practice, with special reference to the abdomen, the chairman, Sir JOHN BRUCE (Edinburgh), said that reputations could be made or marred by the diagnosis and treatment of abdominal disease. The first speaker, Dr. RONALD GIBSON (Winchester), pointed out the pitfalls that beset the general practitioner faced with a patient with abdominal symptoms. The first was to pay more regard to the textbook than to clinical acumen. The major pitfall, from which others stemmed, was failure to do a complete examination and to concentrate solely on the abdomen, assuming that the cause of the symptoms would inevitably be found there. This, said Dr. Gibson, was not only fallacious but dangerous. A history of the illness, a full physical examination, and the use of ancillary diagnostic services were essential for correct diagnosis. A second pitfall following an incomplete examination was that the patient might be sent to the wrong type of consultant for a second opinion. This was not a minor pitfall, as the patient might be operated on when he really had a condition —such as a basal pneumonia—that needed medical treatment. Dr. Gibson listed a number of conditions that might present with abdominal symptoms, including tabes, porphyria, lead poisoning, hypercalcaemia, sickle-cell anaemia, myocardial infarction, torsion of the testicle, and glandular fever.

Surgical Pitfalls

Speaking as a surgeon, Mr. R. V. COOKE (Bristol) stressed the paramount importance of a good history in making a diagnosis. A provisional diagnosis could often be made from a good history and one characteristic sign. If the patient had violent abdominal pain the doctor should consider vascular accidents, such as a leaking abdominal aneurysm or mesenteric thrombosis and embolism, or perhaps acute pancreatitis. Acute pain arising from the gall bladder was always very severe and frequently prevented adequate examination. Pain that developed after food was not always due to disease of the stomach or duodenum; it could result from a colonic lesion.

There were 3,000 deaths annually in this country from acute small-bowel obstruction, said Mr. Cooke. He attributed this to the fact that frequently there were no important physical signs and not much pain, and so there was delayed diagnosis and treatment. Diarrhoea was a symptom that should never be ignored—it might be the first evidence of carcinoma of the colon. Each year 500 patients died in England and Wales as a result of acute appendicitis. Mr. Cooke considered that this mortality could be reduced by earlier diagnosis and earlier operation. Signs and symptoms of a ruptured spleen were often minimal, particularly in children, who often recovered from the initial pallor and shock quite quickly. Faced with a difficult abdominal emergency the general practitioner should call in a consultant for a domiciliary visit without delay.

In the Wrong Bed

Dr. J. M. NAISH (Bristol) spoke of his experiences as a hospital physician. Frequently the patient referred by the general practitioner found himself in the wrong bed. Suffering from a medical abdominal emergency, he might be sent into a surgical ward. In his experience 10% of so-called acute surgical conditions eventually turned out to be medical emergencies. Fortunately the modern surgeon was also medically orientated and was quick to distinguish the two. Dr. Naish listed a number of medical conditions that had been admitted first to the surgical wards of his hospital. Among the biochemical disorders that had been diagnosed initially as surgical conditions because of symptoms referrable to the abdomen were ketosis, uraemia, hyponatraemia, hypercalcaemia (occurring in hyperparathyroidism, thyrotoxicosis, sarcoidosis, and vitamin-D poisoning), porphyria, and multiple myeloma. Heart failure with liver congestion, coronary thrombosis, pneumonia, pleural effusion, and pulmonary infarction were medical conditions that might have abdominal symptoms and be referred to the surgeon. So might Bornholm disease, irritation of the spinal roots (for example, from osteoarthritis, collapsed vertebrae, and osteomyelitis), and diseases of the blood vessels such as purpura, sickle-cell crises, mesenteric angina, and polyarteritis nodosa.

Infancy and Childhood

The assessment of abdominal pain in infancy and childhood was discussed by Professor N. R. BUTLER (Bristol). He explained that the history was usually obtained secondhand through the mother and that adequate examination, particularly in the infant, was frequently difficult. Even obtaining a urine specimen might entail an "all-night sitting." The younger the child, the greater was the danger of perforation of an acute appendix or of gangrene from an intussusception—to which the key in diagnosis was palpation of the abdomen when the baby was feeding and relaxed. Professor Butler said that he had seen more cases of acute abdomen in two years of general practice than in 15 years as a paediatrician. The general practitioner had the advantage of knowing the family, which was a help in deciding if the pain was acute and if so how acute.

Recurrent abdominal pain was present in about 15% of Bristol children aged 7. Professor Butler said that as a result of a survey of Bristol children complaining of abdominal pain Dr. J. Apley had found

The President Elect, Mr. R. V. Cooke, opening the Scientific Exhibition.

organic causes in only 10%. It was the psyche that grumbled rather than the abdominal organs. More abdominal pain was engendered in children today by unsympathetic teachers and insecure parents than ever before. Many such children went on to develop the "periodic syndrome" and later on migraine.

Help from Radiology

Dr. T. LODGE (Sheffield) indicated how the radiologist might help the general practitioner to avoid diagnostic abdominal pitfalls. Radiology, however, did not give the final answer to diagnosis. The findings should be regarded by the general practitioner as no more than a facet of the problem, and considered in the light of his clinical examination and history. Indeed they could be definitely misleading unless they fitted into the clinical picture. On the other hand, "double pathology" might be revealed by the radiologist with the less serious condition providing the presenting symptoms. Dr. Lodge said that he observed many cases of hiatus hernia as incidental findings. In infancy it was of serious significance, but in adults it should be ignored if symptomless.

Recent surveys had shown a high incidence of organic disease in patients with "globus hystericus." Mental disturbances were not unusual in a number of gastrointestinal complaints. The site of abdominal pain in children was frequently misleading. The diagnosis of intussusception could be confirmed by straight radiography of the abdomen and by a barium enema, which under screen control could reduce an intussusception or make its final surgical reduction easier.

In the discussion that followed Dr. NAISH considered that the general practitioner should have access to diagnostic radiological services, but Mr. COOKE disagreed. Dr. NAISH said that it was harmful if not dangerous to do a laparotomy if the patient had a medical emergency such as a coronary thrombosis, pulmonary infarction, diabetic coma, acute porphyria, or hepatitis. Joining in the discussion, Mr. A. DICKSON WRIGHT (London) considered that every acute abdomen with severe pain was a surgical condition, but care should be taken not to do emergency operations on cases of renal colic or pancreatitis.

Vocational Training for General Practice

Wednesday, 12 July

With LORD COHEN OF BIRKENHEAD (Liverpool) in the chair, members of the panel made brief opening statements on "Vocational Training in General Practice." Lord Cohen said that although vocational training had been rejected when incorporated into B.M.A. reports of 20 years ago, it was now the theme of all curricular discussions. Dr. P. S. BYRNE (Milnthorpe) insisted that vocational training must be part of a flexible system, that there must be teachers, and that the new well-trained generalists must escape from the Cameron–Finlay myth. Professor R. SCOTT (Edinburgh) said a vocational training system had to be experimental, and that individual medical schools should get out into the community and use it as their laboratory. More had to be invested in testing methods of training. Dr. R. P. W. SHACKLETON (Southampton) suggested that the regions were the places for vocational training for both the general practitioner and the specialist. The task of postgraduate advisers was to introduce a new pattern of rotational hospital appointments suitable for both. Dr. G. SWIFT (Winchester) thought of the organization of vocational training as a problem for regional hospital boards and local medical committees to deal with together. He emphasized the need for trainees to have opportunities to see each other as well as other practices, and to observe the local authorities at work, and to maintain contact with the university.

Place for Obstetrics

After vigorous discussion on whether general practitioners would do obstetrics in the future and whether this should be a "must" for vocational training, LORD COHEN reminded the meeting that normal obstetrics and the recognition of emergencies was taught to the undergraduate, and this knowledge was available to be built on in the postgraduate period if necessary.

Dr. A. M. GOLDTHORPE (Saskatchewan) asked for what basic type of practice the vocational training was intended. Professor SCOTT thought that students were better trained than they were given credit for—perhaps too well for general practice in that they expected not to be in isolation, to have facilities for investigation and treatment, and to be in direct relationship with the hospital and community centres. Dr. GOLDTHORPE replied that it was not attractive to young men to be trained in hospitals and then excluded from them. In Canada the general practitioner was observed for a year and then allotted duties in the hospital in accordance with his abilities, so that 85% of total medical care was carried out by general practitioners.

Use of Examinations

Asked whether a qualifying examination was of any value at all, Dr. BYRNE said that in spite of 104 diplomas already in existence the Royal College of General Practitioners intended to introduce another. He hoped that it would have a high pass rate and be used not only to see that some teaching rubbed off on the students but as a test of that teaching. Dr. SWIFT said that his education had not taught him how to educate himself, and the qualifying examination should test this. Dr. SHACKLETON pointed out that Yale had no qualifying examination and that each student had his own tutor whose progress reports were used to assess him. The General Medical Council, under Lord Cohen, also thought continuing assessment as important as the examinations.

The role of local health departments in general-practitioner training was considered. Professor SCOTT thought they should be responsible for health centres and should investigate the questions of automation and the use and value of records. Dr. BYRNE wanted to compare health centre practice with good general practice. Ideally the health centre would be associated with a medical school. Dr. SWIFT suggested the one-week visit of trainees to the local health authority, as in Hampshire, was of great help in informing them of facilities and services that were available, but medical officers of health had to be forward-looking too.

Dr. BYRNE thought that general practitioners and practices for vocational training should be selected from applicants by an appointments committee as for any other teaching post. Professor SCOTT tried to select doctors who could stand criticism by both students and patients in the teaching situation. Dr. SWIFT had concluded from trainee courses he had run that many practitioners were natural teachers, while Dr. SHACKLETON emphasized the value of the postgraduate medical centres as meeting-places of the whole profession in recognizing suitable teachers informally.

LORD COHEN concluded that medical education was always striving for an ideal goal which would never be reached. So far the General Medical Council had been able only to observe the new experiments—if it were ever able to initiate them vocational training in general practice would be the first field it would tackle.

Bereavement

Opening the panel discussion on bereavement, the chairman, Professor D. RUSSELL DAVIS (Bristol), said that it was the duty of family doctors to care for the rest of the family as well as the dying patient. Both speakers at the discussion had made systematic inquiries on bereavement—a field previously explored only by writers, poets, and dramatists.

The first speaker, Dr. C. MURRAY PARKES (Tavistock Institute of Human Relations), described studies of bereaved people in London, and said that only one-third of London widows had any contact with a clergyman apart from the funeral service, whereas three-quarters consulted a general practitioner during the six months following bereavement. The number of consultations showed a sharp increase following bereavement, the reasons for seeking advice being different at different ages. Young widows—those under 65—suffered mainly from psychological difficulties, and their consumption of sedatives increased sevenfold during the 18 months immediately after their husbands' deaths. In the older age group, on the other hand, physical symptoms accounted for most of the increase in consultations and there was little change in sedative consumption. The mortality rate of widowers over 65 increased sharply in the six months after bereavement, and studies had shown a 50% increase in deaths from coronary disease compared with the expected rate for married men of the same age. The old idea of dying of a broken heart seemed not to be far wrong.

Dr. Murray Parkes went on to describe the phases characteristic of grief and mourning, during which the widow was initially shocked or numbed, and then suffered from pangs of intense pining. In the final stage there was revival and a gradual return to normal life. There were wide variations in this pattern, and a typical form of grief had been seen in 21 bereaved patients admitted for psychiatric treatment. The reactions in these patients had been precipitated by such factors as overdependence on the dead person, hostility, isolation, and the actual mode of death. Bereaved people could be helped by support before and after the death of a relative and by lending a sympathetic ear. The doctor's task was to treat the whole patient, to allow a reasonable period of grief and mourning, and then to make it clear that there was a time to stop. It was not yet known whether antidepressives should be used or whether they merely postponed the period of grief. Cruse Clubs could help widows and had published two useful booklets.[1]

Ritual Mourning

Mr. GEOFFREY GORER (Haywards Heath, Sussex), author of *Death, Grief and Mourning in Contemporary Britain*, described his own inquiries as a social anthropologist into ritual and deritualized mourning. He pointed out that bereaved people no longer knew how they should behave unless they belonged to a religious group such as Orthodox Jews, members of the Church of Scotland, or Roman Catholics of Irish descent, who still practised ritual mourning. Following a period of grief and mourning bereaved people in these groups adapted well to their loss, and all the evidence—contrary to the speaker's own expectations and personal feelings—suggested that the process of burial of the corpse and ritual mourning was helpful, while cremation was more commonly associated with serious disturbances among the bereaved.

Mr. Gorer went on to say that mourning was deritualized for most people in England today; social disapproval stigmatized the grief-ridden as undesirable, so that they were socially ostracized until they bottled up their feelings, and even outward signs of mourning were not favoured socially. In interviewing bereaved people he had found that they welcomed the opportunity to talk about feelings which had previously been repressed. "Satisfactory normal mourning" consisted of three stages. The first was a short period of shock, which lasted normally up to the burial. Next came a period of intense grief, its length determined by the individual's feelings, since there was now no commonly accepted religious prescription for this. Finally, there was a gradual return to normal life. Among bereaved people who failed to adapt satisfactorily some never entered the second stage because they denied their grief. This was particularly common among widows of professional men. Others never left the second stage, and these included working-class widows over 50, who said with some pride that they would never get over their loss.

Concluding, Mr. Gorer regretted that many doctors appeared to subscribe to the view that grief was morbid. In his opinion it was better to allow the manifestations of grief to work themselves out.

The discussion centred on whether dying patients should be told the prognosis—a proposition supported by Mr. Gorer but contested by several speakers from the floor.

---

[1] *Caring for the Widow and her Family* and *The Widow's Child*, obtainable from Cruse Club Headquarters, 6 Lion Gate Gardens, Richmond, Surrey.

Place of Surgery in Acquired Cardiac Disease

A panel discussion on the place of surgery in acquired cardiac disease was held under the chairmanship of Sir THOMAS HOLMES SELLORS (London). The indications for surgery in mitral stenosis were described by Professor J. F. GOODWIN (London). Valvotomy was required when increasing dyspnoea, haemoptysis, or bronchitis was associated with signs of tight mitral stenosis. Operation should be delayed in the absence of symptoms because of the possibility of restenosis, said Professor Goodwin, but if auricular fibrillation supervened the treatment required was anticoagulation, followed by valvotomy. Pregnant patients with acute symptoms due to mitral stenosis did well following valvotomy. If congestive cardiac failure developed early in the course of the disease this should arouse a suspicion of complications. Doctors should look for early clinical, radiographic, and electrocardiographic evidence of pulmonary hypertension, as valvotomy could reverse this complication if done early enough.

Factors which influenced the success of mitral valvotomy adversely included a rigid mitral valve, valve calcification, an enlarged heart, increasing age of the patient, the possibility of active carditis, and ischaemic heart disease. Patients aged over 50 years did well in the absence of these factors. Restenosis after valvotomy was a problem and seemed to occur less when a valve dilator was used. Professor Goodwin advocated long-term prophylactic sulphonamide therapy after valvotomy.

Professor Goodwin then discussed mitral incompetence. There was much less experience with valve replacement than with valvotomy, and it was still accompanied by a high risk. Patients with mitral incompetence tended to run a more rapid downhill course after the arrest of symptoms but probably had a better prognosis than had been previously thought. They were more prone to such complications as subacute bacterial endocarditis. Mitral regurgitation secondary to papillary necrosis after myocardial infarction was also amenable to surgery.

Aortic Valve Disease

Dr. D. W. BARRITT (Bristol) dealt with aortic valve replacement. The major symptoms of aortic valve disease were dyspnoea on exertion, paroxysmal nocturnal dyspnoea, orthopnoea, angina pectoris, and sudden loss of consciousness. Dr. Barritt reported on a series on 51 patients treated with aortic valve replacement using a Starr–Edwards prosthesis. Seventeen had died in hospital, four had died later as a result of intractable left ventricular failure, cerebral embolus, or myocardial infarction, and 30 patients were still alive. Whenever possible these patients were given anticoagulant therapy.

Mr. R. H. R. BELSEY (Bristol) agreed with Professor Goodwin on the importance of deciding the right time for valvotomy, especially as it had been suggested that the incidence of restenosis was as high as 10%. It was very important that unnecessary operations on unsuitable patients were avoided on the grounds of economics alone.

Mr. D. N. ROSS (London), discussing the selection of patients, suggested that more attention should be paid to the state of the myocardium and that methods should be developed to enable this to be done.

Discussion

The meeting was then thrown open to questions. Dr. D. A. GRIFFITHS (Bristol) asked to what extent multiple valve replacements were done. Mr. Ross said that the other valves were always explored at operation and all mechanical disabilities were dealt with. Mr. BELSEY said that valvuloplasty rather than replacement might sometimes be possible. Professor GOODWIN advocated the use of aortic valve homografts in multiple operations because of the rising risk of embolic complications after multiple prosthetic replacement. Mr. ROSS thought that homografts should be used for aortic valve replacement except when an aortic aneurysm was present, when a patient was very ill and operating time needed to be short, and in multiple valve replacement, where an aortic prosthesis did not add significantly to the risk from the mitral valve prosthesis.

Headache

A panel discussion on headache was chaired by Dr. A. M. G. CAMPBELL (Bristol). The opening speaker, Dr. MACDONALD CRITCHLEY (London), said that headache was probably the commonest symptom in medicine, but fortunately it was rarely due to neurological or cranial disorder. It could be the presenting symptom of many toxic, metabolic, infective, and psychiatric conditions, as well as the sequel of a hangover. It could be trivial and temporary or herald a cerebral catastrophe.

Headaches were caused by alterations in the calibre of the cerebral vessels. An intensive search was being made for metabolic substances capable of causing headache and also for their pharmacological antagonists. Some drugs with an antiserotonin action could relieve headache. Some people never experienced headache, and it might be rewarding to study them.

Headache provided a valuable exercise in differential diagnosis, said Dr. Critchley in conclusion. Careful questioning about frequency, nature, severity, and influencing factors was necessary to discover the cause.

Incidence

Dr. S. J. CARNE (London) described the incidence of headache as a prescribing symptom in 6,000 patients seen in a London general practice. The overall incidence had been 1 in 15 patients (6.6%). Headache was commonest between the ages of 5 and 44. Women suffered more than men and immigrant West Indians more than the native British population. Dr. Carne said that the vast majority of patients associated headaches with some visual defect, with a brain tumour, or with hypertension—though many cerebral tumours did not present with headache and hypertension was seldom a cause. True sinusitis was rarely responsible, though nasal obstruction due to allergy or catarrh might produce headache. Worry and anxiety were potent causes. It was essential in all cases for the practitioner to make a complete examination and to reassure the patient if he found no obvious disease. An *x*-ray of the skull usually satisfied the chronic worrier that his headache had no cerebral cause. In Dr. Carne's experience the commonest causes of acute headache were infections, including influenza and tonsillitis, and in the summer excessive exposure to sun. Chronic headache was frequently associated with migraine, depression, and upper respiratory catarrh.

Psychogenic Headache

Dr. DAVID STAFFORD-CLARK (London) said that a headache was often the presenting symptom of depression and anxiety. The nature of the pain was different in the two conditions, that associated with anxiety being splitting or tearing in nature, while that accompanying depression was dull and like a tight band round the head. Mental tension, worry, and distress could be projected into the symptom of pain. Headache thought to be due to the post-concussion syndrome was experienced by some patients who in fact had never been concussed, but who were reacting to stress.

Ophthalmic Causes of Headache

Ophthalmic causes of headache were rare, said Mr. R. A. BURN (London). Of 1,018 cases referred to him for an ophthalmic opinion only 13% had had pain in the head or eyes, and 39% of these had been cases of anxiety without eye disease. Ocular conditions that cause headache or pain behind the eyes were mainly functional abnormalities of the ocular muscles, followed in frequency by corneal lesions, uveitis, and acute glaucoma. Headache might be due to the strain of accommodation in patients with hypermetropia and presbyopia, but not in those with myopia. In headache of ocular origin the pain was felt in and around the eye. Small children, young people facing the stresses of life for the first time, and older persons with diminished visual activity sometimes suffered from what might be termed "ocular anxiety." They experienced pain of ocular type, but no ophthalmic condition could be found to account for it.

In reply to a question Dr. CRITCHLEY said that hypertension aggravated migraine. Some patients with the condition suffered from cerebral anteriolar sclerosis later in life. He considered that cranial arteritis as a cause of headache was rare below the age of 65. Dr. Carne thought that true allergy was rarely a cause of headache.

Cytotoxic Drugs in the Treatment of Malignant Disease

Cytotoxic drugs in the treatment of malignant disease was the subject of a further "Modern Trends" meeting, with Professor A. G. RIDDELL (Bristol) in the chair.

Professor Riddell described the overall results of systemic chemotherapy as "pretty grim." Many patients responded badly, but very occasionally the outcome was more successful. Choriocarcinoma treated with methotrexate and nephoblastoma with actinomycin D were exceptions to the poor results. It was probably not a good idea to cover operations for cancer with prophylactic cytotoxic agents, because these drugs impaired the immunological mechanisms at a vital time. Professor Riddell reported the use of an immunological approach in conjunction with cytotoxic drugs. Five patients with advanced malignancy had been given 20 mg. of melphalan 10 hours before the intravenous injection of 4×24^9 suspended human spleen cells. These patients had shown a temporary response to treatment. In another patient the spleen had been removed, an extract of the tumour had been injected into a pig, and a suspension of cells from the pig's lymph glands returned to the patient. There had been a dramatic reduction in the site of the tumour. These were tentative steps towards a rational programme.

Choice of Drugs

Dr. J. INNES (Edinburgh) said that the beneficial effects of cytotoxic agents were almost entirely confined to mesodermal neoplasms. The alkylating agents were radiomimetic, and some were fairly specific—for example, busulphan in chronic myeloid leukaemia. The antimetabolites such as methotrexate and 6-mercaptopurine had been introduced as a result of study of the fundamental biochemistry of cells, and had an important place in childhood leukaemia. In a miscellaneous group were urethane, antibiotics, and the periwinkle alkaloids. Generalized therapy was indicated for generalized disease, but radiotherapy was to be preferred for localized lesions. No striking new drugs apart from vincristine and vinblastine had appeared since 1954. Such improvement in results as had been achieved was the result of many clinical trials and a joint therapeutic approach by physicians, surgeons, and radiotherapists.

Perfusion

Mr. C. I. COOLING (London) described the techniques of isolated limb perfusion and regional infusion. In the former the limb was connected to a heart–lung machine and the cytotoxic drug was added to the perfusion fluid in a dose limited only by the tolerance of skin, muscle, and nerve. A tourniquet prevented the drug from reaching the general circulation. Perhaps 10% of patients had good results, though pain was relieved more often. With regional infusion a high dose of drug (usually methotrexate) was given intra-arterially over a period of 7 to 14 days. A dye was used to show the area perfused, and an antidote given intramuscularly helped to lower the systemic level. Good results had been obtained in tumours of the head and neck and of limbs. Dr. Cooling hoped that further research might produce drugs tailor-made for particular tumours, which would improve the value of these useful palliative techniques.

Natural History of Enuresis

Introducing the speakers in the session on the natural history of enuresis, the Chairman, Dr. JOHN APLEY (Bristol), said that, though doctors knew what they meant by the term enuresis, it defied precise definition. With certain qualifications it could be defined as incontinence of urine without demonstrable cause at an age when control had normally been achieved. Enuresis was subdivided into diurnal and nocturnal, primary and secondary; the last having its onset after a period of full control.

Dr. J. W. B. DOUGLAS (M.R.C. Unit for the Study of Environmental Factors in Mental and Physical Illness) described the results of a prospective study of 5,000

The chairman and speakers at the Modern Trends Lecture on Cytotoxic Drugs in the Treatment of Malignant Disease. Left to right, Professor A. G. Riddell (chairman), Mr. C. I. Cooling, and Dr. James Innes.

children from birth to 15 years for investigation of the influence of factors during the first four years of life on the later development of enuresis. The overall incidence of enuresis at the age of 4½ was 13.6% in boys, and 10.6% in girls. Events such as infectious diseases, operations, burns or fractures, and separation from home and family all increased the prevalence of enuresis, so that the incidence in the group exposed to stress was 19%, while it was 7.6% among the remaining children. Stress in early childhood was clearly associated with enuresis later, even on the restricted recording of stressful events that had been possible in the survey.

Investigations

Speaking as a urologist, Mr. Ashton Miller (Bristol) discussed the examination and investigation of enuretic children and said that positive findings were rare. It was, however, important to spot children with underlying abnormalities and to exclude infection, which sometimes caused enuresis in girls. Cystoscopy had been done on a series of enuretic children, and Mr. Ashton Miller had found two types of bladder—each related to a different clinical picture. In children who were wet only at night the bladder had been normal, but in those with urgency and increased frequency of micturition by day as well the bladder had been smaller with a thicker, more muscular wall, and bladder neck hypertrophy. From these findings it had been possible to derive a plan for investigation of enuretic children. If the child was normal by day detailed investigation was unnecessary; if in the second group, and improving by day, it was reasonable to defer investigation as further improvement—first by day and later by night—was likely; but those who failed to improve by day (or even deteriorated) required full investigation.

Psychiatric Factors

Giving a psychiatrist's view of enuresis, Dr. Robert F. Barbour (Bristol) said that, while other body habits were allowed to develop naturally, toilet training was a "must," parental attitudes being typified by Wesley's saying, "Cleanliness is next to godliness." The first task of treatment was to relieve parental pressure on the child. Between the ages of 1 and 3 it was best to wait for spontaneous improvement (giving boys longer than girls), but between 3 and 5 years organic disease had to be excluded. Parents needed reassurance, and simple physiological methods of treatment were appropriate. These included restriction of fluids and waking the child an hour after going to sleep and an hour before the normal time of waking. Drug treatment and alarms could be used from the ages of 5 and 7 respectively.

Closing the meeting, Dr. Apley expressed the hope that Dr. Douglas's study on the effects of stress in early childhood might lead in the future to methods of preventing enuresis.

On Withholding Antibiotics

Thursday, 13 July

Professor C. Bruce Perry (Bristol) took the chair for the discussion on "Withholding Antibiotics."

Professor O. L. Wade (Belfast) had no doubt that the practice of medicine was becoming more difficult, particularly in the use of antibiotics. The organism had to be identified and therapy tailored to it with the help of a bacteriologist. It was becoming difficult to convince students that patients ever recovered from a fever without an antibiotic. Comparing patients with exacerbations of chronic bronchitis to whom antibiotics were given with those to whom they were not, he had found that the duration of the acute phase was not decreased. The mortality from chronic bronchitis had not improved in spite of the introduction of successive antibiotics. He now used them only when the sputum was really purulent, when there was a high fever, or when there was evidence of pulmonary consolidation.

General Practitioner's View

Dr. M. B. Lennard (Bristol) gave the view of the general practitioner who thought that antibiotics should not be withheld. Memories of acute osteomyelitis, mastoiditis, and fulminating pneumonia loomed larger to him than the risks of allergy or resistance. The age of the patient, his medical history (including response to antibiotics previously taken), local knowledge, and the known natural history of the infection were considered by the practitioner. Ultimately, the wisdom of the decision whether to use antibiotics was shown by the therapeutic response.

Antibiotics in Prophylaxis

Professor W. A. Gillespie (Bristol) discussed the use of prophylactic antibiotics. Many studies had shown these to be ineffective in surgical practice because the drugs were too selective, the tissues could be protected from one organism but invaded by another, and drug resistance could develop. However, in certain circumstances, such as dental operations in patients liable to subacute bacterial endocarditis, or patients at risk from clostridial infection after limb amputation, antibiotic cover was amply justified. Sometimes aseptic and antiseptic techniques had proved more effective than antibiotics—for example, in a nursery where babies were treated with hexachlorophene skin infections had been less frequent than when they were given erythromycin. The incidence of breast abscesses in the mother had also dropped on this regimen.

Mr. A. Dickson Wright (London) discussed the age-old propensity for man to dose himself with medicine. Nowadays the medicines tended to have pharmacological effects, and 30% of diseases were said to be iatrogenic.

In the ensuing discussion Professor Wade said he regarded mucolytic agents as unhelpful in chronic bronchitis. The general-practitioner view was that short courses of antibiotics did not mask serious infections, but Mr. J. Angell James (Bristol) thought that mastoiditis could be masked by inadequate treatment of otitis media until meningitis developed. Professor Gillespie reminded the audience that organisms were not killed all that quickly by antibiotics, and that in the Bristol area 60% of staphylococci outside the hospitals were resistant to penicillin.

Diarrhoea

A symposium on diarrhoea was chaired by Mr. W. M. Capper (Bristol). The clinical approach was discussed by Dr. A. E. A. Read (Bristol), who defined diarrhoea as too rapid an evacuation of too fluid stools; the actual number of stools passed daily was of no consequence. The important factors were the colour of the stools and the presence of blood or mucus. The causes of diarrhoea were numerous and included diseases of the large and small bowel as well as generalized conditions such as thyrotoxicosis. Antibiotics, malabsorption syndromes, alcohol, and infections were other possible causes. A careful personal, family, and social history was essential and a complete physical examination should be done in all cases. Rectal examination, tests for occult blood, urinalysis, sigmoidoscopy, and a barium meal should be included in every examination, with bacteriological investigation in times of epidemics. In hospital, tests for malabsorption and thyroid function, and arteriography to detect possible thrombosis and arteriosclerosis of vessels of the large intestine, might be necessary. Dr. Read mentioned the association between certain skin diseases and diarrhoea, and the possibility that virus diseases, small bowel stasis, and genetic disaccharidase deficiencies might be factors in causation.

Use of Radiology

Dr. J. W. Laws (London) explained that radiological investigation was of particular value in aiding the diagnosis of localized lesions in the colon, as in diverticulitis, ulcerative colitis, Crohn's disease, neoplastic disease, and the presence of anatomical abnormalities. Normally a barium enema was done first, and then a barium follow-through if indicated. It was advisable to examine the small bowel radiologically with the patient erect as well as supine, as fluid levels could then be discerned. Other small bowel lesions that could be visualized were stagnant loops, diverticula, strictures, abnormal mucosal patterns, fistulae, and dilatations. Radiology of the small intestine was useful in the diagnosis of conditions in which the mucosal pattern was abnormal, such as coeliac disease, steatorrhoea, Whipple's disease, defective disaccharide absorption, and other malabsorption syndromes.

Pathology of Colonic Disease causing Diarrhoea

The term ulcerative colitis was a misnomer, said Dr. B. C. Morson (London), as it was not primarily a disease of the colon, but rather of the rectum. The colon was shortened not by fibrosis but by thickening of the muscle, and as a result of sustained spasm and hypermotility it could not retain its contents adequately. The mucosal surface was granular, haemorrhagic, and packed with congestive blood vessels—like a hyperaemic burn of the skin treated with a faecal poultice. Later the mucosa became secondarily infected and infiltrated with round cells. Dr. Morson suggested that ulcerative colitis might be a hypersensitivity reaction, possibly to histamine.

Next he defined Crohn's disease as a granulomatous condition affecting any part of the gut from the stomach to the anus. The lesions, unlike those of ulcerative colitis, were discontinuous and were more frequent in the terminal ileum and anal region. They were transmural rather than submucosal and sarcoid foci were present in three-quarters of the cases. Bleeding was less frequent than in ulcerative colitis, which could be distinguished histologically in biopsy specimens. Turning to other causes of diarrhoea, Dr. Morson said that stricture of the splenic flexure occurred in elderly patients as a result of ischaemia of the local vessels. This caused abdominal pain, diarrhoea, and blood in the stools. Diverticulitis was not primarily inflammatory, but was caused mainly by segmental thickening of the circular muscle coat of the colon. Blocking of the diverticula caused stasis and secondary inflammation.

Malignancy in the Lower Bowel

Sir CLIFFORD NAUNTON MORGAN (London) said that the diagnosis of carcinoma of the lower bowel was frequently delayed for as long as six to twelve months because the symptoms were vague and often overlooked. Any change in bowel habit, the passage of blood or mucus per rectum, or the presence of abdominal tenderness in patients after the age of 50 should arouse suspicion. If seen early enough 95% of patients could be saved. Discussing the indications for operation in diverticulitis, Sir Clifford said that surgery should be considered if medical treatment failed, if bleeding was present, or if a mass could be felt. Diverticulitis could be premalignant. Patients suffering from ulcerative colitis for more than five years should be watched for the possible development of carcinoma. Papillomata of the rectum or colon should be removed, as they were also premalignant.

In the discussion that followed Dr. READ said that if unexplained diarrhoea was present for more than 10 days full clinical and laboratory investigations should be done. Sir CLIFFORD NAUNTON MORGAN considered that an exploratory operation should be done on all patients with unexplained rectal bleeding. He never used morphine or codeine for the relief of abdominal symptoms, as these drugs caused spasm of the smooth muscle of the bowel.

Cardiac Emergencies

A symposium on cardiac emergencies was held under the chairmanship of Dr. D. H. DAVIES (Bristol). Dr. D. G. FRENCH (Newcastle, Staffs) based his talk on a six-year experience in a practice of 6,000 patients. He told the meeting that he found an awareness of premonitory symptoms and electrocardiographic studies helped in the diagnosis of myocardial infarction. Among uncommon causes of heart failure he listed silent myocardial infarction, severe iron-deficiency anaemia, and atrial fibrillation secondary to occult thyrotoxicosis. Stokes–Adams attacks, paroxysmal tachycardia, and dissecting aneurysms were seen occasionally. More common was the occurrence of embolism and acute pulmonary oedema in patients with mitral stenosis; he emphasized the importance of the practitioner keeping in mind the patients with this condition, so that the emergencies might be anticipated.

Dr. D. G. JULIAN (Edinburgh) said that the acute myocardial infarction presented a complex of emergencies, of which ventricular fibrillation was the most important. It was best treated immediately with a difibrillator, but if this was impossible external cardiac massage and artificial respiration should be started. Ventricular fibrillation could be prevented by the prompt treatment of ventricular extrasystoles, and tachycardia with lignocaine and procaineamide. Asystole was a difficult form of cardiac arrest to treat, but intravenous isoprenaline might be helpful, or intracardiac pacemaking might be required. The management of shock in myocardial infarction remained a problem. The administration of oxygen and small doses of pressor amines was still the best treatment. At Edinburgh collection of patients with myocardial infarction in one unit with specially trained staff and specialist equipment had resulted in the saving of a fifth of the patients who might otherwise have died.

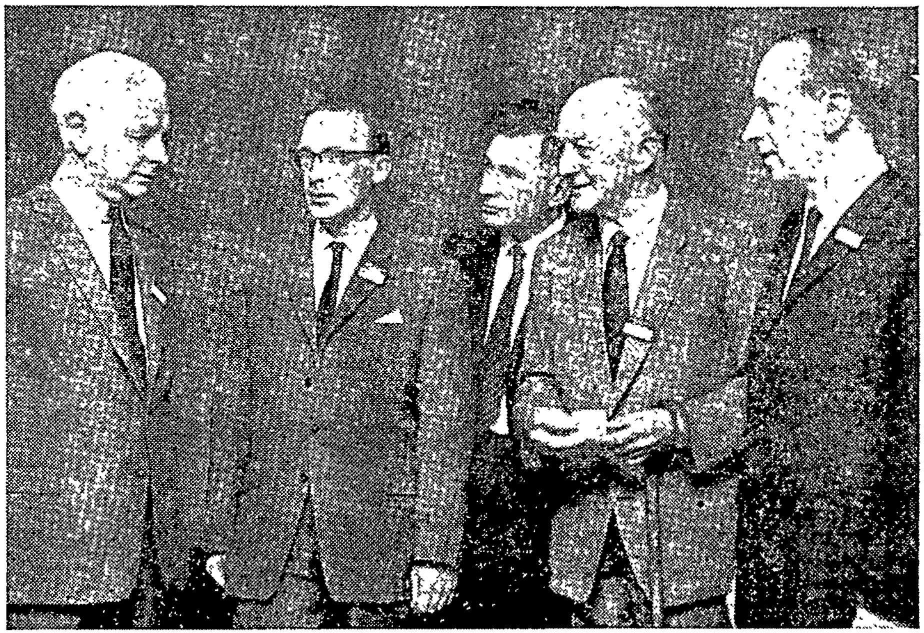
Anaesthetic Emergencies

In discussing complications that might occur during anaesthesia and the immediate postoperative period, Dr. G. W. BURTON (Bristol) emphasized the necessity for supplementing clinical observations with monitoring equipment. He considered that in operations where marked circulatory changes were likely it was essential to have facilities for electrocardiography and electroencephalography, for measuring arterial and central venous pressure, and for taking blood samples. The electroencephalogram was very helpful in deciding whether the circulation to the brain was adequate. The onset of slow waves in the E.E.G. and flattening of the waves was a sign of anoxia.

Other Emergencies

Dr. H. GORDON MATHER (Bristol) dealt with cardiac emergencies other than those particularly associated with ischaemic heart disease and anaesthesia. Acute pulmonary oedema might be due to hypertension, rheumatic heart disease, the sudden onset of atrial fibrillation, silent myocardial infarction, or overtransfusion. It was best treated by intravenous frusemide, digitalis, oxygen, and morphia. Hypertensive crises might occur in the course of long-standing hypertension from any cause; it might be seen in renal disease, pregnancy, phaeochromocytoma, or in adverse reactions to drugs such as monoamine-oxidase inhibitors. Such a crisis could present as acute pulmonary oedema, subarachnoid haemorrhage, acute cerebral oedema, and dissection of the aorta. It was often possible to control the crisis by the use of diuretics, digitalis, and sedatives. If it was necessary to give a hypotensive agent Dr. Mather said he still preferred pentolinium 2.5 mg. intramuscularly, followed by control with guanethidine.

Dr. Mather went on to say that adverse reactions to certain drugs could produce cardiac emergencies. Even well-established drugs such as digitalis could result in arrhythmias of every variety. Arrhythmias could complicate digitalis therapy when the patient had a low serum level of potassium, and adequate supplements must be given. Propranolol, a β-receptor blocker, might induce heart failure or hypertension, and could make bronchospasm worse.



Informal picture of panel members before the discussion on Cardiac Emergencies. (Left to right) Dr. D. H. Davies (chairman), Dr. D. G. Julian, Dr. G. W. Burton, Dr. D. G. French, and Dr. H. G. Mather.

WITHOUT PREJUDICE

As this is my last but one appearance on this page I should begin by apologizing to the many people who have written letters to me and have had no reply. My anonymity makes a correspondence difficult. I have stuck to the anonymity imposed on Pertinax when this column began in January 1963.

Writing under (or over) a pen-name is a respectable convention. When Oliver Edwards brought out in 1957 a collection of his weekly literary pieces from *The Times* under the title of *Talking of Books* neither he nor his publisher dropped the mask of anonymity he preferred to hold in front of his face. I am sure it gave him a feeling of freedom. "Now I can write what I please," he must have said to himself, "and not what in my persona propria I would be *expected* to write."

The first meaning of persona is "a mask, esp. that used by players, which covered the whole head, and was varied according to the different characters to be represented." The meaning was then transferred to the part or character one assumed in the world, from that to a human being performing any function, and later just to a human being. The wrapper round *Talking of Books* had this little message for the curious: "There have been many speculations as to the identity of Oliver Edwards. It is sufficient that he enjoys reading and writing and passing his enjoyment on."

And so do I, though I have nothing like the same range of reading to draw upon. But this is a professional journal, and Pertinax is a professional man with an itch to argue a case for and against it almost matters not what. Point and counterpoint; thesis and antithesis; against pomp, cant, and pretence; for decency and honesty of statement—these have been some of the guide-lines for this column, however much I may have failed to follow them.

I have been embarrassed on at least two occasions by speculations about my identity, but now I am leaving this particular stage I hope I may take my persona and mask into obscurity. But before I do this next week I shall try to answer one or two letters.

* * *

I quite expected criticism of my remarks on psychiatry in my piece of 17 June. But a psychiatrist with his D.P.M. said he was delighted with it. And what scribbler wouldn't be pleased to hear that? "It becomes increasingly obvious, to me at least," he writes, "that psychiatry is going further away from general medicine rather than closer. I am quite certain that much of the cleaving to general medicine by psychiatrists is an attempt to raise their consultant status to the status (real or imagined) of general physicians and surgeons, and all the pomp and ceremony that often goes with them." Well I am glad to have this bit of prejudice confirmed. "The longer I work in psychiatry, and particularly, of course, in a day hospital, the more I realize how much anthropology, sociology, philosophy, and all these bits and pieces which have to do with people living, are needed to do the job properly." He is sure "that medicine should continue to provide the bulk of psychiatrists, however, but that the training should be different." I am sure we shall get a burst of activity when psychiatry comes of age and has a latch-key to its own college.

I drew attention in the same article to the experiments in the U.S.A., and also in at least one centre in Britain, in which the medical profession were training the clergy in psychiatry. I suggested that the parish priest so trained would be a better general practitioner in mental health than the ordinary medical man. My reference was no more than a newspaper report. So I was more than pleased to get from the Revd. John Barton the programme of the Third Pastoral Clinical Training Course for Theological Students which ended last week. It was held under the auspices of the Leeds Regional Hospital Board and the Wakefield "B" Group Hospital Management Committee. Mr. Barton tells me in a letter that they have complete co-operation from regional board, hospital management committee, and the medical profession. "This year we have Anglican, Free Church, and Roman Catholic students in residence." I call that magnificent and heartening news.

Almost by the same post came two letters from New Zealand which one of these days I shall try to answer. A short time ago a leading figure of a sister profession asked me to let him have some hints and tips on a presidential address he had to give. Anyhow, I thought, I am at least leaving this page when people seem to be reading it.

* * *

Then two general practitioners have had a go. One from the far north of England believes that "there are two medico-political bees which appear to be nesting in your bonnet and which have little support in this part of the periphery. The first is your recurrent plea, on various grounds, that the patient should pay something at the time of service, the basic idea being that this somehow improves the quality of medical care. Frankly I do not believe that money will make any difference in the vast majority of doctors." How representative is this enlightened man?

I believe that the economics of the N.H.S. will soon compel the Government to introduce at least some charges as a way of raising more money outside taxation. Apart from this, my plea is based on quite simple human reactions. No one really values anything he gets (apparently) for nothing. My second point is that some element of direct payment increases a sense of responsibility that has been one of the major casualties of the N.H.S. And it should not be difficult to devise ways of exempting children, old-age pensioners, and the derelict.

"The second 'bee' which I spy is your commonly held belief that there is some mystic quality in the doctor–patient relationship which is cemented by money and destroyed by a salary." I think that here I have been misunderstood. My point—I hope I have made it—is that the direct payment of even a small sum at the time of consultation emphasizes the contractual relationship between professional man and client.

And I think that there is more behind it than this. The medical man, theoretically at least, has immense power. After all, he is, within limitations, supposed to have—in fact is licensed to have—power over life and death. I think that Donald Gould is right in thinking that desire for power is something that attracts men into Medicine. Subconsciously the patient needs to control this power with some magic of his own: money has all the appropriate symbolic force for this. And doctors don't really feel comfortable unless they have the accoutrements of power. They are not content with the simple life of the dedicated man. We may deplore this but we should recognize it as one of the facts of medical life.

My correspondent, writing as a "firm believer in the merits of family practice in the old-fashioned sense," says he is content with his lot. "But if I had any choice in my method of remuneration I would prefer to be salaried, and so would quite a few of my colleagues. Perhaps there ought to be a referendum." Well, I think there ought to be a referendum if enough people want it—or indeed if one really wants to discover *what* they want. But does one? Do they?

I know the limitations of working on a salaried basis. No employer of a salaried person can resist the temptation of seeing how cheaply he can obtain his services. And this oddly enough is accompanied by the delusion in the mind of the employer that he is a very generous person. With the State as almost the sole employer of doctors a universal salaried system would, I fear, be against the *financial* interests of the medical profession. If as doctors we want to keep up with the Joneses—and the Joneses are really very nice people—we should aim at being paid from as many different sources as possible. This is enlightened self-interest. (*To be concluded next week.*)

PERTINAX

Correspondence

Letters to the Editor should not exceed 500 words.

Ophthalmic Graves's Disease

SIR,—In a recent leading article entitled "Ophthalmic Graves's Disease" (6 May, p. 329) it was stated that "lid retraction in Graves's disease is mainly due to spasm of the striated levator palpebrae superioris. . . . Increased sympathetic tone may also cause it. . . ." Mr. K. Wybar (24 June, p. 836) does not accept the role of spasm of the levator palpebrae because sympathicolytic drugs—for example, hexamethonium iodide—abolish the lid retraction in thyrotoxicosis. The observation that pharmacological amounts of sympathicolytic drugs can cause ptosis in such patients is not conclusive evidence that increased sympathetic activity is solely responsible for the lid retraction in Graves's disease. While I agree that many of the peripheral manifestations of hyperthyroidism can be attributed to sympathetic overactivity and can be reduced by sympathetic blocking agents, there is no clinical evidence of such overactivity in euthyroid patients with ophthalmic Graves's disease who show lid retraction, often unilateral.

Mr. Wybar also reiterates his previous argument[1] that he finds it difficult to reconcile spasm of the levator muscle with the finding of an increased fat content in the muscle in thyrotoxicosis. Crude estimations of fat content in a muscle do not necessarily correlate with its functional activity.

Pochin[2] has examined the mechanism of lid retraction in Graves's disease in considerable detail. In 12 cases of unilateral lid retraction unassociated with proptosis in Graves's disease he found clear elevation of the lower lid on the affected side in nine cases. He also showed that sympathetic stimulation in man causes lowering, not elevation, of the lower lid,[3] whereas elevation of the lower lid relative to the cornea was found when the upper lid was retracted by levator spasm or in Graves's disease. The pupil on the affected side is not dilated in cases of unilateral lid retraction in Graves's disease, and protagonists of the sympathetic theory of lid retraction must fall back on the assumption of differing thresholds for pupil and lid to sympathetic stimulation, though there is no good evidence for this.

Mr. Wybar states that "there is certainly no consistent evidence that a paresis of elevation of the eye in other conditions is associated with the phenomenon of lid retraction. . . ." In 1927 Collier[4] in an article entitled "Nuclear Ophthalmoplegia, with Special Reference to Retraction of the Lids and Ptosis and to Lesions of the Posterior Commissure," described examples of retraction of the upper lid caused by lesions in the region of the posterior commissure of the mid-brain, often associated with ophthalmoplegia, especially of upward gaze. The underlying disorders were variable—tabes, multiple sclerosis, vascular, degenerative, neoplastic, and encephalitic lesions of the brain stem all having been responsible. Mr. Wybar also mentions that myopathic as distinct from neurogenic lesions causing ophthalmoplegia seldom result in any significant innervational disorder. Several workers have commented on lid retraction in patients with myasthenia gravis[2,4] and in one case[2] the retraction of the upper lid and elevation of the lower lid and ophthalmoplegia improved following neostigmine therapy. Rundle[5] has also provided evidence for the close association between the paralytic variety of lid retraction in Graves's disease and superior rectus function. In certain patients with limited elevation and lid retraction the latter is abolished by directing the gaze downwards.

While I have stressed the evidence for the role of the striated levator palpebrae in the mechanism of lid retraction, I would agree with Mr. Wybar that overaction of the smooth palpebral muscles of Müller may also play a part. I think further investigations of the pathogenesis of the ocular manifestations of Graves's disease are required before we become too involved in speculative arguments.—I am, etc.,

REGINALD HALL.

Royal Victoria Infirmary,
Newcastle upon Tyne 1.

REFERENCES

[1] Wybar, K. C., *Trans. ophthal. Soc. U.K.*, 1953, 73, 639.
[2] Pochin, E. E., *Clin. Sci.*, 1939, 4, 91.
[3] —— ibid., 1939, 4, 79.
[4] Collier, J., *Brain*, 1927, 50, 488.
[5] Rundle, F. F., *Med. J. Aust.*, 1953, 2, 605.

Mental Health Services for Children

SIR,—Your thoughtful leader (3 June, p. 585) raises many important points which indicate the complexity of the subject. Custom encourages the use of "mental health" but Vickers[1] has observed that often the term means "mental ill-health." Both from experience of general practice and of child psychiatry I am aware of the need for more beds and units—some of this need must be met if only to lighten the load and lessen crises in children's departments—yet I would question your emphasis on the lack of psychiatric training, which is put forward as the most urgent aspect in a mental health service for children. To suggest that others are just waiting for psychiatric opinion (often equated with psychodynamic formulation) and are lost without it is to misjudge the situation and the skill of doctors and others dealing with children in trouble.

Indeed, the most significant part of your leader would seem to be contained in the following words: "it is often a matter of chance whether serious emotional disorder in children is treated within a medical, social, educational, or judicial framework." This fact is not merely a cause for lament but an opportunity for research. How many children are treated or dealt with, in which category, by whom, and with what results?

My own impression is that intervention in the total family situation often helps enormously. The psychiatric role is an adjuvant and excipient, with psychotherapy for the child being the least of the burden. Research must be directed not merely within the psychiatric context. Here child psychiatry has not merely a contribution to make, but also a lesson to derive. It must be seen against the limitations of psychiatry generally. The boundaries of psychiatry must be closely examined by those who would advance its claims. The emphasis on "mental health" as if it were indeed the obverse of "mental illness" has led to the prominence of concepts which only sometimes seem to have relevance to the larger field.

Possibly the Seebohm Committee will cast light on the role of the family doctors in the family service which must embrace medico-social factors affecting the mental health of children—and their families. The problem is administrative as well as partly training. In addition to the supportive functions which you stress, and only some of its present commitments, psychiatry can possibly assist most by helping to formulate some of the questions and evaluate the results.—I am, etc.,

Birmingham 13. BERNARD BARNETT.

REFERENCE

[1] Vickers Sir Geoffrey, Address Birmingham Health Week, 5 June 1967.

Carcinogenic Properties of Ortho-dianisidine

SIR,—It was mentioned in the "Medical News" column of the *B.M.J.* (31 December 1966, p. 1663) that ortho-dianisidine was now to be subject to official regulation owing to its suspected carcinogenic properties. This chemical is used routinely in laboratories and hospitals in the glucose-oxidase technique. We therefore wondered what "medical tests" were thought necessary, since many of us using this technique have been pipetting 1% solutions of *o*-dianisidine in alcohol by mouth daily for some years now, while being unaware of its suspected carcinogenic properties. We should also be interested to know exactly what the evidence is which has incriminated ortho-dianisidine.

We feel that the answers to these questions would be of great value if brought to public attention in your columns, since in our experience those engaged in research seem quite unaware that there is any hazard involved in the use of ortho-dianisidine or tolidine.—We are, etc.,

OMER KARRAR.

Department of Biochemistry,
Oxford

DAVID JENKINS.

University Laboratory of
Physiology,
Oxford.

*** See leading article at p. 189.—ED., *B.M.J.*

Local Government Reform and the Health Services

SIR,—I was interested to read Miss Elizabeth Burney's article (1 July, p. 41). She does not seem to want to preserve the medical officer of health. Having neatly whittled down his duties, she then calls what remains "a hodge-podge of sanitary and statistical responsibilities." She entirely forgets that the majority of medical officers of health are appointed principal school medical officers, and has thus conveniently neglected this important branch of preventive medical care.

In the last paragraph the statement is made that "More scope could be given to professional administrators to obtain top jobs in the community health services for which the medical profession is not necessarily more suited than any other." On the basis that "health" is defined as a state of total mental, social, and physical well-being and not just an absence of disease, one wonders who are these "others" who are going to guide the community health services. Presumably the social worker can deal with the social problems and the psychiatric social worker with the mental problems, but outside the medical and nursing professions are there any good professional administrators who can really evaluate the priorities for the total social, mental, and physical health of the community?

It takes time and a great deal of expertise to learn how to run the community health services, and the last person we would want in charge is an economist who is always thinking how to save the rates. Miss Burney writes, "Whether there would still be anybody called the medical officer of health, or what his status would be, matters very little." Already there is a good deal of disenchantment from doctors in the present medical services. They have been cut out of the Review Body and have been told by the Management Side of the Medical Whitley Council that they are administrators first and doctors afterwards. It would be as well if some of those who plan the health services of the future would travel to the industrial areas and see how much clinical work is actually being done in the preventive medicine field. Of course we must accept change in the future, and it is likely that the family doctor will take over some of this work, but it will not happen very quickly unless the under-doctored areas receive a new influx of family doctors. The situation at present is not too grim in the county boroughs, but in the northern industrial county districts the writing is already on the wall, and there are very few junior doctors in the preventive medicine field. The immunization figures will fall; the screening for disease and the study of the epidemiology of disease will be reduced or non-existent; and the school health service (not mentioned in Miss Burney's article) will become no service at all. There are many other health tasks which will no longer be properly evaluated throughout this country.

My final advice to Miss Burney is that, before she renders the medical officer of health redundant by 1975, she makes sure that there is someone to put in his place. There is no very great evidence at present, particularly in the industrial areas, that these fine, non-medical, professional administrators really exist who can staff the top jobs in the new community health services.—I am, etc.,

P. O. NICHOLAS.

Bolton,
Lancs.

Idiopathic Haemochromatosis

SIR,—Your leading article (25 February, p. 446) and Dr. W. H. Crosby's letter (20 May, p. 507) indicate the varying practice in the management of the first degree relatives of patients with idiopathic haemochromatosis and also underline our uncertainty of the natural history of the disorder in affected relatives. Some apparently believe that "all affected relatives should be treated by multiple venesections" while others reserve such therapy "for those with histological evidence of tissue damage as well as siderosis."

"Affected" relatives may be detected by measurement of the serum iron and serum total iron binding capacity (T.I.B.C.), by estimation of iron absorption, by hepatic biopsy, or by quantitative tests of total body iron storage using iron-chelating agents. Hepatic biopsy permits an estimation of the amount of excess storage iron and this is usually graded arbitrarily—for example, 0 to 4.[1] Relatives with grades 0 to 1 iron storage in the liver have normal iron stores.[2 3] Those with grade 2 iron deposition have approximately 2 g. of storage iron as measured by repeated venesection[4] and, we believe, should be observed without therapy unless serial biopsies or chelation tests reveal evidence of increasing iron storage. We have observed several such patients for up to five years without evidence of increase in iron storage (unpublished data). Relatives with grades 3 or 4 iron deposition on liver biopsy usually have 10 g. or more of excess storage iron[4] and, we believe, should be treated by venesection therapy irrespective of the presence of tissue damage, since such iron loading usually antedates the development of hepatic fibrosis.[5]

In our experience quantitative tests of iron storage using diethylenetriaminopenta-acetic acid allow more exact assessment of the degree of excess iron storage than does liver biopsy, and serial tests provide a more useful guide to the effect of therapy than do the serum-iron, T.I.B.C., or the haemoglobin concentration.[4]—I am, etc.,

L. W. POWELL.

University of Queensland
Department of Medicine,
Royal Brisbane Hospital,
Brisbane, Australia.

REFERENCES

[1] Scheuer, P. J., Williams, R., and Muir, A. R., *J. Path. Bact.*, 1962, **84**, 53.
[2] Bothwell, T. H., Cohen, I., Abrahams, O. L., and Perold, S. M., *Amer. J. Med.*, 1959, **27**, 730.
[3] Powell, L. W., *Aust. Ann. Med.*, 1966, **15**, 110.
[4] —— and Thomas, M. J., *J. clin. Path.*, 1967, in press.
[5] —— *Quart. J. Med.*, 1965, **34**, 427.

Pressurized Aerosols in Asthma

SIR,—We have been interested in the recent correspondence (10 June, p. 699) dealing with bronchodilator aerosols, particularly those containing adrenaline, isoprenaline, or orciprenaline as the active component. Many writers have inferred from clinical observations that this form of bronchodilator therapy is contributing to a proportion of unexpected deaths among asthma sufferers. This has generally been attributed to the cardiac actions of these sympathomimetics. Much of the evidence that has been advanced to implicate these sympathomimetic amines as the cause of sudden death in asthmatics who have used them is anecdotal, and has been strongly criticized by others who have noted no incidence of fatalities directly attributable to these amines. The reports of clinical attempts to study this problem[1-4] are welcome.

As laboratory pharmacologists, we have undertaken some investigations on this subject, using animal experimentation. One aspect of our investigations was prompted by the suggestion that the interaction between large doses of sympathomimetics used as bronchodilators may promote deleterious cardiac effects. A considerable amount of work has been done on blood-pressure effects of large doses of these drugs, and of the interactions between them. With a single drug, or with combinations of them, long-continued administration leads to the development of tachyphylaxis. Our observations of their cardiac actions indicate that they follow the same pattern.

In experiments in cats infusions of adrenaline, isoprenaline, or orciprenaline were given over considerable periods of time at gradually increasing rates. This was done to mimic the possible effect of excessive use of aerosol preparations. In these experiments we have detected no sign of cardiac toxicity. In fact after the infusions had continued for some time the tachycardia which was produced initially by all three drugs declined despite increases in the rates of infusion. This development of tachyphylaxis (or tolerance, or resistance, to give alternative names which may be more familiar to clinicians) to the cardiac actions of the three sympathomimetic amines probably diminishes the risk of cardiac toxicity arising from their use. Furthermore, the effects of single intravenous doses of any one of these drugs during the continuous infusion of another were less the longer the duration of the infusion, indicating that the tachyphylaxis was crossed. This finding does not support the contention that the interaction between sympathomimetic bronchodilators may lead to an increased risk of cardiac toxicity.

The details of these investigations will be published elsewhere. In reporting this brief summary we wish to ally ourselves with those who seek to provide a basis of fact about the possible risk of sympathomimetic amines in asthmatics and to detract from the uncritical acceptance of clinical impressions.—We are, etc.,

JUDITH M. ATKINSON.
M. J. RAND.

Department of Pharmacology,
University of Melbourne,
Parkville N.2,
Victoria, Australia.

REFERENCES

[1] Gandevia, B., *Med. J. Aust.*, 1966, **2**, 381.
[2] —— and Robertson, M., ibid., 1967, **1**, 136.
[3] Patrick, P. R., and Tonge, J. I., ibid., 1966, **2**, 668.
[4] Dornhorst, A. C., and Hodge, R. L., *Brit. med. J.*, 1967, **2**, 441.

SIR,—Recent correspondence in your columns concerning the side-effects reported in patients with asthma after excessive use of aerosol bronchodilators is of widespread and general importance (6 May, p. 375, and 10 June, p. 699). Likewise the importance of the comment from the Committee on Safety of Drugs Publication No. 5 in the Adverse Reactions series drawing attention to the dangers associated with overdosage of pressurized aerosols has been emphasized by its reproduction in "Today's Drugs" (1 July, p. 37).

The problem really is why do so many asthmatics use such large amounts of bronchodilators ? I have no doubt that the answer is simply that the vast majority of patients have never been properly instructed in the use of these aerosols ; although some pharmaceutical firms issue instruction notes on their use, these notes are often understandably inadequate, as frequently only actual demonstration and personal instruction will suffice for many patients. Indeed, the number of patients whom I see in my clinic for the first time already using one of these aerosols who have been correctly instructed in its use is usually very small. It takes only about five—or perhaps ten—minutes of careful instruction to teach a patient how to use an aerosol.

It is known from a number of clinical trials that one activation will usually produce a sufficient dose of bronchodilator to achieve significant relief of bronchospasm. There is no evidence to suggest that the degree of response is directly proportional to increasing the size of dose. Therefore several puffs in quick succession which fail to relieve bronchospasm almost certainly do so because the agent is not being fully inhaled into the bronchial tree, but is probably being absorbed through the buccal or upper respiratory tract mucosa. Under these circumstances large doses can be absorbed with the possibility of developing the now well-known toxic effects without achieving relief of the bronchospasm. It cannot be too strongly emphasized that persons using pressurized aerosols should be properly trained in their use, and instructed that if no relief is obtained from one or two actuations at an interval of not less than one minute no further relief should be expected from additional activations of the aerosol, and other assistance should be sought.—I am, etc.,

Leeds. GORDON EDWARDS.

Nebulizers

SIR,—I should like to thank Dr. B. M. Wright (20 May, p. 508) for his information regarding the details of evaluating the performance of nebulizers. However, for routine testing by untrained persons I would suggest that the method I described, with the flow meter between the cylinder and the nebulizer, should be adopted—this in fact being the way in which the nebulizer is used in the treatment of patients.—I am, etc.,

I. S. BRUCE.

Department of Anaesthetics,
General Hospital,
West Hartlepool,
County Durham.

Typhoid Fever—30 Years On

SIR,—I read with much interest Dr. J. M. Morfitt's letter in your journal (24 June, p. 839). An almost identical epidemiological parallel was discovered in Edinburgh during 1965 when typhoid fever occurred in a 65-year-old housewife 31 years after her husband had typhoid, and who had subsequently remained an unknown intermittent urinary carrier. A report of this episode, which threw further doubt on the reliability of the Vi agglutination test for the detection of chronic typhoid carriers and also demonstrated shortcomings in the Food Hygiene (Scotland) Regulations,[1] was recently published under the title "Typhoid Fever—Thirty Years After."[2]—I am, etc.,

J. C. M. SHARP.

Health and Social Services
Department,
Edinburgh 1.

REFERENCES

[1] "*The Food Hygiene (Scot.) Regulations*," Statutory Instrument, 1959, No. 413, London.

[2] Sharp, J. C. M., *Hlth Bull. (Edinb.)*, 1967, 25, 3.

Human Vibriosis

SIR,—The articles on human vibriosis by Dr. W. D. White, and by Dr. J. H. Darrell, Mr. B. C. Farrell, and Dr. Rosemary A. Mulligan (29 April, pp. 283 and 287) were of great interest to us. We should like to record a similar case seen at this hospital a few months ago.

A 5-month-old girl was admitted with a history of convulsions. On examination she was pyrexial, with a temperature of 106° F. (41° C.), with marked dehydration and peripheral vascular failure. Generalized twitching was present, and the abdomen was slightly full. The results of investigations were as follows: Haemoglobin 13.3 g./100 ml., P.C.V. 41%, W.B.C. 19,000, N. 8%, L. 68%, M. 20%, metamyelocytes 4%. The film was suggestive of a severe toxic process. Serum Na 138 mEq/l., K 6.3 mEq/l., HCO 10 mEq/l. (the blood culture findings are detailed below). Cerebrospinal fluid normal. Rectal swab negative for *Staphylococcus aureus*, *Shigella*, *Salmonella*, and specific *Escherichia coli*.

Despite intensive therapy with intravenous fluids, hydrocortisone, and chloramphenicol she continued to deteriorate and died seven hours after the onset of symptoms.

At post mortem (by Dr. G. A. Stirling) the jejunum and ileum were found to be inflamed and contained bloodstained watery faecal material. A segment of ileum, 12 cm. long, was dark in colour, suffused with blood, and appeared necrotic. The mesenteric vessels were patent. The appendix was healthy, but the mesenteric lymph nodes were enlarged. The caecum was congested, but the remainder of the colon and the rectum appeared normal. The peritoneum was congested and there was a small amount of brown fluid in the peritoneal cavity. The lungs were collapsed and there were a few petechial haemorrhages in the pleura, pericardium, oesophagus, and gastric mucosa. The remaining organs showed no abnormalities apart from slight fatty change in the liver, and some oedema of the brain.

Microscopically the gastric, jejunal, and ileal mucosae were infiltrated with acute and chronic inflammatory cells ; no specific features were noted. The colon appeared normal. The lungs showed interstitial pneumonia in some areas. Acute fatty change was apparent in the liver and tubular degeneration in the kidneys.

An organism similar to that described by Dr. Darrell and co-workers was isolated from the blood culture bottles ("liquoid" broth) after 48 hours' incubation anaerobically, and in 10% carbon dioxide. It appeared as pin-point transparent colonies on the blood agar plates subcultured from the "liquoid" broth and incubated overnight anaerobically and in 10% carbon dioxide. Growth on the carbon dioxide plate was more profuse than on the anaerobic, and none appeared on the aerobic plate.

The organism stained easily by Gram's method and appeared predominantly as Gram-negative spirals with lesser numbers of curved rods. Subculture proved difficult, but best results were obtained on sloppy blood agar slopes incubated in 10% carbon dioxide. This vibrio was oxidase- and catalase-positive and grew at 42° C., thus falling into the group of "related vibrios." It was resistant to penicillin but sensitive to tetracycline, chloramphenicol, and erythromycin on disc testing. Mr. Moylan Gambles of the Central Veterinary Laboratory, Weybridge, kindly confirmed the identification and considered this organism to be closely related to *V. coli*.

It is difficult to assess the significance of the isolation of this vibrio, but the absence of other findings and the similarity to cases described in the U.S.A.[1] suggest that this infant was suffering from vibrionic enteritis. Our post-mortem findings resemble those of Lochte[2] on an adult from whom a "related vibrio" was also isolated.

We should like to thank Dr. M. J. Wilmers and Professor A. C. Cunliffe for permission to publish this case.

—We are, etc.,

RACHEL G. EVANS.
J. V. DADSWELL.

Department of Paediatrics,
King's College Hospital,
London S.E.5.

REFERENCES

[1] Wheeler, W. E., and Borchers, J., *Amer. J. Dis. Child.*, 1961, **101**, 60.

[2] Lochte, W., personal communication (quoted by W. E. Wheeler and J. Borchers), 1961.

Integrated Training Schemes

SIR,—Mr. P. W. R. M. Alberti is to be congratulated on his article on integrated training schemes (8 July, p. 101). I am sure he is right to mention that any training scheme is dependent on the concentration of units into larger area centres, where there would then be sufficient S.H.O. and registrar staff for these schemes to be initiated. These teaching programmes must give not only adequate clinical and operative training but also instruction for the higher examinations ; and they must include the facility of rotation into other units, designed to broaden the trainee's experience within his specialty. In these enlarged centres there would be sufficient consultant staff to allow the development of special interest in subsections of the specialty, in addition to routine work, to give a comprehensive training programme. For instance, in E.N.T. three of these subsections might be special otology, soft-tissue neck surgery, and audiology. The last two in this respect have been sadly neglected in a specialty which until recently has run the risk of becoming excessively ossific-centred.

In suitable units Mr. Alberti mentions G.P. clinical assistant participation. I would suggest that for these appointments and for the greater specialization that will in itself result within large group practices there could be courses for general practitioners in area specialty centres. Finally, both these training schemes hinge, in my opinion, on available senior registrar staff, who would be able to participate in these training schemes as well as deal with some of the clinical and operative work of their various chiefs. I feel it is this grade of doctor who should be rotated to include central establishments, where their training would include further facilities for teaching and a discipline for research. I only hope that Mr. Alberti's timely reminders will be heeded by those who are now deliberating specialty training at central level.—I am, etc.,

Middlesbrough. M. HOROWITZ.

SIR,—I must take issue with Mr. P. W. R. M. Alberti on some points in his article (8 July, p. 101).

(1) "If training is to be centred about large institutes, then inevitably there will be no juniors in the periphery. This need not be a bad thing, and in many instances will only stabilize an already current situation." This takes no account of potential general practitioners not normally requiring integration in training schemes for specialists, and for whom there is no room in larger centres. Why should they not work in peripheral hospitals under adequate supervision by the larger number of consultants Mr. Alberti rightly favours ?

(2) "Some services will be centralized . . . as communications improve so the need for small isolated units will diminish." Public service communications are in fact deteriorating, not improving: patients who are not car owners are already finding difficulty in attending hospital from remote country districts.

(3) "Hospitals might therefore be built where they can be manned, rather than where political pressure dictates." They should be built where they are needed following political pressure exerted on the Government by local M.P.s etc., endeavouring by their good reputation to attract junior staff to work there.

(4) "Consultants and general practitioners will have to work much closer together." How ? General practitioners are already too few and overworked (a fact recognized by the Minister and by the last Review Body's recommendations). Married women graduates might be encouraged to do a little more, but medically qualified mothers of small children cannot provide a substitute for the thousands of junior staff the "large institutes will siphon off from the periphery," and who do so much of the routine and emergency work, especially at night.

I could say a great deal about rotating schemes, much of it highly critical, but Mr. Alberti and I agree they should not ideally require change of residence. I doubt whether this is so important if there are absolutely no unnecessary expenses or *unexpected* removals.

Finally, I agree warmly with Mr. Alberti's strictures on the requirements for higher degrees and the Colleges' approval of undesirable posts as suitable for training. I share his feelings that at present specialist training is far too haphazard, and that a shorter organized course of training may mean harder work during that time but at least could be linked to the very high probability of a consultant post in the future, owing either to retiral of an older man or to the creation of a new post planned years in advance from statistical forecasts already available to the Ministry if it would but seek them.—I am, etc.,

Princess Elizabeth
Orthopaedic Hospital,
Exeter.
J. E. WOODYARD.

Oculogyric Crises Due to Phenothiazines

SIR,—During the past year I have seen three young people with oculogyric spasms which I considered to be caused by phenothiazines. Two of these patients were seen during the past week.

The patients were aged 15, 19, and 21 years. All presented in the same way, with oculogyric crises and hyperextension and rotation of the neck recurring every few minutes and accompanied by persistent mydriasis.

The first two patients were suffering from subtertian malaria, and were being treated with chloroquine. Prochlorperazine (Stemetil) was given in each instance because of vomiting. In the first patient, a girl of 15, the spasms started after two doses of 10 mg. Pentobarbitone (Nembutal) 100 mg. was given by mouth, and the attack ceased after about an hour. The second patient, a 19-year-old male, was given prochlorperazine 5 mg. at midday on the day of admission, then 12.5 mg. intramuscularly at 4 p.m. the same day, and repeated on the following day at the same time. Spasms started at 6 p.m. and continued for an hour after giving pentobarbitone 200 mg. The third patient, who was suffering from infectious hepatitis, was given perphenazine (Fentazin) 4 mg. on admission to hospital because of vomiting, and this was repeated the following afternoon. Spasms commenced two hours later. He was given 150 mg. pentobarbitone, following which spasms persisted for about an hour.

These cases are reported to emphasize the risk of using phenothiazines in young people. Jaundice might be expected to potentiate this drug effect, and it is suggested that malaria, chloroquine, or both might do likewise.—I am, etc.,

J. R. HARRIES.

P.O. Box 2223,
Nairobi,
Kenya.

National Kidney Centre

SIR,—In view of recent press reports about the closure of the National Kidney Centre I feel constrained to use your columns to place on record a fuller statement of the reasons for closure of the National Kidney Centre on 1 July 1968.

The National Kidney Centre was set up in November 1966 as a non-profit-making charitable trust with its sole aim to determine whether the rate of expansion of home dialysis with a minimum of medical support could be achieved in the British Isles. It was never intended to compete with the National Health Service, as has been suggested, and indeed it was hoped from the outset that the centre would be able to co-operate with the N.H.S. dialysis programmes wherever possible, to ensure the advancement of this form of treatment. Unfortunately the official attitude of the Ministry of Health has prevented any official co-operation with N.H.S. dialysis units.

To date the centre has been responsible for the training and subsequent maintenance in the home of 27 British nationals and four non-British nationals, utilizing the staff of one doctor and three trained nurses. No hospitalization requirements with dialysis have been necessary during the nine months of its function, and all patients are in good health. The feasibility of expanding home dialysis with integration into existing local community dialysis facilities from a specialist training centre has been successfully demonstrated in the United States.

However, its present failure in this country has not been due to shortage of funds or resources but simply to the inability to find a suitable formula to bridge the dogmatic distinction separating medical practice inside and outside the N.H.S. Full details of the results obtained and methods used will be published in due course. A preliminary report is in the press.[1]—I am, etc.,

London N.3.
STANLEY SHALDON,
Medical Director,
National Kidney Centre.

REFERENCE

[1] Shaldon, S., and Oakley, J. J., *Proc. Europ. Dial. and Transpl. Ass.*, 1967, in press.

Psychological Factors and Ulcerative Colitis

SIR,—I was delighted to read your leading article (1 July, p. 1) and the paper by Dr. F. Feldman and colleagues (p. 14) on psychiatric studies of patients with ulcerative colitis. I have long ceased to believe in the concept of "psychosomatic medicine," which in my opinion is a confession of ignorance on the part of the profession regarding the aetiology of these conditions.

The concept that a disease such as ulcerative colitis, with its intractable diarrhoea, blood loss, and exsanguination of the patient, could be psychogenic in origin has always appeared to me to be utterly absurd. Recent advances in medical treatment such as steroid therapy and salazopyrine and such successful surgical procedures as colectomy for the removal of the diseased area of bowel have confirmed my belief that the psychosomatic approach is wholly wrong. The spectacle of these severely ill people being subjected to extensive psychotherapy seems to me the negation of all common sense, especially in the light of the new knowledge we now possess in treating this condition. It is equally true with other so-called psychosomatic illnesses, which will no doubt prove to have a physical basis on further investigation.

I note that Dr. Feldman and his colleagues conclude their very comprehensive investigation by stating that there is now a "central problem of whether primary psychosomatic disease exists, and, if so, how it can be explained." I submit that this conclusion is a victory for common sense and that the whole theory of psychosomatic medicine should be subjected to a thoroughgoing analysis, to see on what scientific basis its theories rest.—I am, etc.,

Hornchurch,
Essex.
D. D. COWEN.

Unexpected Foreign Body

SIR,—Dr. G. B. Stein (1 July, p. 51) raises an important matter—the difficulty arising in making a diagnosis when a non-opaque denture has been inhaled—and has a point in suggesting that they should not be allowed to be made.

However, among the innumerable objects which are accidentally inhaled there are many that are radiotranslucent or so small as to be easily missed. Dr. Stein's case report, like several previous reports, including my own,[1] serves to remind us that should a patient who has been unconscious subsequently develop pulmonary symptoms the possibility of a foreign body being present should always be in mind, and that lack of radiological confirmation is no guarantee that one is not present. When real doubt exists the patient should be referred for bronchoscopic examination.—I am, etc.,

Midhurst, Sussex. VINCENT T. POWELL.

REFERENCE

[1] Powell, V., *Thorax*, 1965, 20, 48.

"Swallowed" Endotracheal Tube

SIR,—The report by Mr. J. A. S. Dickson and Mr. G. C. Fraser (24 June, p. 811) of five cases of neonatal endotracheal tubes acting as foreign bodies in the oesophagus is of considerable interest. These infants recovered from neonatal asphyxia despite failed endotracheal intubation. How many others are subjected to this procedure unnecessarily?

It seems to be a current fashion that the diagnosis of neonatal asphyxia demands that an immediate attempt should be made to intubate the trachea. I am sure this is a wrong approach. This aggressive attitude may be harmful to the infant in three ways. Firstly, because the attempt can actually delay oxygenation of the blood, not only by wasting valuable time but also by mechanically obstructing an otherwise effective gasp. Secondly, it may produce reflex inhibition of respiration. Thirdly, even relatively experienced resuscitators cannot always avoid soft-tissue damage. Add to this the more bizarre complications, such as those cited in the report, and it ought to be obvious that intubation of an infant's trachea should not be undertaken without good reason. Failure to respond to oxygen properly administered by bag and facemask[1] (or the Samson[2] or Cardiff[3] resuscitators) in the correct extended position, preceded by careful toilet of the nose and pharynx, might be a justifiably good reason. The mere diagnosis of neonatal asphyxia in itself is not.—I am, etc.,

Wrotham, Kent. J. V. I. YOUNG.

REFERENCES

[1] Brews, A., *Manual of Obstetrics*, 1963, 12 ed., p. 674. London.
[2] Samson, H. H., *Med. Proc.*, 1963, 9, 158.
[3] Longworth Scientific Instrument Co. Ltd.

Urinary Infection Presenting with Jaundice

SIR,—We have read with interest the article "Urinary Infection Presenting with Jaundice" by Drs. A. B. Arthur and B. D. R. Wilson (4 March, p. 539). This prompts us to report a case of our own.

A female infant born prematurely (birth weight 1.4 kg.) has been in hospital since birth and survived seven severe infections in the first seven months of life. These were: omphalitis (*Staphylococcus aureus haemolyticus*), rhinitis, bronchitis (*Pneumococcus*), bilateral otitis media (*Proteus vulgaris*), rhinitis, sinusitis maxillaris (*Proteus vulgaris*), pyelonephritis (*Escherichia coli*), bronchopneumonia, bilateral maxillar sinusitis (*Staphylococcus albus*), and enterocolitis (*Escherichia coli* $O_{111}:B_4$).

The fifth of these infections, pyelonephritis, which she had at 3 months of age, was associated with jaundice. The total serum bilirubin was 8.7 mg. per 100 ml. (direct van den Bergh 4.2 mg./100 ml.). The other infections which this child had were by no means less severe, and caused by a variety of organisms, yet only the pyelonephritis was associated with jaundice. This seems to support the view put forward by Drs. Arthur and Wilson.—We are, etc.,

Department of Paediatrics,
University of Pécs,
Pécs, Hungary.

T. HEIM.
G. KAROLINY.

Drug Treatment Centres

SIR,—The statement in your leading article (20 May, p. 455) that "numerically small are the methedrine and L.S.D. users, the chlorodyne drinkers, glue sniffers, and people dependent on barbiturates" is probably correct for the younger age groups if one excludes the abuse of the Drinamyl type of drug (although methedrine and L.S.D. are both becoming increasingly popular). As regards the middle-aged, however, barbiturate dependence can by no means be regarded as a numerically small problem, and in that age group it is second only to alcoholism. Barbiturates are prescribed in enormous quantities, increasing year by year—for example, from 15 millions in 1961 to over 17 millions in 1965. This makes them readily available agents for overdosage, and the steady rise of barbiturate deaths by suicidal and accidental overdosage in previous years[1-3] is still continuing—from about 515 (suicide) and 140 (accident) in 1956 to approximately 1,490 and 525 respectively in 1965. Among nonfatal suicide attempts barbiturates are the most widely used agent, accounting, for example, for 60% of admissions for suicide attempts to various general and psychiatric hospitals in a personal study carried out a few years ago.[2] In a recent Australian study Drs. F. A. Whitlock and J. E. Edwards (27 May, p. 576) found that barbiturates were the agents employed in approximately four out of five cases of "impulsive" suicide attempts. Just as drunkenness is relatively more common among alcoholics than among social drinkers so the risk of barbiturate overdosage affects chiefly (though of course not exclusively) those taking the drug regularly to excess (and hoarding supplies).

Locket[4] estimates that 4–6% of all cases of acute barbiturate poisoning admitted to his unit were barbiturate addicts. Thus the high number of people dying from or admitted for acute barbiturate poisoning probably reflects the prevalence of barbiturate dependence, chiefly among women. This conclusion is supported by findings such as that among 38 female drug addicts (almost all middle-aged) admitted to the St. Bernard's unit in 1962–3 there were 10 barbiturate addicts and 11 more dependent on Drinamyl,[5] and of 69 female addicts admitted between 1962 and 1964 (by then an increasing proportion of young amphetamine and heroin-cocaine addicts were admitted) a minimum of 29 were dependent on barbiturates.[6] During 1966 alone, outside hospital, I saw 23 barbiturate addicts, but it is only quite recently that I came across a youngster who had sniffed glue regularly for a few weeks when he was unable to get hold of other drugs. Although a few youngsters mention that occasionally they had temporarily tried glue sniffing without much "reward," in this country this form of drug abuse seems to be quite rare and can surely not be placed "numerically" or in any other aspect of importance alongside barbiturate dependence.

Barbiturate abuse and addiction must not be overlooked when at present it is mainly the young amphetamine, cannabis, and heroin-cocaine abusers who make headlines; and all too often one comes across barbiturate addicts who have been investigated for a long time for "epilepsy" without having ever been questioned about their use of barbiturates and the possibility of withdrawal convulsions. —I am, etc.,

M. M. GLATT.

St. Bernard's Hospital,
Southall, Middlesex.

REFERENCES

[1] Brooke, E. M., *Lancet*, 1956, 1, 150.
[2] Glatt, M. M., *Bull. Narcot. (U.N.)*, 1962, 14, 19.
[3] Brooke, E. M., and Glatt, M. M., *Med. Sci. Law*, 1964, 4, 277.
[4] Locket, S., *Clinical Toxicology*, 1957. London.
[5] Glatt, M. M., *Nursing Mirror*, 1965, 120, 1.
[6] George, H. R., and Glatt, M. M., *Brit. J. Addict.*, 1967, 62, 147.

Liquor Bilirubin Levels

SIR,—I note with some interest the correspondence by Dr. A. F. Fleming on liquor bilirubin levels (24 June, p. 840). As he states, there are both chemical and spectrophotometric methods in use at the present time for the estimation of bilirubin in liquor amnii. He goes on to point out the difficulties of these methods and the likely sources of error and finishes with an appeal for a quantitative method which expresses the results in terms of µg. of bilirubin and not as a ratio or optical density measure.

A method developed in this hospital[1] does, I believe, satisfy many of the objections which Dr. Fleming raises, in that it uses the extreme solubility of unconjugated bilirubin in chloroform as a means of extracting this substance from liquor. Reduction of the chloroform volume brings about a fourfold concentration of the bilirubin. By the use of the spectrophotometer and a standard curve, the quantity of bilirubin present can be measured in terms of absolute units. The method is simple to carry out, and if one wishes to express the result as µg. of bilirubin per mg. of protein, as Fleming suggests, this could be easily done. Using this method we have examined over 120 samples of liquor. With one exception there has been an extremely good correlation between liquor bilirubin and foetal condition. These results will be published in due course.—I am, etc.,

G. W. PENNINGTON.

Sheffield and Region
Endocrine Investigation Centre,
Jessop Hospital for Women,
Sheffield 3.

REFERENCE

[1] Pennington, G. W., and Hall, R., *J. clin. Path.*, 1966, 19, 90.

Ehlers–Danlos Syndrome

SIR,—In my article on the heterogeneity of the Ehlers–Danlos syndrome (3 June, p. 612) I suggested that spontaneous rupture of large arteries occurs only in patients with a distinct "arterial" type of this syndrome, and I also stated that I intend to publish a separate article on this "arterial" type of the Ehlers–Danlos syndrome.

In their letter about my findings Dr. S. G. Elkington and Dr. P. H. Beighton (24 June, p. 843) claimed that all patients with Ehlers-Danlos syndrome should be regarded to be at risk through arterial bleeding.

To reply in full to all the points raised by your correspondents I would have to write almost the whole of my as yet unpublished paper. In brief, our disagreement, if any, seems to stem from the fact that they refer to "the risk of arterial bleeding" while I wrote about "*spontaneous* rupture of large arteries." Our interpretation of some of the published reports on arterial complications in Ehlers–Danlos syndrome also differs, because, unlike them, I find it impossible to identify the clinical type of the syndrome in the patients described.—I am, etc.,

A. P. BARABAS.

Norfolk and Norwich Hospital,
Norfolk.

Infant-scalp Vein Needles

SIR,—At least 18 months ago house-officers at the Royal Victoria Infirmary, Newcastle upon Tyne, started to use these little sets in circumstances where rapid intravenous infusions are unnecessary—for example, in maintenance electrolyte therapy and in the slow administration of low-molecular-weight dextrans. If the needle blocks, as it commonly does after two or three days, it may be quickly and relatively painlessly changed; a quiff of cotton-wool and a squirt of Nobecutane hold it in place.

Perhaps because of this usually short life of these needles "chemical" phlebitis is uncommon. Most infusion needles are still too irritative. In a recent unpublished survey conducted by two colleagues and myself the "complication" rate—that is, phlebitis, cellulitis, leakage, and thrombosis—reached 50% in the case of certain plastic cannulae. An early warning sign of phlebitis is a sharp squeak of protest from the patient when the infusion is suddenly speeded up.

The removal of a drip needle from a severely inflamed vein is often followed by thrombosis, and was perhaps the situation encountered by your correspondent (1 July, p. 48). If, as the needle is withdrawn, 1–2,000 units of heparin and 10–25 mg. of hydrocortisone are injected thrombosis is often prevented and the vein saved for another day—or night.—I am, etc.,

M. L. SNAITH.

Derbyshire Royal Infirmary,
Derby.

Diet and Diverticulitis

SIR,—I find it difficult to understand the apparent criticism of the letter of 2 July 1966, p. 50, by Dr. T. L. Cleave and myself, relating diverticulitis to the consumption of refined carbohydrates, as contained in the letter of Dr. E. H. Goulston (6 May, p. 378). He agrees that no case of diverticulitis has ever been reported from Ethiopia, where it is known that the grain eaten consists mostly of teff (a kind of millet) taken unrefined, but refers to the infrequent occurrence of diverticulosis. If diverticulosis has been seen at Addis Ababa this is exactly what one might expect, because in that capital considerable amounts of white flour are now being consumed,[1] and we should expect cases of diverticulitis to follow in due course, as happened in the American Negro people referred to in our letter. For, in conformity with my own "rule of 20 years," advanced after observing the length of time spent in towns by Zulus before they develop diabetes, as set out in our joint work,[2] it would seem that a definite period of time is also needed before a refined diet can lead to overt diverticular disease.

Dr. Goulston asks if barium enema studies have been performed on Zulus. I am happy to supply the following recent figures for such examinations:

Urban[3]	King Edward VIII Hospital, Durban.	218 Barium enemas	4 cases of diverticular disease.
Rural[4]	Eshowe and Empangeni Hospitals in Zululand.	100 Barium enemas	No case of diverticular disease.

Though these figures are significant at the 5% level, I should like a still larger series; even so, these results certainly indicate that diverticular disease is emerging precisely as was observed in the American Negro people, as mentioned in our letter.—I am, etc.,

G. D. CAMPBELL.

Durban,
South Africa.

REFERENCE

[1] Ethiopia, 1959, *Nutrition Survey*, U.S. Interdepartmental Committee on Nutrition for National Defence, Bethesda.
[2] Cleave, T. L., and Campbell, G. D., *Diabetes, Coronary Thrombosis and the Saccharine Disease*, 1966. Bristol.
[3] Quantrill, J. R., *S. Afr. J. Radiol.*, 1966, 4, 9.
[4] Bostock, J. P., Personal communication, 1966.

I.V.P. in Renal Colic

SIR,—The value of this measure is admirably assessed by Mr. James A. Rhind (1 July, p. 24), and even if some night radiography is entailed there is more justification for doing it than in much of the radiography at present carried out at night as "emergency." Immediate I.V.P. in renal colic usually provides a conclusive diagnosis, a good guide to management, and a baseline from which to assess if conservative methods are adopted.

I too have observed therapeutic effect, due presumably to the diuretic effect of the contrast. When this happens pain can be severe, and ready analgesia should be available if patient control on the *x*-ray table is to be maintained. The amount of ionizing radiation used by this technique is not likely to be in excess of what would be used in "cold" investigation, especially as single-film pyelograms usually suffice in interval-check examinations.—I am, etc.,

DAVID J. MITCHELL.

Royal Albert Edward
Infirmary,
Wigan, Lancs.

Chloroquine

SIR,—Recently Professor A. W. Woodruff, of the London School of Hygiene and Tropical Medicine, commented, in answering a query in the *Practitioner*,[1] that "It is now generally agreed that chloroquine should not be used as a prophylactic but should be reserved for the treatment of acute malarial attacks . . . unfortunately strains resistant to it have recently emerged and it is considered best to try to avoid encouraging the emergence of further resistant strains."

This is excellent theoretical advice, but how far is it applicable in practice? Many sources, official and non-official, in East Africa recommend chloroquine for prophylaxis because there is known to be proguanil–pyrimethamine resistance locally and as yet none to chloroquine. As a result I believe the majority of the prophylactic-consuming public takes a 4-aminoquinoline. For a small number of others to take proguanil helps the main problem but little and exposes them personally to the slight risk of a malarial attack.

If agreement is as general as Professor Woodruff avers—and the U.S. Army would seem another notable dissentient—then what we need is a massive campaign to depopularize chloroquine in the minds of very numerous doctors throughout the tropics, not to mention some malariologists. Failing this, the isolated informed voice will be crying in the wilderness and exposing the individual patient to slight risk on theoretical grounds which it is unfortunately too late to apply.—I am, etc.,

P.O. Box 20693,
Dar es Salaam,
Tanzania.

H. DE GLANVILLE.

REFERENCE

[1] Woodruff, A. W., *Practitioner*, 1967, 198

Appointments Systems

SIR,—Is is not high time that the idle pretence of an appointment system operating in hospitals should be dropped? I am tired of listening to the complaints of patients who have been given an appointment for a certain time and then have been kept waiting two or three hours beyond the appointed time. I send patients mostly to two teaching hospitals of deservedly high reputation and things are no different there.

I once telephoned an appointments clerk myself, and the charming young lady gave me a certain time for a patient. An hour or so later I telephoned again for another patient and I was given exactly the same time. When I pointed out that the consultant could not possibly see more than one patient at a time, I was met by the excuse that some patients do not turn up and "the doctor must not be kept waiting."

I have even had it reported to me by patients that 20 or 30 of them had been given the same time to attend. This seems to me pure deception. An appointments system which gives the same time to all the patients is no appointments system at all. Why then should it pretend to be? We might at least be honest and disclaim any pretence at an appointments system, that would at least be honest, but what happens now is pure humbug and deception.—I am, etc.,

London W.1.

A. J. HAWES.

Diabetes in the Tropics

SIR,—In his excellent paper on the above topic (17 June, p. 747) Professor S. R. A. Dodu stated that 20% of diabetic patients reporting for the first time to the Korle Bu Hospital in Accra confirmed their suspicions by "tasting their urine." May I mention yet another sign of glycosuria I have observed when several diabetic patients, reporting similarly in Sierra Leone, another tropical area, said they had noticed "many ants in their chamber pots the next morning"?—I am, etc.,

Plaistow Hospital, London E.13. A. F. TUBOKU-METZGER.

Portable Pharmacy

SIR,—I possess a portable pharmacy similar to that described by Dr. P. W. Mathew (3 June, p. 641). The measurements are 11½ × 8 × 10 in. (29 × 20.3 × 25.4 cm.). It is probably a hundred years old. Many are of greater antiquity.

One was offered recently at an antique shop in Towyn, North Wales, for £40. *Fama habet* that a leading London auctioneer sold the same article later for £600.

I trust that Dr. Mathew's box has a similar remote lineage.—I am, etc.,

High Wycombe, Bucks. G. S. W. EVANS.

Blood Pressure Monitoring

SIR,—It is at least 40 years since a medical practitioner in charge of an antenatal patient became ashamed if his patient's abnormal rise of blood pressure went undetected.

The report of Dr. W. E. Miall and Mr. H. G. Lovell (10 June, p. 660) raises the question of how long all patients are to wait before the medical profession comes to regard itself responsible for seeing that each patient has the blood pressure examined yearly, and if necessary an attempt made to return the blood pressure to the safe zone.—I am, etc.,

London S.W.19. AMY M. FLEMING.

Muscle Stiffness and Vitamin C

SIR,—With reference to the published findings of Drs. L. Corbett and A. Barr (8 July, p. 113) on muscle stiffness and vitamin C, I regret to note that the dosage scheme found effective by me had not been followed—namely, 500 mg. of vitamin C *in one dose* one hour before the unaccustomed exercise—and 400 mg. *in one dose* directly after it.—I am, etc.,

London S.W.7. I. H. SYED.

Folate Deficiency in the Elderly

SIR,—Attention has been drawn to this subject in the *B.M.J.* (10 June, pp. 652 and 670).

During a recent trial concerning the efficacy of total-dose infusion of iron dextran in correcting iron deficiency anaemia in the elderly[1] serum folate levels were estimated, using the method described by Spray,[2] on the patients before and six weeks following treatment. The patients' age range varied from 69 to 89, half being treated in the day hospital and half as in-patients. The serum folate range in 37 pre-infusion subjects was 1–19.7 mμg./ml. (mean 5.3; S.D. 3.4 mμg./ml.), and at six weeks post-infusion their range was 1.5–26 mμg./ml. (mean 4.6; S.D. 2 mμg./ml.). Six pre-infusion patients had values below 3 mμg./ml. and nine post-infusion patients had values below 3 mμg./ml. Twenty-eight patients with an initial serum folate level below 6 mμg./ml. had a mean haemoglobin of 61% (S.D. 11 mμg./ml.) and six weeks after treatment had a mean haemoglobin of 75% (S.D. 11 mμg./ml.), while nine patients with initial folate levels over 6 mμg./ml. had a mean haemoglobin of 65% (S.D. 8 mμg./ml.) and a post-treatment haemoglobin of 75% (S.D. 11 mμg./ml.).

Attempting to correct iron deficiency in the elderly by total-dose infusion of Imferon (iron dextran) does not seem to influence the serum folate levels of the patients concerned, and probably the initial serum folate level does not influence their response to iron dextran as judged by the haemoglobin rise. However, as serum folate levels probably do not accurately reflect tissue state, the diagnosis or exclusion of folate deficiency on serum folate levels alone appears unjustified.—I am, etc.,

JAMES ANDREWS.

West Middlesex Hospital,
Isleworth,
Middlesex.

REFERENCES

[1] Andrews, J., Fairley, A., and Barker, R., *Scot. med. J.*, 1967, 12, 208.
[2] Spray, G. H., *J. clin. Path.*, 1964, 17, 660.

Sliding Board for Severely Disabled Patients

SIR,—Now that the more severely disabled are able to drive, with the introduction of automatic gear change in smaller cars, greater independence can be obtained by the use of a sliding board. Whereas before it was necessary for tetraplegics to be lifted bodily into their cars, now they can transfer from wheelchair to motor car, if not entirely alone, with the minimum of assistance.

A "sliding board" has been developed by several tetraplegics and paraplegics at the Chaseley Trust for Disabled Ex-Servicemen at Eastbourne, and is made in their own workshops by them. It is constructed quite simply and cheaply from selected wood covered with Formica, which provides a smooth non-abrasive sliding surface. A small cushion may be placed under the buttocks as extra padding, but we find that the board is sat upon for so short a time that this is not usually necessary.

Although we have not tested the board among geriatric or other types of disabled patients, we feel sure that they too could easily benefit from it, and apart from use with the car it can also come in handy in the house to transfer from bed to chair, chair to lavatory, etc.

The ideal size was found to be 2 ft. 6 in. by 6 in. by ¾ in. (76 cm. × 15 cm. × 1.9 cm.). Further information about the sliding board can be obtained from Handcarved Signs, Chaseley, Southcliff, Eastbourne, Sussex.—I am, etc.,

MARY SEIFFERT,
Senior Physiotherapist,
The Chaseley Trust.

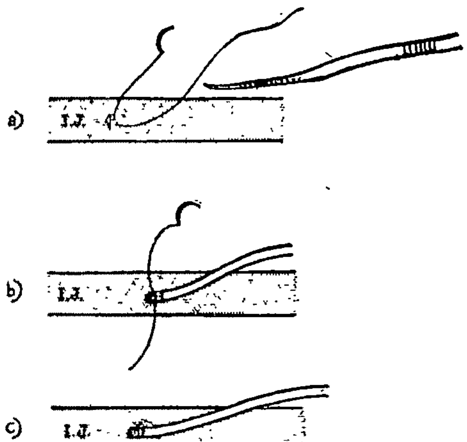
Eastbourne, Sussex.

Ventriculo-atrial Shunt for Hydrocephalus

SIR,—Ventriculo-atrial shunt procedure is now the commonly accepted treatment for progressive hydrocephalus in infants. It appears to be the common practice to tie the internal jugular vein over the venous catheter during the operation. Tying the internal jugular vein will result almost certainly in formation of a thrombus between the site of ligature and the beginning of the superior vena cava. This thrombus may be an important factor in causing septicaemia and in blocking the shunt mechanism.

It is quite feasible to insert a venous catheter in the internal jugular vein without tying that vein.

The internal jugular vein is dissected above the sterno-clavicular joint and two loops of thread (No. 40) are passed around it. The two loops are pulled apart to stretch the vein and a suture is placed in the vein wall between them using 4/0 silk on an atraumatic needle. This is left untied (see Fig). A small nick is made in the vein wall by sharp-pointed scissors just distal to this suture. The venous catheter is introduced through this and pushed in until the tip is believed to be in the atrium. The loose ends of the suture in the vein wall are now tied over the nylon ring in the venous catheter. If the nick in the vein wall is small enough no further sutures are needed. The scalp wound is closed next and the neck wound is closed last, after the loops of thread round the vein are removed.



Showing the technique of inserting the venous catheter into the internal jugular vein (I.J.).

The first two patients in which this technique was used are alive and well six months after the operation. There was no leakage of blood from the site of insertion of the venous catheter into the vein.

The venous catheters used were made by The Holter Company, Bridgeport, Penn., U.S.A., and the valves used were those made by Mr. Stanley C. Wade and Mr. Ronald Dahl for Mr. Kenneth Till.

—I am, etc.,

VASANT TALWALKER.

Bombay, India.

Annual Representative Meeting

Sir,—May I, through the courtesy of your columns, express my protest at what occurred on the last day of the Bristol A.R.M.?

Very many of the motions down for debate under the heading "Hospital and Consultant Services" were glossed over, without debate or discussion of any kind, as a matter of expediency. Thus whole blocks of motions, at least two of which concerning distinction awards for consultants (501 and 608) contained important matters of principle, were accepted as references to Council without the Representative Body being given the opportunity to hear argument on both sides, so that the representatives' own views could be formed, altered, or augmented.

Why, when the Association claims to speak for all sections of the profession, was this allowed to happen? The short answer is that the Representative Body ran short of time. It ran short of time because some few Divisions were allowed a disproportionate length of platform time, endlessly discussing points of detail which should have been dealt with or referred to the appropriate committee.

I refer particularly to the debate on the new constitution, which time and again descended to the level of "Shall we have By-law No. so-and-so, Subsection C, paragraph 3, second sentence, first line, fourth word, or not." I also refer, however, to the debate on General Medical Services, much of which was concerned with detail, important in itself, but properly dealt with by the G.M.S. Committee in session, not by the Representative Body in debate.

It should be unnecessary to reiterate, but evidently it is, that the A.R.M. is concerned with matters of principle, and that it delegates detailed debate to the committees reporting to it. Perhaps the chairmen of the committees concerned, together with the chairman of the Agenda Committee, would note these strictures, so that in future years we as a Representative Body may be given the opportunity of discharging our duties adequately.—I am, etc.,

J. D. Shapland.

Modbury,
South Devon.

Casualty Department—or G.P. Service?

Sir,—The letter by Mr. B. J. Preston and his co-authors (1 July, p. 46) makes somewhat depressing reading, though their experience is probably typical of many hospital casualty departments in large towns.

Of the six categories of patient listed by Mr. Preston it would seem that only visitors to London (8% of his casual attenders) should be considered as eligible for casualty. Four of the other groups (more convenient to go to hospital; patient already attending the hospital for another condition; patient wanted a second opinion; and no general-practitioner surgery on that day) should not normally be accepted at casualty, though exceptionally those in the last group might be seen once and then referred back to the general practitioner. As to difficulty in registering with a general practitioner, there should be some reservation in accepting many of these patients' statements. Registration in central London can be difficult, but a fair proportion of such patients have simply been too feckless or thoughtless to bother about finding a general practitioner. This, indeed, is borne out by Mr. Preston's statement that 25% of all patients resident in that area (excluding visitors and those in transit) are not registered with a general practitioner. With certain doctors' lists as loaded as they are, and with the present miserable system of capitation, it is hardly surprising that some general practitioners are disinterested in collecting more "heads." Other doctors are understandably resentful that people, long resident in an area, often fail to register until they are ill.

The right answer to this problem is not to convert the hospital casualty department into a glorified health centre, but to take steps to ensure that general practitioners are encouraged to provide a proper service and that the public uses that service responsibly. At the present time there is increasing tendency for patients to bypass the general practitioner. It is virtually a daily experience for casualty doctors and nurses to be told by patients that they have "paid their stamps" and are "entitled to treatment." However much these mistaken beliefs may motivate a largely ignorant and politically misguided public, it is surely the doctor's task to ensure that he does not encourage such widespread abuse of the hospital service. In saying this I am mindful of the fact that daily attempts to "educate" the public, however appealing such an enterprise may seem to politicians and the more starry-eyed of our colleagues, are largely doomed to failure. Nurses and doctors, tiring of the need to argue with patients about their eligibility to attend casualty, often find it simpler to capitulate to public demand.

The problem posed by Mr. Preston and his colleagues does not, in my opinion, argue for the "open door" in casualty, but is surely one of the many cogent and forceful arguments which the profession should advance in demanding root and branch reform of the N.H.S. One hundred per cent. free-at-the time medicine, with its total failure to differentiate the urgent and vital from the more trivial and unimportant, is the chief reason why the N.H.S. is cracking up. Continuation of this type of service, with increasing disenchantment of doctors, must eventually lead to massive breakdown in medical standards.—I am, etc.,

Reginald S. Murley.

London W.1.

Psychological Medicine Group Conference

Sir,—Discussing Section 29 of the Mental Health Act, 1959, Dr. Morris Markowe (10 June, p. 703) claims that the survey of compulsory admissions to 27 psychiatric hospitals conveys a "false impression."

The principal facts (unpalatable to many) reported in the original paper[1] and in a subsequent letter[2] may, however, be conveniently tabulated as follows:

Admissions to Psychiatric Hospitals During 1963

Total	Informal	Sect. 29	Sect. 25	Sect. 26
National Figures				
173,718	138,575 (80%)	22,184 (13%)	8,170 (5%)	2,059 (1%)
Sample of 27 Psychiatric Hospitals				
31,540	24,041 (76%)	4,261 (13·5%)	2,510 (8%)	491 (1·5%)

The psychiatric hospitals in the sample were not specially selected as implied in the report of the Psychological Medicine Group Conference (*Supplement*, 20 May, p. 119); instead two were chosen randomly from each of the 15 regions in England and Wales (three did not complete the questionaries). The sample's representativeness is illustrated by the close approximation of the percentage figures in the national and sample groups. The 1964 national figures are comparable to those of 1963 with respect to Sections 29 and 25,[3] and in these years Section 29 was used more than twice as frequently as Section 25, which is contrary to the letter and spirit of the Mental Health Act.

Is the position all that different now? In 1966, Barton and Haider concluded that "some 5,000 people are now being admitted to psychiatric hospitals in England and Wales annually without adequate scrutiny of the need for compulsion."[4] It will be interesting to observe the impact of the circular letter of 4 October 1966 from the Chief Medical Officer of the Ministry of Health to medical administrators of psychiatric hospitals which emphasized restricting "the use of the powers under Section 29 to the minimum." Dr. Markowe might perhaps care to examine this point for possible inclusion in his forthcoming report.

Unfortunately, it is impossible to reach any general conclusions from analysis of the figures for Shelton Hospital, which has always shown a marked preponderance of Section 25 over Section 29 admissions. In my view this is due to several factors which have been fully elaborated elsewhere,[5] and which if adopted nationally might reduce the proportion of Section 29 admissions to a generally acceptable level.

Meanwhile, in the absence of further conclusive evidence to the contrary, I am inclined to support Dr. Barton's contention[6] that "the present Act is not obsolescent" and that "it is being misused."—I am, etc.,

J. C. Barker.

Shelton Hospital,
Shrewsbury.

REFERENCES

[1] Enoch, M. D., and Barker, J. C., *Lancet*, 1965, 1, 760.
[2] —— ibid., 1965, 1, 1161.
[3] *Brit. Hosp. J. soc. Serv. Rev.*, 1965, 75, 1384.
[4] Barton, R., and Haider, I., *Med. Sci. Law*, 1966, 6, 147.
[5] Barker, J. C., *Brit. Hosp. J. soc. Serv. Rev.*, 1965, 75, 1577.
[6] Barton, R., *Lancet*, 1966, 2, 1417.

Merit Awards in General Practice

Sir,—Surely the time for your closing the correspondence in the *B.M.J.* on this topic is long overdue.

Reading letters on it under different headings week after week gives the impression that you are under pressure from sections of the medical establishment.—I am, etc.,

S. H. F. Howard.

Barton-on-Humber,
Lincs.

Obituary Notices

D. IOAN-JONES, B.SC., M.B., B.S., F.R.C.S.

Mr. D. Ioan-Jones, emeritus surgeon to the United Cardiff Hospitals, died in Cardiff on 27 June. He was 70.

David Ioan-Jones was born in 1897, and was educated in the University of Wales, graduating B.Sc. in 1919. For his clinical studies he came to London and entered the Westminster Hospital, qualifying with the Conjoint diploma in 1921, and graduating M.B., B.S. three years later. He became house-surgeon and house-physician at the Westminster and surgical registrar to Sir Stanford Cade and the late Mr. Rock Carling. He took the F.R.C.S. in 1929, and in 1932 was appointed assistant surgeon to the Cardiff Royal Infirmary, where he remained until his retirement as senior surgeon in 1963.

As time went on Ioan-Jones won the complete confidence of the profession, and the demands on his services grew almost beyond endurance. Then in 1936 came a sudden break. He had to be admitted to Midhurst Hospital, and while there he had to undergo a thoracoplasty, performed by his old teacher, the late Mr. Tudor Edwards. He made a complete recovery, and was back at work in 1938 at the same intensity until he retired in 1963. For many years he covered a huge mileage, both day and night, especially during the war years, and he always made himself available to serve others.

In 1953 he was vice-president of the section of surgery at the Annual Meeting of the B.M.A., and in 1960 he was appointed for a period of five years as representative of the University of London on the court of governors of the University College of South Wales and Monmouthshire, Cardiff.

As a general surgeon David Ioan-Jones was outstanding, both in his clinical assessment and in his techniques. His rapid gentle movements inside the abdomen were a real pleasure to observe, as was the speed with which he tied his reef knots. He was one of the pioneers in performing adrenalectomy in cases of breast cancer, and the records were carefully kept. Despite his vast surgical experience he could not be persuaded to put pen to paper. One felt that this was a great loss. He used to say that there are too many people doing this. After a hard day's work he preferred to relax with his wife and friends, for he enjoyed good company.

A man of tremendous courage and dignity, he never sought favours by flattery. It is natural to believe in great men. The world is upheld by the veracity of good men ; they make the earth wholesome. David Ioan-Jones was one of these in his own quiet dignified way. "He is great who is what he is from nature." This tranquillity was made possible by the ideal home life that was his blessing.

We extend our deepest sympathy to his wife, Barbara, and his daughter, Mrs. Mathias.—R. D. O.

W. BRIGGS, M.B., B.S., F.R.C.S.

Mr. W. Briggs, a former consultant surgeon to Blackburn Royal Infirmary, died on 2 July. He was 87.

Walter Briggs was born in Blackburn on 15 June 1880. He entered Owen's College, Manchester, in 1897, graduating M.B., Ch.B. in 1902 with second-class honours in the Victoria University, which still included Owens College, University College, Liverpool, and Yorkshire College, Leeds. Two years later he gained the additional qualification of M.B., B.S.Lond. In the meantime he had held resident posts at the Blackburn Royal Infirmary. In 1905 he went to Vienna, then the Mecca of postgraduate education. While there he met, and became engaged to, Miss Florence Taylor, an Australian-born pupil of the great piano teacher Leschetizky. In 1908 Miss Taylor came to Blackburn to become Mrs Walter Briggs, abandoning the idea of a career as a concert pianist for a marriage of great happiness. Their hospitable Blackburn home was always full of the sound of music. In the 1930s my wife and I spent many enjoyable evenings in Blackburn, where I was allowed to play the second piano part to Florence Briggs as soloist in well-known concertos and other works arranged for two pianos.

Walter Briggs started his career in Blackburn as a single-handed general practitioner, but was soon appointed to the honorary staff of the Blackburn Royal Infirmary as assistant surgeon—probably first acting as anaesthetist, as the custom was in those days. The first world war was a turning point in his career. He joined the 64th Casualty Clearing Station as a surgical specialist. The nucleus of this unit was recruited in the Western Command, and for a short time was attached to the 2nd Western General Hospital, Manchester, before going to France in 1917. In 64 C.C.S. Walter Briggs served with distinction with the rank of acting major, being mentioned in dispatches, and there came under the influence of the late Sir Ernest Rock Carling and the great Harvey Cushing, who was working near by at 46 C.C.S. (Mendinghem). In Harvey Cushing's *Surgeon's Journal* there are brief references to these encounters—"To tea with Carling and Briggs" (15 October, 1917). "A full operating day, Briggs and Carling from No. 64 looking on" (Saturday, 20 October 1917). After the war Walter Briggs gradually relinquished general practice, and on the retirement of Mr. R. Y. Aitken became the sole consulting surgeon in the Blackburn area. His wise leadership in the clinical and administrative affairs of the Blackburn hospitals became undisputed. In 1928–9 he was chairman of the Blackburn Division of the Bristol Medical Association, and in 1945 he was elected president of the Manchester Surgical Society, a signal honour for a surgeon from a non-teaching centre. In his earlier years his surgical interests, which were always wide, were for a time focused on orthopaedics. He organized and took charge of the first orthopaedic clinic established in Blackburn with a unit for long-stay patients in the municipal hospital at Queen's Park. During this period he attended regularly the meetings of the British Orthopaedic Association. Later, when the Blackburn Royal Infirmary appointed its first specialist orthopaedic surgeon, Walter Briggs's surgical repertory had become restricted to the procedures of major abdominal surgery and the surgery of malignant disease. His technique in the operating-theatre always showed how deeply he had been influenced by watching Harvey Cushing at work in France. In 1950 Walter Briggs was elected to the Fellowship of the Royal College of Surgeons of England under the "twenty years" rule. This distinction could have come to him much earlier, if by chance he had been an M.R.C.S. A change in the regulations made it possible for the College to recognize him at the age of 70, at the end of his active surgical life.

Walter Briggs was one of the original members of the Manchester Regional Hospital Board, on which he served for seven years, from 1948 to 1955. On his retirement from the affairs of surgery he made several voyages up the Amazon as a ship's surgeon. His devoted wife died in 1954. He is survived by his daughter, Mrs. Arthur Carter, of Darwen, five grandchildren, and four great-grandchildren.—H. P.

J. R. writes: As a general practitioner closely associated with Mr. Briggs for 33 years, I would add my appreciation of a man who was not only a close personal friend but also a very esteemed colleague. Mr. Briggs was that rare person who had great integrity, professional honesty, absolute devotion to medicine and surgery (for he was a general practitioner before he became a consultant in surgery), and an appreciation of the realities of life. He loved the fine things of life : flowers, good music, good literature, a beautiful day, and, above all, the Lake District, which he knew intimately. He was also a sportsman, both actively as a young man and later as a spectator.

Mr. Briggs's professional ability was great as a diagnostician and as a surgeon. To have him to see a case in a consultative capacity was a great experience both for the patient and for the general practitioner concerned. His skill in diagnosis and his understanding of the human problems involved were a pleasure to doctor and patient alike. For many years he was honorary consulting surgeon to Blackburn Royal Infirmary, where his name is held in great respect and awe, and where a ward is named after him. With the advent of the National Health Service in 1948 he stayed on as a consulting surgeon for two more years, until he was 70. He was a member of the hospital management committee and one of the first members of the newly formed North-west Regional Hospital Board, where his great gifts of knowledge and personal charm helped to launch this enterprise.

Mr. Briggs had lived with his daughter since the death of his wife, and looked after quite a large garden until August 1966, when his health began to fail. He bore his last illness with great fortitude and bravery, and with the spirit which had guided him all through his long life. To have known him so intimately was a great and rare privilege.

Brigadier R. V. FRANKLIN, O.B.E.
M.B., B.CH., B.A.O., A.M.S.(RET.)

Brigadier R. V. Franklin, a former inspector of training, Army Medical Services, died suddenly on board his yacht on 2 July. He was 64.

Robert Vincent Franklin, son of Lieutenant-Colonel R. J. Franklin, R.A.M.C., was born at Aldershot on 27 January 1903, and was educated at the University of Dublin, graduating M.B., B.Ch., B.A.O. in 1925. He went to sea for a short time as ship's surgeon before joining the R.A.M.C. in 1926 and specializing in otology. He was sent to India in 1927, where he served until he was sent to Burma and the Far East during the second world war. He was mentioned in dispatches, and in 1945 was appointed O.B.E. After serving in Germany and Egypt he returned to Britain for a period of four years as assistant director of medical services in Scotland and northern England before going out to Singapore in 1952. In 1953–4 he served in Korea as deputy director of medical services and then returned to Britain as inspector of training, Army Medical Services, from 1955 to 1960, when he retired from the Army and again took up a position as ship's surgeon.

R. M. H. writes: Bob Franklin first went to sea in 1926 because of his tremendous love of it, which never forsook him, and it was fitting that his passing should have occurred while yachting. After a life afloat he joined the R.A.M.C. and became an E.N.T. specialist, at which he was extremely gifted. With promotion came more administrative responsibility. His close co-operation with the Royal Naval medical services gave him infinite pleasure.

On his retirement from the Army with the rank of brigadier he joined Cunard, and served as surgeon and principal medical officer in their *Parthia, Media, Sylvania, Carinthia, Mauretania, Queen Mary,* and *Queen Elizabeth.* He was a strict disciplinarian, and his departments ran well. Clinically he was sound, and even after many years with administrative work he could still perform general surgery admirably. His zest for the social life made him an incomparable shipmate, and his table from the passengers' angle was always sought after for its wonderful conviviality. There is no doubt about it that those who go to sea possess a quality of human understanding that other spheres miss, and Bob Franklin possessed this in wide measure.

H. L. GULATI, M.R.C.S., L.R.C.P.
D.O.M.S.

Dr. H. L. Gulati, a general practitioner and ophthalmologist and former London County Councillor, died suddenly on 13 June. He was 70.

Harbans Lall Gulati was born in the Punjab in 1896 and received his medical education at Lahore. In 1916 he became an officer in the Indian Medical Service and saw service on the North-west Frontier. In 1920 he worked his passage to England. His medical degrees were not recognized here, and he had not only to take his matriculation and qualifying exams again but had once more to go completely through medical school. Entering Charing Cross Hospital Medical School, he qualified with the Conjoint diploma in 1926. Almost at once he took up general practice in Battersea and remained in active practice there for over 40 years up to the time of his death.

Dr. Gulati entered politics in 1934 and became a Conservative member of the borough council, serving on committees concerned with health, libraries, national savings, and a variety of other subjects. In 1940 he became a magistrate and served regularly on the South-western Petty Sessional Division thereafter. During the second world war his social work, particularly for children and old people, is well remembered. He was active in pioneering the "meals-on-wheels" service, and in the St. John and Red Cross organizations. In 1945 he took the D.O.M.S., and soon afterwards began his association with the Royal Westminster Ophthalmic Hospital.

In 1947 Dr. Gulati resigned from the Conservative party over their antagonistic attitude to the National Health Service. Shortly afterwards he joined the Socialist Medical Association, and became its secretary. Joining the Labour party, he soon found himself on the borough council once more. In 1955 he fought the London County Council elections, and was returned as a member for South Battersea. Later he became prospective Parliamentary candidate, but pressure of work made him give up active politics and he never achieved his ambition of getting into Parliament.

Lall, as he was known to practically everyone, was a great man. He faced problems squarely, and overcame them with a combination of strength, industry, and tact. The shortest encounter with him left a lasting impression. He was held in awe by many and in great esteem by his patients, many of whom travelled great distances to see him after leaving the district. He was a fighter and had a remarkable zest for life, and loved good food and good company. He seldom spoke of his early days in England, when he arrived penniless and without friends or relatives. He did unskilled work, often at night, to put himself through medical school, and he vowed others would not have to suffer similar adversity. For this reason he later became an active member of the management committee of the Indian Y.M.C.A. and saw this institution completely replanned and rebuilt. He was also a Freemason. Recently he had returned from Japan and had produced a paper on the legal system of that country, and at the time of his death he was writing his autobiography.

He is survived by his widow, two sons, one of whom is in the medical profession, and one daughter.—R. L. G.

Colonel P. J. RYAN, M.C., M.A., M.SC.
M.B., B.CH., B.A.O., A.M.S.(RET.)

Colonel P. J. Ryan, formerly of the Army Medical Service, died peacefully at Rye Hospital on 29 June—his eightieth birthday—after a distinguished medical career in the Army.

Peter John Ryan was born in Ireland on 29 June 1887, and received his medical education at the University of Dublin, graduating M.B., B.Ch., B.A.O. in 1911. A keen sportsman, he enjoyed hunting, fishing, polo, yachting, and skiing, and won many trophies at golf. A rugger player, he captained Lansdowne Rugby Club in Dublin. In his leisure moments he was a keen bridge player, winning an international trophy. He was one of the last batch of regular Army officers who joined the R.A.M.C. in 1914 by free competition, but before doing so he had travelled round the world twice as a ship's doctor and had learned much about men. He served in the first world war and was awarded the M.C. in 1918 and mentioned in dispatches. He was also thrice awarded the Croix de Guerre. He served during the 1936–7 campaign against the Fakir of Ipi on the North-west Frontier of India, and between the two world wars saw active service in Egypt, Mesopotamia (Iraq), and India, again being mentioned in dispatches. He commanded "A" company at the R.A.M.C. depot for several years. In the second world war he served as A.D.M.S. of North Wales district of Western Command, where I first met him at Shrewsbury headquarters, and served under him for three years.

Peter Ryan as an officer and doctor and in his whole life was a man of the highest moral, ethical, and Christian standards, and in his Army work and administration he lived up to them to the hilt. He was energetic and conscientious in everything he did and ordered to be done, giving and demanding efficiency in every detail by himself and those under him alike. He was one of those men of whom one can truthfully say one was glad to have known and worked with him. In retirement he was full of energy and efficiency in his beautiful home and garden at Icklesham in Sussex. He had become very interested in horticulture, winning many awards at local shows. His continued enthusiasm for efficient activity found outlets by his participation in village life and affairs. He was a member of Icklesham parish council, chairman of several local charities, including the Icklesham almshouses—the modernization of which was almost entirely due to his tireless negotiation and hard work. For many years he was chairman of Queen Mary's Home for Retired Army Nurses, and president of Pett and District British Legion. He was also the honorary treasurer of Area I Sussex Home Physiotherapy Service, into the inauguration of which service, and to the running of it afterwards, both he and his wife poured much energy. He also organized the covenant scheme for St. Anthony's Roman Catholic Church in Rye.

It is good that he lived to such a grand old age to enjoy useful work after his professional retirement, but his loss is still a very great one, and our sympathy goes out to his widow, two daughters, and five grandchildren, all of whom loved him dearly and will greatly miss him.—R. M. P.

C. J. LEWIS, M.D., M.R.C.P., D.P.H.

Dr. C. J. Lewis, a general practitioner at Walsall, died on 20 June. He was 69.

Charles John Lewis was born in Birmingham on 28 April 1898, and was educated at King Edward's School and Birmingham University, graduating M.B., Ch.B. with honours in 1921, and taking the Conjoint diploma the same year. After house appointments at Birmingham General Hospital and the Queen's Hospital for Children in London he proceeded M.D. in 1922 and took the M.R.C.P. two years later. He went into general practice at Cradley Heath, Staffordshire, in 1927, and in 1934 took the D.P.H. He came to Walsall in 1932, where he worked hard in a large industrial practice, combining this with the posts of medical officer to the G.P.O. and as one of the town's parish poor-law doctors. He also at one time held the posts of anaesthetist to Burntwood Military Hospital, and clinical assistant at Birmingham Skin Hospital.

Dr. Lewis put in a lifetime of hard and devoted work in the Midlands up to the onset of his illness in February of this year. He was due to retire at the end of June, and was planning many projects to be fulfilled during his retirement. He was a keen member of the B.M.A., always taking an active and enthusiastic part in Divisional meetings. His hobbies included gardening—orchids and carnations being his principal interest—and china, particularly that of Staffordshire, Chelsea, and Nantgarw. He is survived by his wife and two adopted daughters, to whom we extend our deepest sympathy.—W. B. McC.

J. STIRLING, M.A., M.D.

Dr. J. Stirling, formerly in general practice at Aldridge, Staffordshire, died in Walsall General Hospital on 3 June at the age of 73.

John Stirling was born in Alexandria, Dunbartonshire, in 1893, and received his education at the Vale of Leven Academy. As a young man he ran a boys' club at Bonhill North United Free Church, and from this stemmed his deep interest in the welfare of young persons, which continued throughout his life. After a short period as a schoolmaster he enlisted in the R.A.M.C., from which he was discharged after a serious accident which left him with a permanent disability. He never complained, and never allowed the disability to interfere with his activities. It was after his Army service that he decided to study medicine, and he entered Glasgow University, where he graduated M.B., Ch.B. in 1920, and M.A. in the same year. He proceeded M.D. in 1931. He settled in general practice in 1921 in Aldridge, where he remained for the whole of his professional life. He was the perfect general practitioner, devoted to his patients and beloved by them all.

Dr. Stirling had a wide range of interests, and for many years he was a very active member of Walsall Hospital Management Committee. He was a magistrate and took a particular interest in the juvenile court. For some years he was medical officer at Druids' Heath Approved School, and then chairman of the managers, and was an accepted authority on the problems of juvenile delinquency and the work of approved schools. He was a founder member and past president of Aldridge Rotary Club, one of the founders, and for many years chairman, of the Aldridge Community Association, and an enthusiastic exponent of Scottish dancing. In 1925–6 he was president of the Walsall Burns Club. He was a divisional surgeon in the St. John Ambulance Brigade for upwards of 40 years, and throughout the second world war he was medical officer in charge of Aldridge First Aid Post. From 1938 to 1941 he was chairman of the Walsall and Lichfield Division of the British Medical Association. A keen gardener, he was never happier than when sharing his plants and flowers with his friends, so many of whom have treasured memories in the form of plants which started their lives in his lovely garden. Throughout his life he was a sincere and devoted member of the Presbyterian Church, and for a great many years he was Session Clerk of Walsall Presbyterian Church. His two outstanding qualities were friendship and leadership: his friendship was loyal, lasting, and completely unselfish, and his leadership was by personality, example, persuasion, and explanation, but never by dictation.

To his widow and to his two sons (one of whom was in general practice with him) his many friends and associates extend deep and sincere sympathy.—F. L. R.

T. E. JAMES, M.R.C.S., L.R.C.P.

Dr. T. E. James, a general practitioner of Clydach Vale, Rhondda, died at his home on 1 June after a long illness. He was 65.

Thomas Ellis James was born in Clydach Vale on 14 April 1902, and received his medical education at the Welsh National School of Medicine, Cardiff, qualifying with the Conjoint diploma in 1927. He spent a short time as an assistant at Cilfynydd, Pontypridd, before returning to Clydach Vale to build up his own practice single-handed. He worked exceedingly hard, and by the start of the National Health Service had succeeded in creating a large practice spreading well beyond Clydach Vale into neighbouring districts. In 1953 he entered into partnership and continued his work in the practice where he knew his patients so well. One of his greatest assets was an encyclopaedic memory for all his patients and their interrelationships, and this enabled him to be a real family doctor and to help his patients in so many ways other than in purely medical matters.

Dr. James was active outside his practice, and was chairman of the North Glamorgan and Brecknock Division of the British Medical Association in 1961–2, a past-president of the Rhondda Medical Society, a past chairman of the Rhondda Rotary Club, and also served on many local committees. He was a serving officer of long standing of the St. John Ambulance Brigade. A superb raconteur and after-dinner speaker, he will be remembered by many.

All his patients—and many who were not patients—held Dr. James in great esteem. He was kind to everyone and always ready to help. On his retirement on 31 March of this year his patients and friends showed their appreciation by presenting him with a substantial testimonial. Although he was aware of the inevitable outcome of his long illness, he bore it with great courage and without complaint.

All extend their deepest sympathy to his widow and their family.—D. C. S.

A. H. FERGUSON, B.A., B.M., B.CH.

Dr. A. H. Ferguson, a general practitioner in Lincoln, died suddenly on 27 June. He was 49.

Alan Hudspeth Ferguson was born at Anfield Plain, County Durham, on 22 June 1918, and was educated at Newcastle Grammar School and Nottingham High School, gaining a scholarship at Wadham College, Oxford, where he obtained first-class honours in physiology before proceeding to clinical studies at the London Hospital. He graduated B.M., B.Ch. in 1942. After an appointment as house-physician at the Norfolk and Norwich Hospital he served during the second world war as captain in the R.A.M.C. After demobilization in 1946 he entered general practice in Lincoln.

Alan Ferguson ("Fergi") gave a quite exceptional quality of medical care to his patients. His work was his answer to the critics of family practice, especially to those who complain of diminishing public confidence in general practitioners. This was due in large measure to the time he was prepared to devote to them and the energy he put into his own continued medical studies. These and a degree of self-discipline obvious to all who knew him enabled him to develop a particularly personal type of family practice rarely found in these days, especially in urban districts. Such an approach naturally made him sought after as a general-practitioner obstetrician, an aspect of work which he enjoyed. His competence and knowledge of his patients enabled him to accept justifiably much responsibility, thus sparing many of them unnecessary investigation and treatment. His work left little time for committees, but for many years he was a member of Lincoln No. 2 Hospital Management Committee.

Those who came to knew Fergi well were, at first, surprised by his wide range of reading, and were glad when in recent years he took up photography to add a special interest to his brief travels in Europe, often motivated by his interest in history. His sudden death will be a great loss to Lincoln, and his many patients, colleagues, and friends will miss his guidance and dedication. We extend our deepest sympathy to his wife and his two sons, one of whom is studying medicine.—E. P. M.

News and Notes

EPIDEMIOLOGY

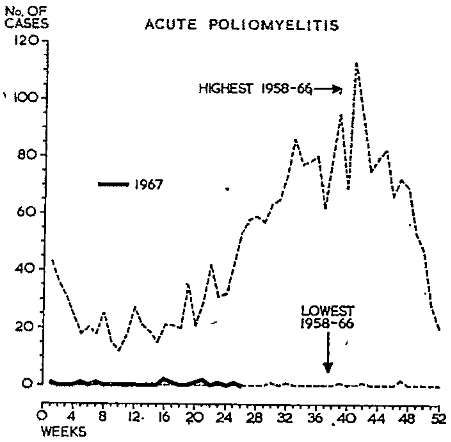
Eire in First Quarter

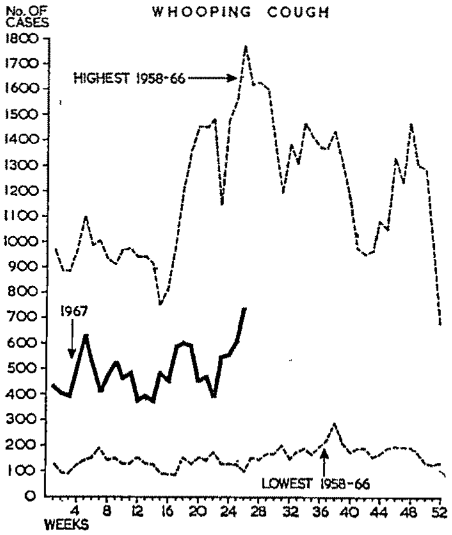
The birth rate in Eire during the first quarter of 1967 was 20.5 per 1,000 population, being 0.5 below the rate for the preceding first quarter. The infant mortality rate was 25 and the neonatal mortality rate was 15 per 1,000 registered births, and these rates were 2 and 3, respectively, below the rates for the first quarter of 1966. The death rate was 11.2 per 1,000 population, being the lowest rate for any recent first quarter.

Deaths from the principal infectious diseases included 43 from influenza, 33 from gastroenteritis under 2 years, 2 from measles, and 1 from whooping-cough. Deaths attributed to cancer numbered 1,230, and of these 512 were due to malignant neoplasm of the digestive system and 222 to malignant disease of the respiratory system. There were 1,447 deaths from coronary and arteriosclerotic heart disease and 741 from other myocardial degeneration.

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of acute poliomyelitis and whooping-cough in England and Wales. Figures for 1967 are compared with the highest and lowest figures for each week in the previous years shown.





INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **1 July** (No. 26) and corresponding week 1966.

Figures of *cases* are for the countries shown and for Greater London. Figures of *deaths* and *births* are for the whole of England and Wales (London included), Greater London, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0		0	0	1	0	
Dysentery ..	514	58	96	20	6	542	151	75	15	9
Encephalitis, acute ..	0	0		0		3	2			
Enteric fever:										
Typhoid ..	0	0	1	0		4	0	0	0	
Paratyphoid	1	0	6B	0		4	0	0	0	
Food-poisoning	132	43	8	4		206	27	27	1	
Infective enteritis or diarrhoea under 2 years				16	66				15	36
Measles* ..	5,762	342	37	136	118	6,867	717	77	111	117
Meningococcal infection ..	8	1	3	0	1	7	0	5	2	
Ophthalmia neonatorum	8	1	1	0		15	0	1	0	
Pneumonia† ..	76	7	57	2		81	13	52	0	2
Poliomyelitis, acute:										
Paralytic ..	0	0	0	0		0	0	0	0	
Non-paralytic	0	0	0			0	0	0		
Puerperal fever§	76	37	1	0		87	38	9	0	
Scarlet fever ..	293	57	10	16	7	375	37	39	14	11
Tuberculosis:										
Respiratory ..	241	51	21	9		256	54	33	11	
Non-respiratory ..	56	11	4	4		57	15	12	2	
Whooping-cough	740	93	55	10	56	403	68	30	18	2

DEATHS	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0		0	0	0	0		0	0	0
Dysentery ..	0	0		0		0	0		0	
Encephalitis, acute ..					0					0
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	5	1	1	0	1	7	1	0	0	1
Influenza ..	3	0	0	0	1	2	0	0	0	0
Measles ..	0		0	0	0	0		0	0	0
Meningococcal infection ..			0					0		
Pneumonia ..	535	83	10	12	12	418	74	19	12	10
Poliomyelitis, acute ..	0	0		0	0	0	0		0	0
Scarlet fever ..	0		0	0	0	0		0	0	0
Tuberculosis:										
Respiratory ..	25	6	0	0	2	34	5	2	0	5
Non-respiratory ..				0	0				0	0
Whooping-cough	0	0	0	0	0	1	0	0	1	0
Deaths 0-1 year	266	58	19	11	7	304	55	14	8	9
Deaths (excluding stillbirths)	9,132	1433	515	122	150	9,083	1427	510	111	128
LIVE BIRTHS	16,272	2715	933	297	518	16,255	2727	909	254	
STILLBIRTHS	219	26	15			244	39	20		

* Measles not notifiable in Scotland, whence returns are approximate. † Includes primary and influenzal pneumonia. § Includes puerperal pyrexia.

Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available.

Dysentery	Week Ending 30 June	Week Ending 7 July
Bedfordshire	27	**21**
Bedford M.B.	17	**16**
Durham	18	**31**
Gloucestershire	24	**18**
Bristol C.B.	15	**18**
Greater London	58	**80**
Ealing	14	**12**
Islington	6	**11**
Redbridge	4	**11**
Southwark	3	**12**

Dysentery (Contd.)	Week Ending 30 June	Week Ending 7 July
Lancashire	92	**97**
Manchester C.B.	12	**15**
Preston C.B.	3	**18**
Eccles M.B.	11	**14**
Northumberland	32	**30**
Ashington U.D.	19	**15**
Morpeth R.D.	13	**13**
Somersetshire	4	**17**
Clutton R.D.	2	**14**
Surrey	14	**27**
Warwickshire	62	**38**
Birmingham C.B.	19	**15**
Coventry C.B.	31	**13**
Yorkshire West Riding	39	**51**
Bradford C.B.	13	**19**
Leeds C.B.	17	**17**

Dysentery (Contd.)	Week Ending 30 June	Week Ending 7 July
Edinburgh	36	**22**
Glasgow	34	**21**
Stirling County	0	**13**
Food-poisoning		
Essex	7	**19**
Halstead R.D.	0	**10**
Greater London	43	**163**
Hillingdon	29	**136**
Lancashire	20	**29**
Liverpool C.B.	8	**11**
Caernarvonshire	0	**13**
Llandudno U.D.	0	**13**
Denbighshire	0	**60**
Wrexham M.B.	0	**60**
Glasgow	2	**10**

PARLIAMENT

Abortion Bill Through the Commons

[FROM OUR PARLIAMENTARY CORRESPONDENT]

Almost a year after its second reading, on 22 July 1966, the Medical Termination of Pregnancy Bill has finished the course in the House of Commons. It went through by a majority of about two to one—roughly that which had sustained it throughout two all-night sittings—just before noon on Friday, 14 July. The final vote was: for 167, against 83.

The Bill now faces equally stiff opposition in the House of Lords. By the time this is read the second reading stage there will be over, and prelates, politicians, and practitioners in the peerage will have declared their intentions towards it.

Conscience Clause

In this connexion, the most significant event in the final 14-hour marathon in the Commons was the indication given by the sponsor, Mr. DAVID STEEL, Liberal M.P. for Roxburgh, Selkirk, and Peebles, that the conscience clause (Clause 4) was bound to be reconsidered in the Lords.

The last amendment discussed was a proposal to delete from the clause the provision that in any civil or criminal action the burden of proof of conscientious objection should rest on the person claiming it. The amendment was put forward on the ground that the clause departed from the principle that the burden of proof should rest with the person making the charge.

Mr. STEEL, opposing the change, said the Royal College of Obstetricians and Gynaecologists and the British Medical Association had now come forward with certain views, but there had not been time to take all the advice necessary and to consider the implications of their suggestions. They had accepted, in their correspondence with him, that this would probably have to be dealt with in the House of Lords.

The Minister of Health had said it was the view of a substantial body of the profession that the clause was unnecessary and raised unnecessary complications. He (Mr. Steel) thought they should continue to try to secure a clause that would satisfy those who believed there should be some clear conscience clause in the Bill. But in providing a conscience clause they must be careful not to leave a loophole for an open defence that could not be substantiated.

He recognized the concern that had been expressed about the wording of the clause, and was not closing his mind to representations. All the views put forward would be carefully considered by him and the leaders of the medical profession when they considered what amendments should be made to the Bill in its passage through the Lords.

After hearing the Government view that it was desirable to have this safeguard, and that the proviso should be retained, the House rejected the amendment by 139 votes to 70, and eventually gave it a third reading and dispatched it to the other House.

Care of the Elderly

The Minister of Health, Mr. KENNETH ROBINSON, who has consistently answered the anonymous charge of maltreatment in the Health Service with a demand for names and places, has now been given the names of the hospitals concerned in the book *Sans Everything* and has asked for sufficient detail to facilitate independent inquiry. He has also accepted that there is a fear of reprisals among nursing staff if they make complaints and is discussing with the Royal College of Nursing how to dispel it.

These consequences of the publicity which the book attracted were made known to the House of Commons in a debate on the care of the elderly on 11 July. Mr. Robinson said he had now asked for sufficient particulars to relate each hospital to a specific section of the book, so that hospital board chairmen could arrange for inquiries to be carried out by a legally qualified chairman from outside the National Health Service, assisted by other persons unconnected with the hospital concerned. More generally, managers of all hospitals have been asked to make searching inquiries into the possibility that any form of inhumanity, particularly in the treatment of elderly patients, might exist in any of the hospitals for which they were responsible.

Mr. Robinson emphasized that no one at this stage could say with certainty that any of the allegations were true or untrue. Should it prove that even a single charge of brutality or inhumanity was substantiated he welcomed its exposure. But the other side of the balance sheet should not be overlooked. The method of presentation—a series of anonymous charges against unidentifiable persons in unnamed hospitals—had caused unmeasurable distress and anxiety not only to nursing and other staff but to relatives and friends of patients, present and future.

Complaints from Nurses

On the suggestions that nursing staff and others were afraid to come forward with complaints for fear of reprisals, he said his first reaction had been to dismiss this possibility out of hand. He had since seen the questionary published in the *Nursing Mirror* of 16 June, and a selection of replies. These had convinced him that such fears did exist, at least among a small minority, and he was considering what might be done to dispel them. Senior officers of the Ministry had discussed this with the President of the Royal College of Nursing, and they would be considering what further action would be appropriate.

"I have no evidence," he summed up, "that any patients are deliberately ill-treated, as alleged in *Sans Everything*. I am ready and anxious to investigate anything which can be investigated. I am determined that if there are malpractices in any hospital they shall be uncovered and eliminated." And he promised that nurses who came forward would be given all the protection that he could.

Hospital Commission?

Miss MERVYN PIKE, Opposition leader on social topics, endorsed the views of Professor ABEL-SMITH that there should be a hospital commission responsible for investigating complaints, and an inspectorate similar to that in the education service, which could be equally valuable in health and welfare. There should be more spending on hospitals. The shortage of beds and pressure on resources was aggravated because too many old people had to be kept in hospitals and mental homes because they had nowhere else to go. Many more homes were needed for old people. In far too many places there were long waiting-lists, inadequate and unsuitable buildings, and untrained and overworked staff. A recent article in the *British Medical Journal* had argued that a unified health service should be fitted in with any reformed local government structure. Much could be done also to prevent overlapping in the local authority services. It was a delusion that the inevitably escalating demands of the future could be met by relying on steeply rising taxation to pay the social welfare bill. In face of the present difficulties the B.M.A. had decided to plan an alternative health service. Parliament should realize that the time had come to take a good hard look at the alternatives to the present system.

Geriatric Services

Mr. ROBINSON, recalling his request on regional hospital boards in 1965 to give geriatric and psychiatric services "a due and early share" of resources available, said there was already some evidence of progress. In 1966 there were 59,186 geriatric and chronic sick beds. The regional boards estimated that in 1970 there would be 63,048, an increase of 7%, which would keep pace with the rise expected in the elderly population.

There had also been a considerable strengthening of medical staffing: the number of consultants specializing in geriatrics had risen by nearly 40%—from 115 in 1964 to 156 in 1966. The challenge of this specialty was being more widely appreciated, and this should be helped by a new development among teaching hospitals. Most of the London undergraduate teaching hospitals had recently undertaken, or proposed, to provide full hospital services to their local communities, including geriatric patients. This would mean that geriatric care would benefit from the stimulus of a large teaching hospital. He was glad to note that the Royal College of Physicians had recently recognized the value of the specialty by setting up a geriatric committee.

Money the Core

Dr. M. P. WINSTANLEY (Cheadle, Lib.) said a crucial point in the whole problem of the care of the elderly was the existing situation of divided responsibility. There was a "fairly urgent need for the appointment of an old persons' officer whose sole duty would be to make himself or herself aware of the size of the problem in the area, identify the people, and ensure that the various sources of assistance and health were integrated." They must speed up the end of the tripartite system within the Health Service. If they persisted in having these organizational divisions, they would never get the kind of integration they wanted. He concluded by saying that all discussions came down to one thing in the end: money. Unless more money was spent on the provision of resources for the care of the elderly, no amount of talking would do any good.

Dr. SHIRLEY SUMMERSKILL (Halifax, Lab.) declared that the money should come entirely out of the national income and that more of the national income should be spent on health.

Dr. DAVID KERR (Wandsworth, Central, Lab.) disagreed with the idea of a hospital commissioner. The value of the book they had been discussing lay in the message implicit throughout that the whole hospital system should be thrown open to public gaze. Such occurrences as the book described would then not occur.

MEDICAL NEWS

Appointments to Personal Chairs

Dr. E. J. FIELD has been appointed to a chair in experimental neuropathology, personal to himself, at the University of Newcastle upon Tyne.

Dr. Field, who is 52, graduated M.B., B.S. from the University of Durham in 1938. After holding house appointments he became the surgical registrar and demonstrator in anatomy at Newcastle and later senior demonstrator and lecturer in anatomy at St. Bartholomew's Hospital Medical College. He proceeded to the M.S. in 1944 and the M.D. in 1946, and in the same year he was appointed lecturer in anatomy at Bristol University. After working at the Institut Pasteur, Paris, and in the University of Geneva he took the Ph.D. (Bristol) in 1953. He returned to Newcastle in 1958 as senior lecturer in neuropathology, and in 1961 he was appointed honorary director of a newly established Medical Research Council Group on Demyelinating Diseases. This group was converted into a Medical Research Council unit in 1965, Dr. Field continuing as the honorary director. His research on immunology and autoimmune disease has dealt especially with multiple sclerosis and experimental allergic encephalomyelitis. Transmission studies with multiple sclerosis material both in vivo and in tissue culture have recently led to an interest in "slow" virus diseases.

Dr. D. S. MUNRO has been appointed to a personal chair of clinical endocrinology in the department of pharmacology and therapeutics at Sheffield University. Dr. Munro, who is 42, graduated at Aberdeen University in 1947, and after appointments as house-physician at Aberdeen Royal Infirmary and as assistant in the department of materia medica in the university became M.R.C.P. in 1949. On demobilization from the R.A.M.C., in which he served as a junior medical specialist in the Far East, he was registrar in medicine to the Aberdeen teaching hospitals, and in 1953 he was appointed lecturer in therapeutics at Sheffield University. From 1957 to 1958 he was Research Fellow in Endocrinology with Dr. E. B. ASTWOOD at the New England Medical Centre, Boston, Massachusetts. On returning to Sheffield he was promoted senior lecturer in 1959 and became reader in clinical endocrinology in 1965. He was elected F.R.C.P. this year. His M.D. thesis on clinical applications of isotope dilution techniques was accepted in 1956. He has also published papers on electrolyte metabolism in Addison's disease and on applications of the use of radioactive isotopes in the study of body composition. Recent research interests have been in the bioassay of thyroid stimulating substances and on the nature and significance of the long-acting thyroid stimulator of hyperthyroidism.

Clinical Biochemistry Chair

Dr. H. LEHMANN, University biochemist to the Cambridge United Hospitals, has been pre-elected professor of clinical biochemistry from 1 October. Dr. Lehmann was educated in Dresden and studied medicine at the Universities of Freiburg, Frankfurt, Berlin, and Heidelberg, obtaining awards for anatomy at Frankfurt and for gynaecology at Berlin. (In 1964 he delivered the Ludwig Aschoff lecture at Freiburg and was made an honorary professor of that university.) Because of the political atmosphere in 1933 in Germany he went to Basle for his M.D., and then returned to Heidelberg to work under Professor OTTO MEYERHOF. From Heidelberg he went to Cambridge and became a research student at Christ's College. In 1938 he obtained the Ph.D., was awarded the Darwin Prize of Christ's College, and was elected a Beit Memorial Fellow.

Shortly after the outbreak of the war he worked as a medical officer, first in Essex, and then for several years in the R.A.M.C., mostly in India Command. After the war he went to Uganda for two years to work at Makerere College on hookworm anaemia. On his return he spent a year as a consultant pathologist at Pembury Hospital in Kent and then joined St. Batholomew's Hospital, where he remained for 13 years. He continued to make contributions in the field of abnormal haemoglobins, and in 1962 the Medical Research Council set up a unit concerned with this subject, and made him honorary director. This unit, now at the Cambridge University department of biochemistry, has recently been made the World Health Organization Centre on Abnormal Haemoglobins. In 1963 Dr. Lehmann rejoined the biochemistry department at Cambridge as its University biochemist to Addenbrooke's Hospital, and was made a Fellow of Christ's College.

Kidney Centre to Close

The National Kidney Centre at Finchley, N. London, has decided not to take on any new patients and will close within a year. Responsibility for 27 patients already receiving treatment has been assumed by the Ministry of Health. The centre was set up last November as a private concern to treat patients by dialysis in their own homes. In a statement on 13 July the Ministry reported that a deputation from the centre "indicated that they now accept the Ministry's view that the centre is not viable without the full medical resources of a hospital." Dr. Stanley Shaldon, the medical director, proposes to relinquish his post by 1 July 1968. (A letter from Dr. Shaldon appears at p. 241.)

Medical Research Council

Professor A. W. Kay, Regius Professor of Surgery at Glasgow University, and Professor R. A. Gregory, F.R.S., George Holt Professor of Physiology at Liverpool University, have been appointed members of the Medical Research Council. They succeed Professor Sir Hedley Atkins, P.R.C.S., and Professor W. D. M. Paton, F.R.S., who retire in September on completing their terms of office.

Opening of Medical Centre

The new postgraduate medical centre at Good Hope General Hospital, Sutton Coldfield, which Professor Sir Max Rosenheim opened on 15 July, has been completed at a cost of £27,000. The greater part of this sum was donated by a local benefactor, but the Birmingham Regional Hospital Board also made a substantial contribution (see *B.M.J.*, 9 July 1966, p. 123). Facilities include a fully equipped lecture theatre, with accommodation for just over 100, a library, seminar-room, and a common-room, as well as the usual administration offices. The centre will be used by the hospital senior medical staff for interdepartmental rounds and teaching sessions. Courses, in addition to regular lectures and demonstrations, are expected to be held for general practitioners. It is hoped that the centre will be integrated with others in the Birmingham area, so that courses for higher degrees can be run in conjunction with other hospitals.

Central Health Services Council

Subjects discussed in the report for 1966 of the Central Health Services Council (H.M.S.O., 3s. net) include the visiting of children in hospitals, expansion of screening for cervical cancer, and the need for psychiatric beds in teaching hospitals. During the year the Council set up a new committee to consider the functions of the district general hospital. A new subcommittee on acute poisoning was also set up. In a statement introducing the report the Minister of Health, Mr. Kenneth Robinson, acknowledges the help given by the council throughout the year.

British Empire Cancer Campaign

The annual general meeting of the British Empire Cancer Campaign for Research was held on 4 July in the Assembly Hall of the Royal Commonwealth Society, the Duke of Devonshire presiding. Some 200 members of fund-raising committees in all parts of the country attended. The Nuffield Trophy, awarded for the best fund-raising efforts made during the year, was presented to Lord Rowallan on behalf of the Glasgow committee. Professor T. Crawford, director of the department of pathology, St. George's Hospital Medical School, has succeeded Professor R. W. Scarff as honorary secretary, and Viscount Mills has succeeded Sir Joseph Lockwood as honorary treasurer.

"Medical Directory"

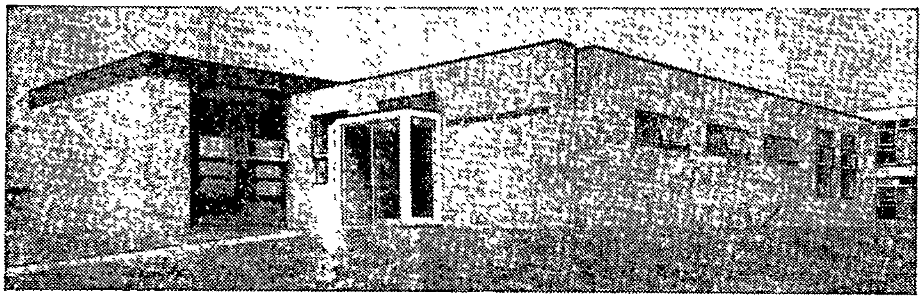
The posting of the annual schedule for the *Medical Directory*, 1968, has been completed. It is desired to include the names of all fully and provisionally registered medical practitioners living or working in the British Isles, and also the names of British-qualified doctors living or working abroad. All such practitioners who have not received the schedule are asked to communicate at once with the Editor, *Medical Directory*, 104 Gloucester Place, London W.1, stating full name and year of qualification.

People in the News

Dr. Geoffrey Templeman, Vice-Chancellor of Kent University, has been re-elected Chairman of the Universities Central Council on Admissions for the period 1 August 1967 to 31 July 1970.

Grants and Awards

The Ministry of Health has made a grant of £3,454 to enable Professor M. Roth, of the University of Newcastle upon Tyne, to undertake an investigation entitled "Psychometric Screening of the Aged in the Community."



Medical Centre at Good Hope General Hospital, Warwickshire.

News in Brief

The Worshipful Company of Barbers of London is appealing for £300,000 to rebuild the Barber-Surgeons' Hall in Monkwell Square, London Wall. Cheques should be sent to Mr. John H. L. Trustram, 31 Bedford Street, London W.C.2.

Members of Regent House at Cambridge University decided last week by 244 votes to 213 that they would not raise overseas students' fees. Oxford University has also rejected the Government's decision.

The World Health Organization supported 1,276 projects in 1966 in 152 countries and territories.

Recent Publications

The *Compendium of University Entrance Requirements* for first degree courses in the United Kingdom in 1968–9 has been published by the Association of Commonwealth Universities. Copies can be obtained from Percy Lund, Humphries & Co., Ltd., The Country Press, Priestman Street, Bradford 8, price 14s. 6d. (post free in the United Kingdom). The compendium does not supersede the official publications of individual universities.

Coming Events

British Occupational Hygiene Society.—Conference on health hazards in docks and shipyards, 12–13 September, University of Newcastle upon Tyne. Details from honorary scientific secretary, Mr. D. C. Murphy, Medical Department, Esso Refinery, Fawley, Southampton.

Institute of Diseases of the Chest.—Course in respiratory diseases for medical senior registrars and registrars, 18–22 September. Fee £7. Applications to Mr. R. A. Perkins, Institute of Diseases of the Chest, Brompton Hospital, London S.W.3.

British Association for Social Psychiatry.—Seminar, 24–30 September, Queen's College, Oxford. Details from Conference Secretary, 62 Great Cumberland Place, London W.1.

Societies and Lectures

For attending lectures marked ● a fee is charged or a ticket is required. Applications should be made first to the institution concerned.

Monday, 24 July

Institute of Laryngology and Otology.—5.30 p.m., combined staff consultation clinical meeting.

Tuesday, 25 July

Royal Postgraduate Medical School.—4 p.m., Mr. G. C. Knight : Whiplash Injuries and Cervical Spondylosis.

West Suffolk Hospitals Postgraduate Centre.—At Outpatient Hall, West Suffolk Hospital, 8.15 p.m., clinical meeting.

Wednesday, 26 July

B.B.C.—1 Television.—11.15 p.m., medicine today: Heart Failure. (Sponsored by A.S.M.E.)

Stoke Mandeville Hospital.—12.15 p.m., Sir Max Rosenheim: Investigation of Hypertension in a Young Adult.

Friday, 28 July

Royal College of Physicians of Edinburgh.—5 p.m., Mr. N. G. C. Hendry: Medicine and the European Economic Community.

Royal College of Surgeons of England.—5 p.m., Victor Bonney lecture by Mr. S. Way: Gynaecological Oncology before and after Victor Bonney.

Royal Postgraduate Medical School.—10.15 a.m., Research in Progress.

Saturday, 22 July

Cambridge University Medical School.—At Chesterton Hospital, 10.30 a.m., all-day symposium: Urological Problems in the Elderly.●

Appointments

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—P. Kellett, M.R.C.S., M.A.N.Z.C.P., D.P.M. (consultant psychiatrist, St Audry's Hospital, Melton); P. S. Dhasmana, M.B., F.R.C.S., D.L.O. (consultant E.N.T. surgeon, Norwich, Lowestoft, and Great Yarmouth Hospital group).

EASTERN REGIONAL HOSPITAL BOARD.—K. M. Parry, M.B., D.C.H. (senior administrative medical officer, Eastern Regional Hospital Board in Dundee).

FRENCH HOSPITAL AND DISPENSARY.—G. H. Jantet, M.B., F.R.C.S. (honorary consultant surgeon).

MANCHESTER REGIONAL HOSPITAL BOARD.—J. M. Abraham, M.B., M.R.C.P., D.C.H. (whole-time or maximum part-time consultant paediatrician, Oldham and District, and Ashton, Hyde and Glossop groups of hospitals); M. Ata, M.B., M.R.C.P.Ed., M.C.Path. (whole-time or maximum part-time consultant pathologist (with special experience in haematology), Rochdale and District group of hospitals); D. A Pitkeathly, M.B., M.R.C.P.Ed. (whole-time or maximum part-time consultant rheumatologist, in regional board hospitals and the United Manchester Hospitals); G. G. Hay, M.B., D.P.M., D.C.H. (whole-time or maximum part-time consultant psychiatrist, Bolton and District group of hospitals); E. A. Allcock, M.B., F.R.C.S., F.R.A.C.S. (whole-time or maximum part-time consultant surgeon, South Cheshire group of hospitals); J. H. Green, M.B., M.Ch.Orth., F.R.C.S.Ed. (whole-time or maximum part-time consultant traumatic and orthopaedic surgeon, Salford group of hospitals); Shiela G. Maddock, M.B. (whole-time consultant physician in geriatrics, Salford group of hospitals).

MINISTRY OF OVERSEAS DEVELOPMENT.—G. R. Randall, M.B., B.S. (medical and health officer, South Pacific Health Service).

MORGAN-HUGHES, J. A., M.D., M.R.C.P. (consultant neurologist, National Hospitals for Nervous Diseases and North-west Metropolitan Regional Hospital Board).

NATIONAL HOSPITALS FOR NERVOUS DISEASES.—H. Merskey, D.M., D.P.M. (consultant physician in psychological medicine).

NORTH-EAST METROPOLITAN REGIONAL HOSPITAL BOARD.—Suzanne L. Alexander, M.B., B.S. (consultant dermatologist, Ilford and District group).

NORTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD.—R. P. Britt, M.B., M.C.Path. (consultant pathologist, Hillingdon Hospital); D. C. Adamson, M.R.C.S., F.F.A. R.C.S. (consultant anaesthetist, Luton and Dunstable and Associated Hospitals); Audrey A. Boutwood, M.B., M.R.C.O.G. (consultant obstetrician and gynaecologist, Elizabeth Garrett Anderson Hospital); L. N. Allen, M.B., F.R.C.S. (consultant surgeon, Edgware General Hospital); J. A. Morgan-Hughes, M.D., M.R.C.P. (consultant neurologist, National Hospitals for Nervous Diseases and Bedford General Hospital); F. E. Loeffler, M.B., F R.C.S., M.R.C.O.G. (consultant obstetrician and gynaecologist, Central Middlesex and Willesden General Hospitals).

Universities and Colleges

BRISTOL

At a special degree congregation held on 13 July in the Great Hall of Bristol University on the occasion of the annual meeting of the B.M.A., the Chancellor, The Duke of Beaufort, conferred the degree of Doctor of Medicine *honoris causa,* on Mr. A. Lawrence Abel, Member of Council, B.M.A., Professor Hamid Ali M. Khan, Immediate Past-president, B.M.A., and Mr. Robert V. Cooke, President of the Association. The Public Orator was Professor T. F. Hewer, professor of pathology in the University. (Pictures in *Supplement,* pp. 83 and 85.)

CAMBRIDGE

FINAL M.B.—*Part II:* [1,2,3]C. E. Ackroyd, [1,2,3]G. M. Addison, [1,2,3]F. C. Arrow, [1,3]Q. R. Bailey, [1,2,3]E. J. Barrington-Ward, [2,3]L. A. L. Baxter, [1,2,3]J. A. Bell, [1,3]P. S. Bennett, [2]A. B. Bevan Jones, [1,2,3]D. J. Bevington, [1,2,3]S. R. Bloom, [1,2,3]J. P. Bolton, [1,2,3]C. M. Britton, [1,2,3]K. G. E. Brown, [1,2,3]R. C. Brown, [1,2,3]M. R. Buckley, [1]G. W. S. Burgess, [1,2,3]R. Canepa-Anson, [1,2]A. G. M. Carless, [1,3]J. H. Casson, [1,2,3]J. A. Chapman, [1,2,3]J. G. Collier, [1,2,3]J. R. O. Collin, [1,2,3]J. R. Cove-Smith, [1,2,3]D. R. Davies, [1,2,3]G. G. Davies, [1,2,4]R. J. Davies, [1,2,3]E. P. Davis, [1,2]N. M. S. Dutton, [1,2,3]J. P. Dymond, [1,2,3]P. D. M. Ellis, [1,2,3]C. A. Ellison, [1,2,3]J. B. Endacott, [1,2,3]M. G. Falcon, [1,2,3]Mrs. L. A. Farebrother, [1,2,3]M. J. B. Farebrother, [1,2,3]I. W. Fawcett, [1,2,3]K. W. M. Fulford, [1,2,3]J. C. Ganz, [1,2,3]D. G. Garden, [1,2,3]H. Garmany, [1,2,3]A. D. N. Gelson, [1,2,3]P. H. Gentle, [1,2,3]J. F. Gordon, [1,2,3]W. H. Goss, [1,2,3]W. B. Graham, [2,3]A. G. Gray, [1,2]R. H. B. Grey, [1,2,3]J. J. Halliday, [1,2,3,4]J. C. Hammonds, [1,2,3,5]H. M. Hargreaves, [1,2,3]B. D. W. Harrison, [1,2]M. E. Hatfield, [1,2,3]A. J. W. Hilson, [1,2,3]G. I. Hodgkinson, [1,2,3]J. F. Hollingshead, [1,2,3]J. A. C. Hopkirk, [1,2,3]R. A. C. Hughes, [1,2,3]J. D. Humphreys, [1,2,3]N. J Ireland, [1,2,3]R. J. G. Irons, [1,2,3]D. I. Johnston, [1,2,3]R. O. Kahan, [1,2,3]G. Keele, [1,2,3]C. S Kolb, [1,2,3]C. Lawrence, [1,2,3]T. R. Lee, [1,2,3,6]R. Lendrum, [1,2,3]I. A. F. Lister Cheese, [1,2,3]D. Lloyd Jones, [1,2,3]A. B. Loach, [1,2,3,6]J. F. Macfarlane, [1,2,3]G. A. MacGregor, [1,2]C. G. Marks, [1,2,3]P. M. Martin, [1,2,3]R. S. Maurice-Williams, [1,2,3]C. Metcalfe-Gibson, [1,3]J. Miller, [1,2,3]I. S. Milne, [1,2,3]B. W. R. Moore, [1,2,3]J. M. Morgan, [1,2,3]D. S. Nairn, [1,2,3]J. H. Newman, [1,2,3,4]R. J. Nicholls, [1,3]J. R. Norman, [1,2,3]W. M. C. Oh, [1]F. S. Pagan, [1,2,3]J. Pearson, [1,2,3]R. M. Pearson, [1,2,3]R. M. Peregrine-Jones, [1,2,3]D. J. Peters, [1,2,3]J. G. Pickering, [1,2,3]M. S. Povey, [1,2,3]K. G. Poyner, [1,2,3]R. J. Preece, [1,2,3]P. J. Quinton, [1,2,3]P. A. M. Raine, [1,2,3]W. A. Ramsahoye, [1,2,3]C. W. G. Redman, [1,2,3]J. C. Richardson, [1,2,3]T. Rigby-Jones, [1,2,3]W. M. Roberts, [1]F. G. V. Scotchman, [1,2,3]M. E. Setchell, [1,2,3]D. E. P. Shapland, [1,2,3]J. A. Shave, [1,2,3]J. R. Shelley, [1,2,3]J. R. Sibert, [1,2,3]M. Silverman, [1,2,3]J. S. Simpson, [1,2,3]T. H. D. Smyth, [1,2,3]D. E. Stableforth, [1,2,3]M. C. Stallard, [1,2,3]C. J. G. Sutton, [1,2,3]R. I. A. Swann, [1,2,3]D. R. Tant, [3]J. P. Tate, [1,2,3]R. B. Tattersall, [1,2,3]J. B. Thompson, [1,2,3]R. J. Thompson, [1,3]G. M. Thomson, [2,3]I. G. Thwaites, [1,2,3]P. Torkington, [2,3]C. F. Tredgold, [1,2,3]T. A. Trevelyan, [1,2,3]J. E. Trowell, [1,2,3]N. H. Tucker, [1,2,3]D. Vasey, [1]G. H. Warrick, [1,3]D. A. Webb, [1,2,3]N. M. White, [1,2,3,4]N. E. Williams, [1,2,3]R. C. N. Williamson, [1,2,3]K. F. Winterbottom, [1,2,3]P. B. Wood, [1,3]R. A. L. Young, [1,2,3]Mrs. G. D. Yudkin, [1,2,3,6]J. S. Yudkin.

[1]Passed in principles and practice of physic. [2]Passed in principles and practice of surgery. [3]Passed in obstetrics and gynaecology. [4]Distinction in physic. [5]Distinction in surgery. [6]Distinction in obstetrics and gynaecology.

GLASGOW

M.D.—J. A. N. Emslie, [2]W. Hamilton, [2]J. G. R. Howie, Jean O. Struthers, Jean R. Nairn, [2]J. A. Boyle, G. A. G. Christie, P. G. Gaskell, [1]R. B. Goudie.

CH M.—C. M. Davidson.

PH.D.—*In the Faculty of Medicine:* J. Armour, K. Boddy, M. Rahman.

M.B., CH.B.—E. A. Adeleye, A. Adrain, Jennifer A. Aitken, Surendra Amin, Valerie-Margaret K. Arthur, Margaret C. Barr, R. H. Baxter, M. I. Ben-Amer, C. B. Boyle, C. J. Browne, T. W. Bryson, [2]P. C. Buchan, [2]J. A. Burton, G. M. Callaghan, [2]K. C. Calman, Isobel P. B. Campbell, I. A. Carmichael, Isobel D. Christie, Sheila A. Clark, T. Clark, K. McM. Cochran, D. I. Cooper, G. MacC. Cunningham, Moira M. D. Currie, R. Dalling, Elizabeth C. Dalziel, D. C. Davidson, Barbara S. Davis, B. M. A. Dodhy, W. Dunlop, B. P. Dunn, [1]J. S. Dunn, A. C. Ferguson, Helen R. Ferrie, J. D. P. Findlay, A. Fisher, W. S. Fleming, J. A. Ford, J. R. Goldring, [2]R. A. Gordon, Alice B. Graham, J. F. Haggis, C. L. Hales, Elisabeth R. Hamil, D. J. Hardy, Edith M. Hastings, Maureen J. H. Hawthorn, J. Higgins, W. S. Hillis, C. W. Imrie, Sandra Ingram, A. S. Jamieson, J. H. Johnston, Eve C. Johnstone, J. W. Kerr, B. W. Knox, N. Krasner, A. Leckerman, Teresa B. Leyden, J. D. Lorimer, G. McAllister, Christobel W. McArthur, J. N. MacAskill, D. L. McBride, T. J. McCann, S. McCormick, S. W. McCreath, J. McDonald, [1]I. R. McDougall, T. McFarlane, W. A. Mackintosh, A. Macleod, M. Macleod, R. McMahon, G. H. Macpherson, K. J. McQueen, Q. J. McQuoney, G. J. McSherry, Rosemary McSherry, W. J. Mackie, W. Marsh, R. C. Menzies, Constance C. Methven, E. A. Mills, [2]Grace G. Mitchell, [2]I. A. R. More, W. M. Morrison, T. S. Murray, B. K. Nath, J. C. O. Obanye, [2]G. Oram, P. S. Orr, A. I. Pack, J. L. W. Parker, Rosemary G. Paterson, R. S. Paton, B. Persaud, [2]R. O. Quin, Isobel A. Rae, L. E. Ramsay, Mary H. Ramsay, J. A. Richardson, Mary G. Robertson, H P. Robinson, I. Rogers, R. P. Saberwal, [2]K. W. McK. Scott, [2]P. D. R. Scott, R. T. A. Scott, W. R. Short, R. G. Simpson, K. S. R. S. Y. Too, H. Smart, W. P. Soutter, Christian A. MacG. Spark, Elizabeth M. Stark, [2]R. D. Stevenson, Sarah A. Stewart, Patricia H. G. Thomson, Charlotte M. Tolmie, Mary J. Torbet, J. G. van Bavel, G. A. B. Waddell, G. M. Watson, Janet G. Watson, [2]Diana M. Watt, J. P. White, Marjorie L. Wood, R. F. M. Wood, F. D. Wren, Mary A. Wright, D. F. Yule.

[1]With honours. [2]With commendation.

LONDON

Professor P. C. C. Garnham has been appointed to the Heath Clark lectureship for 1968.

Dr. N. G. Trott has been appointed to the readership in physics as applied to medicine ten-

New Issues of Specialist Journals

BRITISH JOURNAL OF PREVENTIVE AND SOCIAL MEDICINE

Contents of the July issue are as follows:

Deliberate Self-poisoning in the Oxford Area. J. Grimley Evans.
Acute Poisoning and its Prevention. J. D. P. Graham and R. A. N. Hitchens.
Medical and Social Needs of Patients in Hospitals for the Mentally Subnormal. I. Leck, W. L. Gordon, and T. McKeown.
Indices of Obesity derived from Body Weight and Height. T. Khosla and C. R. Lowe.
A Community Study of Urinary pH and Osmolality. W. E. Waters, M. Sussman, and A. W. Asscher.
The Value of the Erythrocyte Sedimentation Rate as a Screening Test. G. Pincherle and J. Shanks.
Secular Changes in the Physique of Aberdeen Mothers, 1950–64. A. M. Thomson, W. Z. Billewicz, and R. M. Holliday.

Volume 21, No. 3. Yearly subscription (4 numbers) £3 3s., abroad £3 10s.

BRITISH JOURNAL OF OPHTHALMOLOGY

Contents of the July issue are as follows:

Pathology of Posterior Polymorphous Degeneration of the Cornea. Gwyn Morgan and Alan Patterson.
Iris Dysgenesis with Other Anomalies. R. A. D. Crawford.
Angle-closure Glaucoma and Inverse Astigmatism. J. McLenachan and D. F. C. Loran.
On a New Method to Cure Cataract by Extraction of the Lens. Jacques Daviel, translated by W. G. Pearce.
Surgical Safety of Prophylactic Peripheral Iridectomy. W. H. G. Douglas and Ian M. Strachan.
Idiopathic Acquired Lacrimal Drainage Obstruction. R. Dalgleish.
Visual Defects in Cases of Down's Syndrome and in Other Mentally Handicapped Children. P. A. Gardiner.
Cerebro-retinal Degeneration due to Carbon Dioxide Poisoning. David Sevel and Arnold Freedman.
Evaluation of Conjunctival and Nasal Bacterial Cultures before Intra-ocular Operations. John Nolan.
Keratoconus Posticus Circumscriptus with Indentation of the Lens. Hari Charan.
Choroidal Malignant Melanoma in a Child. Samuel T. Jones.
Plastic Reconstruction of the Upper Eyelid. S. V. M. Surya Rao, K. Vengala Rao, and C. Venkataramy Reddy.
Ophthalmological Synopses.
Crytoextractor and Cryopexor. M. M. S. du Toit.
Iris Retractor for Use with Cryoextractors. M. M. S. du Toit.
Reviews. Notes.

Volume 51, No. 7. Yearly subscription (12 numbers) inland £8 8s., overseas £9. With *Ophthalmic Literature* and Index (7 numbers) inland £15, overseas £16.

MEDICAL AND BIOLOGICAL ILLUSTRATION

Contents of the July issue are as follows:

Progress in Artificial Voice Aids. Bernard W. Watson.
A Bronchoscopist's View of Bronchial Anatomy. Peter Stradling.
Hyperbaric Oxygen Therapy: Its History and Current Scope. B. G. B. Lucas.
A Comparative Assessment of Optical and Fibre Gastroscopes. L. A. Kont and George Berci.
Deglutition in the Newborn. J. P Farriaux and G. Milbled.
An Experiment in University Teaching—Part I. G. E. Kenshole.
Schlieren Photography of an Ultrasonic Beam. Clive F. J Croot and Richard Robbins.
Audi Partem Alteram. Equipment and Methods. Journal Abstracts. Book Reviews. Motion Pictures and Other Media.

Volume XVII, No. 3. Yearly subscription (4 numbers) £3 3s., abroad £3 10s.

able at the Institute of Cancer Research, Royal Cancer Hospital.

The title of reader in anaesthetics has been conferred on Dr. M. K. Sykes in respect of his post at the Royal Postgraduate Medical School.

MANCHESTER

FINAL M.B., CH.B.—[3]G. N. Athey, R. P. Barley, D. P. Bentley, A. R. Blackburn, T. Bolton, Christine M. Bradley, G. W. Bradley, J. F. Bray, R. D. Brosnan, G. Neil Brown, F. E. Burke, J. S. Canavan, M. A. M. B. Carmi, P. A. Chadderton, Ann M. Cunningham, J. Currie, T. L. Davies, [1]D. P. Deakin, R J. Dobbs, J. F. Eastwood, M. R. Fleisher, Rosalind J. Forbes, I. Green, M. J. Hamilton, P. L. Harris, Janet Haworth, H. J. Holly, M. B. Holmes, P. E. T. Isaacs, Jennifer R. James, D. H. A Jones, M. J. Lewis, L. J. Libman, J. N. Longrigg, [2]Ian MacLennan, J. F. Mansfield, Anne S. Marsden, P. B. Miller, J. E. Milson, C. J. Monks, D. Neary, J O'Donnell, J. O'Grady, G. H. Platt, Sylvia Rimmer, R. J. Salem, Jacqueline Shadlock, Anne R. Shakibai (née Horsfall), Janet A. Sneddon, [1]S. G Spiro, T. J. Stahl, G. Stores, Olga P R. Stores (née Meir), O. T. Tang, A. Thornton, Carol A. Tomlinson, R. M. Towey, P. J. Travis, Jane S Wilkinson, R. J. Williams, A. N. Woodward, Janet N. Wynroe, Sheena D. Wyse, Veronica A Youngs.

[1]Awarded distinction in obstetrics and gynaecology. [2]Awarded distinction in paediatrics. [3]Awarded distinction in surgery.

WALES

WELSH NATIONAL SCHOOL OF MEDICINE

M.B., B.CH.—[1 2 3 4 5]E. M. Eronini, M. B. Ablett, Angelina M. Bako, J. W. Blizzard, Siân Bramley, P. D. Bull, B. Davies, H. C. Davies, T. R. Davies, E. M. Downes, K. M. Evans, R. H. L. Galliver, G. E. Griffith, Anne M. Hailwood, Julia C. Harper, Morfydd E. R. Harries, J. Hill, [6]Helen E. Hughes, K. D. Hughes, N H. Jiwa, P. H. Jones, W. H. L. Jones, D. M. Joynson, A. R H Kidy, Susan King, P. A. Knoyle, [7]O A. Ladipo, R. C. Levy, C E. Lewis, A Lielmanis, [8]L K. Lightfoot, T. Lyon, C. J. L. Morgan, K. R. Murrin, S. E. Mushin, G. C. Oghuagu, F. N. Oosman, D A. Owen, [2 3]E. W. Owen, P. Patel, H. G. Rees, Dorothy C. J. L. Morgan, K. R. Murrin, S. E. Mushin, C. M. Rhydderch, R Rhydderch, E. Roberts, D G. Salter, T. E. A. Salubi, D. Shelling, Jillian B. Smith, R. W. J. Smith, R. A Sparks, R. S Ubhi, T. B. Webb, K. G. Whittle, Eunice E. M. Williams, [6]G. J. Williams.

[1]With commendation. [2]With distinction in pharmacology and therapeutics. [3]With distinction in pathology and bacteriology. [4]With distinction in social medicine and public health. [5]With distinction in medicine. [6]With distinction in surgery. [7]With distinction in physiology. [8]With distinction in human anatomy.

LIVERPOOL

In Congregation on 8 July the honorary degree of D.Sc. was conferred on Sir Robert Aitken, M.D., D.Phil., F.R.C.P., F.R.A.C.P., vice-chancellor, University of Birmingham; vice-chancellor, University of Otago, 1948–53; regius professor of medicine, University of Aberdeen, 1939–48; chairman, Committee of Vice-Chancellors and Principals, 1958–61; and the honorary degree of M.Sc. on Dr. R. J. Minnitt, F.F.A. R.C.S., F.R.C.O.G., inventor of the Minnitt gas-and-air machine for use in childbirth.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At an extraordinary meeting of the Council held on 12 July with Sir Hedley Atkins, president, in the chair, Diplomas of Fellowship were granted to the following candidates:

R. M. Burton, R. D. Gardner, G. Willett, B. M. Thomas, E. E. Douek, A. B. Richards, R. M. Simons R. V V. Baker, P Hill, B. K. Sood, M J. K. Hudson, M. T. Reynolds, J. M. Dinham, H. G Naylor, P. Anderson, M. E. Cavendish, R S. Dawkins, J. L K. Bankes, J. W. Carswell, Margaret W. Childe, W. S. C. Cox, F. T de Dombal, R. J. Lavelle, N J. Knight, G. B R Vaughan, R. Phillips, J. E. F. Bruce, D. P. H. Caldwell, N. R. A. Trickey, T. A H. English, G. Deane, E M Oxley, D. J D T Pinto, B T Williams, O. O A. Ajayi, E. L. Datnow, J. V H Kemble H. W. S. Pigott, K Hardinge, R Sanders, M. J. Knight, F S. Zeerah M A. Abu el Ela, T. K. Goonatillake, L. Kumarasinghe, A. el M. Y. Soliman, W. N F. Boughey, R N. Radhakrishna, J. Attard, J. P. S. England, A. M Gordhandas, H S Chhabra, A. R. B. El Zawawi, M. Khan, N. H. Mahindrakar, A N. Mitra, S. L. Sandhir, P. A. Wirasinha, J. D. Wrighton, J. R. N. Curt, A. K. Das, P. G. Johnson, S. B. Mukkadap, P. H. Pattisson, S. M. Shah, M. L. Singh, B. D. Smith, M. J. Abberton, M R. Baylis, S. Bhattacherjee, T. D. Chatterjee, H. V. Coop, C. B d'A Fearn, N. G. Kundu, C. J. Langridge, A D W. Maclean, M. A. Melsom, M. A. Mirza, A. Abdel-Halim Montasir, D. R Raje, P. A. Rashid, A. P. Ray-Choudhuri, D. Sengupta, R. P. Wilding, S. Ahmad, Z Ahmad, R. G. Ainley, J E. Casaletto, A. V. Choudhrie, R. E. Cudmore, E. N. Gleave, J. R. Hoare, B. Z. Katalinić, M. W. McLain, R Mapstone, I. A. Miller, U. S. Mishra, T. B. Poliness, P H. Shah, P. Sukhum, J. S. R. Baxter, P. K. Chaturvedi, N. St. J. P Dwyer, F. Hainsworth, D. W. Jackson, S. D. Kate, D. P. E. Kingsley, B. S. Kuming, M. D. Lee, M. P. McBrien, Averil O. Mansfield, J. J. H. Mulnier, O. P. Pahuja, S. P. Parbhoo, W. J. C. C. Rich, A Roy, J. B. E. Stephenson, J. A. Wattie, P. S. Bajaj, S. L. Biddulph, I. D. Brown, D. M. Chaplin, S V Darbar, I P. Elhence, P. Fan, K. M. Fung, B. H. L. Gibson, Y. V. Ginde, M A. Hannon, J. C. D. Hair, L. A. J. Hughes, D. J. Kirkpatrick, D E. Leask, A. J. McEwan, A J. B. Missen, M P. Mohansingh, J. M. Parekh, R. D. Prabhu, J E. L. Sales, P. C. Shah, J. R South, R Thammadi, R H. Weeks, H. T. Williams, N. J. Barwell, E A. Benson, F. P. Blake, R. A. D. Booth, D W. Cairns, P. K. J. Gerard, M. M. Hegarty, M. J. S. Hubbard, K. V. Kapur, A. M. Karmody, R N. Katariya, N. C. M Locke, P. D. Moynagh, M. O'Driscoll, J. L. Robinson, R. N. Sapsford, J. Spivey, W. S. Taor, P. F. Catts, F. C. Y Cheng, N. B. Dave, S. P. B. Donnan, Ming-Sum Lau, E. P. N. J. O'Donoghue, S. G. A. Shah.

A Diploma of Fellowship in the Faculty of Anaesthetists was granted to J. E. Gunning.

Sir James Paterson Ross, Bt., delivered an address to the new diplomates.

At a quarterly meeting of the Council held on 13 July Sir Hedley Atkins was re-elected president for the ensuing year. Professor R. Milnes Walker and Mr. H. C. Edwards were elected vice-presidents for the ensuing year.

Mr. H. Osmond-Clarke was readmitted and Mr. G. Qvist, Dr. A. J. Whitaker, Mr. D. Ranger, and Dr. W. D. Wylie, were admitted as members of the council.

Professor D. W. Hill was admitted as the Research Professor in Ophthalmology.

Professor Robert B. Duthie, The Nuffield Professor of Orthopaedic Surgery, Oxford, was admitted to the Fellowship *Ad eundem*.

The Hallett Prize for 1964 was presented to Mr. Nadaraja Ganeshananthan (University of Ceylon).

The deaths of Mr. D. Ioan-Jones and Sir Claude Frankau (past members of the Court of Examiners) were reported with deep regret.

The Hallett Prize was awarded to Dr. A. L. G. Peel (University of Cambridge).

The award of the Nuffield Prize (Faculty of Anaesthetists) to Dr. Jennifer A. Jones, of Charing Cross Hospital, was recorded).

Mr. F. A. d-Abreu (Westminster Hospital), Mr. J. M. Pullan (St. Thomas's Hospital, Mr. E. J. Radley-Smith (Royal Free Hospital), and Mr. L. P. Jameson Evans (Birmingham) were re-elected, and Mr. R. E. Horton (Bristol), Mr. R. H. Livingston (Belfast), and Mr. F. G. Smiddy (Leeds) were elected to the Court of Examiners for the ensuing three years.

Sir Thomas Holmes Sellors was appointed the Gordon-Taylor Lecturer for 1968.

Professor A. Paufique (Lyons), was appointed the Pocklington Memorial Lecturer for 1968.

The election of Lord Brock of Wimbledon as a Trustee of the Hunterian Collection was reported.

Dr. Hisako Ikeda, was appointed senior lecturer in the Godfrey Robinson Unit in the Research Department of Ophthalmology.

The following diplomas were granted, jointly with the Royal College of Physicians of London, as follows:

DIPLOMA IN PATHOLOGY.—V. L. Gurubacharya, W. J Naudé, V S Pathmanathan, R. N. Perera, P. M. Soldin, N Trikha, K M. M. Wai.

DIPLOMA IN ANAESTHETICS.—M. F. M. Aboudi, A. Afrasiabi, R Ahmad, S K. Alam, A. A A. Al-Khayatt, Margaret J Ansell, Rachel G. Bailey, M A. Baluch, G. Bandyopadhyay, E. H D'A. Banister, G E J Banks, D C. P Barkhouse, L. Baron, S M Basu, M S Batra, A. Beitner, A N. Bond, Juliet D Boyd, R. Buchanan, Alice M. K. Chang, R. R. Chatrath, B. B. Chaudhuri, Shashi Chhabra, A J Christie, A. B. Conyers, Dorothy M. Crawford, S Datta, P. B. Deaner, J. A. Dharmarajah, Mary M. Dixon, R. A. K. Doshi, H M. Drake, Sandra M. Dymock, A. G. C. Findlater, G. D. Flowerdew, Anne Forsyth, T. A. Fraser, P S. Gadgil, A. M. Gandhi, Bina Ghosh, Purnima Ghosh, R. Gopalkrishnan, Jennifer B. Green, A J Greig, S. A Haider, C. B. Hall, D H. Harley, Khalda, Hasnain, T. E. J Healy, Janet E Hunter, A. Hussain, H. A. T. Hyderally, Elizabeth M. Iddon, B. S. Irani, Alak L. Jaiswal, L. A G. Jayasekera, K. Jeevaratnam, R. F. Johnston, C. W Joshi, Bernadette A. Keane, R. C. Keays, F. B. Kotwall, N. Kundu, S A. Latif, S W. Lim, S Ling J. McV. Loudon, R. S. Lurie, G F. Mackenzie, N. K. Mathur, Rajni Mehra, Qamar-uz-Zaman Mian, S. Y. Mirsadgady, S G Murtaza, M. Nissen, F. V O. Noël, Maureen A. O'Brien, Kathleen J Packer, Kathleen M. Page, G. M. Patel, A. Plant, V J. Pratt, F Prodhan, B R. Puddy, J. M. Purchas, S. Quadir, A H. Rahman, A. K. Ray, A. Razak, Indira Sahay, J. P. Sedgwick, P. R. Sen Gupta M. Shafiq, K. D. Shah, I. Siddiqi, Kuljit Sidhu, U. P. Singh, J A. S. Smith, I. A. Sutherland, M A. Tayyab, Julia Tertishnaja, S. W. J. Theophilus, J. Thorburn, J. E. Threlfall, M E. Tolley, Felicity K. E. Tunbridge, S. V. Vakil, T. K. Waddell, J. S. Walker, Pamela O. White, D. H. Wickenden, Elizabeth Wilkinson, D. Williams, Elisabeth M. Williams, E. H. Wilson, Man-Lee Yeung, A. N. M. Ziaduddin.

Correction

Thoracic Medicine.—We regret that Dr. D. A. J. Tyrrell's contribution to the recent conference at the Royal College of Physicians (1 July, p. 43) was inaccurately reported. The passage should have read as follows:

"At the second morning session the chairman Sir CHRISTOPHER ANDREWES, F.R.S., introduced Dr. D. A. J. TYRRELL (Common Cold Research Unit, Salisbury), who outlined the types of virus known to cause respiratory infection in man. Many of these were very selective in their choice of host cells, and their study had been simplified by the introduction of organ cultures of human respiratory epithelium. Dr. Tyrrell went on to classify respiratory viruses. The myxovirus group included the viruses of influenza, causing clinical influenza, but also colds, bronchitis, and bronchopneumonia; respiratory syncytial virus, causing bronchiolitis in infants and mild colds in older subjects; parainfluenza 1, causing croup, but also pneumonia and colds; parainfluenza 2, causing croup and minor respiratory infection; and parainfluenza 3, causing pneumonia and bronchitis in children, but mild colds in many cases.

Among other types, the rhinoviruses caused common colds and occasionally bronchitis, and the Coxsackie and adenoviruses mainly sore throats or feverish colds. Sore throats were often due to streptococcal infection. Respiratory viruses could survive in air for short periods only, and are spread most commonly by coughing and sneezing, but hardly at all during speech or normal breathing."

Deaths

Dart.—On 23 June 1967, in Launceston Hospital, George Herbert Dart, M.D., M.R.C.P.Ed., D.P.H., D.T.M.&H., aged 82.

Neumark.—On 12 July 1967, at St. Mary's Hospital, Paddington, Ernst Neumark, M.D., of 73 Lawn Road, London, N.W.3, aged 55.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON W.C.1. TELEPHONE: 01-387 4499. TELEGRAMS: *Aitiology, London W C 1.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C 1, on receipt of proofs.

ADVERTISEMENT AND SUBSCRIPTION ORDERS should be addressed to The Manager at B.M.A House, London, or at 415 Bourke Street, Melbourne, Victoria, Australia.

MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the British Medical Association, B.M.A. House, London, or to the Scottish Secretary, B.M.A., Scottish Office, Drumsheugh Gardens, Edinburgh.

BRITISH MEDICAL JOURNAL

LONDON SATURDAY 29 JULY 1967

Pointers

Subarachnoid Haemorrhage: Psychiatric morbidity high in 261 cases studied by Dr. P. B. Storey (p. 261).

Vitamin-B_{12} and Psychiatric Symptoms: Only memory impairment seemed related to the deficiency in Dr. Ralph Shulman's series of 27 patients (p. 266).

Cerebral Infarction: Dr. S. K. Battacharji and colleagues find no support for stenosis alone playing a decisive part in pathogenesis (p. 270).

Another Smoking Hazard: Bronchoconstriction due to irritant action of smoke particles, probably mediated through the vagus, according to Dr. G M. Sterling (p. 275).

Humidifying Oxygen: Dr. B. J. Freedman found Woulfe's bottle method adequate (p. 277).

Heparin and Anginal Pain: Intravenous administration produced same effects as placebo in patients studied by Dr. C. J. Bulfitt (p. 279).

Calcium Infusion Test: Dr. J. V. Lever and colleagues found that calcium retention is not conclusive evidence of osteomalacia (p 281).

Sickling and Haematuria: Dr. O. O. Akinkugbe from Ibadan in Nigeria reports four cases showing radiological evidence of renal papillary necrosis (p. 283).

Case Reports: Association of Guillain-Barré syndrome with chronic lymphatic leukaemia (p. 286). Gas in portal vein (p. 288).

Rubella: Serological method for demonstrating recent infection described by Dr. J. E. Banatvala and his colleagues (p. 286).

A Case for Cannabis? Leading article (p. 258).

Clinicopathological Conference: Diarrhoea and Goitre—Case Demonstration at the Royal Postgraduate Medical School (p. 293).

New Appliances: Mr. H. B. Eckstein describes a new urinary diversion appliance (p. 297).

Coronary Care Unit: Dr. B. L. Pentecost and colleagues describe the organization of a unit in a general hospital (p. 298).

Annual Scientific Meeting: Final report of scientific proceedings (p. 300).

Pertinax: Without Prejudice (p. 304).

Post-concussional Sequelae: Letter from Dr. J. Schorstein (p. 305).

Abortion Bill: Lords Debate (p. 316).

Overseas Conference of B.M.A.: Report, *Supplement*, p. 101.

General Medical Council: Meeting of Disciplinary Committee (*Supplement*, p. 104).

Doctors and Clergy: Annual meeting (*Supplement*, p. 107).

Bristol Annual Meeting: Annual Dinner of B.M.A. (*Supplement*, p. 108).

Changed Character of Osteomyelitis

In the last 25 years the clinical picture of haematogenous osteomyelitis has changed dramatically for the better. As this period corresponds with the development and wider use of antibiotics, much of the credit has been given to them. Though some critics fear that the old cycle of fulminating septicaemic disease will begin again once there are sufficient antibiotic-resistant organisms circulating in the world,[1] antibiotics at present are the most potent weapon in the treatment of osteomyelitis, and their benefit has been enormous. The appropriate antibiotic will sterilize the bone abscess, thus reducing the local thrombosis in the bone and the size of the sequestra. As the small sequestra left after treatment may be absorbed, open sinuses and mixed infections have become rare. Massive sequestra are uncommon, and multiple recurrences of infection are now rare. The two conditions leading to a persistent sinus are a mixed bacterial infection in a cavity whose walls cannot collapse.

Whether antibiotics are responsible for all the present success of treatment is questionable, for whether in Europeans, Indians, or East Africans[2] the disease has changed to a less dramatic form. It is reasonable to assume that at least in advanced societies an improvement in the general health and hygiene of the community, particularly in infants and adolescents, has reduced the number of primary foci from which haematogenous osteomyelitis might spring. Minor infections are better treated, impetigo is rare, dental and tonsillar care is better. But these improvements alone do not suffice to explain the diminished severity of the disease in poorer populations. Clearly there are other factors at work, and they are not easy to explain.

While the more easily diagnosed septicaemic form accompanied by multiple foci of bone infection and positive blood culture has become rare, osteomyelitis in its modern subacute and benign form has become a trap for the unwary. Infantile osteomyelitis, though less common, may remain true to its old form. It is more often due to streptococcal infection than is adolescent osteomyelitis. Systemic disturbances are often less than the local physical signs would suggest, the disease being characterized by massive oedema of part of a limb and rapid separation of a large sequestrum, sometimes of the whole metaphysis of a long bone. This tragedy may have occurred before adequate antibiotic therapy has had time to act. A broad-spectrum antibiotic must be given at once in suspected cases without waiting to establish the correct one by laboratory studies.

In adolescence, still the most common age at which osteomyelitis develops, a subacute form of the disease is now more often seen than formerly. As before, the epiphysis remains the site of infection, the lower femoral epiphysis being most frequently attacked, and a history of trauma is still obtained in about half the cases. The onset is gradual. The patient is reluctant to use the limb, so that the physician may confuse the disease with early poliomyelitis or juvenile rheumatism. As the most

© *British Medical Journal*, 1967. All reproduction rights reserved.

serious error in the treatment of osteomyelitis is delay in the administration of an antibiotic, treatment should not await resolution of the doubt about the diagnosis. Better a cured child with an undiagnosed disease than a sick child with osteomyelitis. Radiology is of no value in establishing the diagnosis early, changes not usually being visible until between the seventh and tenth day. The important features are tenderness in the vicinity of an epiphysial line, local evidence of inflammation, especially oedema, and a raised erythrocyte sedimentation rate. The rise in the white cell count may be slight and delayed. True, an increase in the neutrophil/lymphocyte ratio may be more important as a diagnostic sign in the early stages, but it later returns to normal. Blood culture is negative in most cases. Estimation of the antibody titre is of little value.

Suspected cases must be given adequate doses of a broad-spectrum antibiotic and put at rest with local immobilization of the affected part. It is possible in some cases to abort the disease so effectively that the radiological evidence may be doubtful and merely consist of local rarefaction on the metaphysial side of the epiphysial plate. If the systemic manifestations of infection continue, it may be wise to change the antibiotic, but this will usually mean that pus has formed. Usually subperiosteal, it is indicated by an increase in the local oedema, and demands surgical incision. If subperiosteal pus is found, there is no need to drill the underlying bone; the medulla has become decompressed already. A specimen of pus should be taken in order to establish the appropriate antibiotic. The edges of the wound may be lightly drawn together, and after some delay it will usually heal with the minimum of scarring. Continuation of antibiotic therapy to avoid mixed infection and to prevent a recurrence of inflammation is necessary. Therapy should continue for a minimum period of four weeks after the onset of the disease.

Osteomyelitis in the adult from a cause other than injury is extremely rare, but it may be encountered in debilitating diseases, among which diabetes is well recognized. As L. R. I. Baker and his colleagues recently reported,[3] other debilitating diseases such as neutropenia secondary to systemic corticosteroid therapy may be rare precipitating causes, as also may hypogammaglobulinaemia.

Much remains obscure in the epidemiology of osteomyelitis, and further studies of its incidence in this and other countries are needed. While antibiotics have drawn its sting, their use does not wholly explain the changed pattern of the disease. They do need to be given early. Treated within the first three days, osteomyelitis may remain a benign disease.

[1] Winters, J. L., and Cahan, I., *J. Bone Jt Surg.*, 1960, 42A, 691.
[2] Harris, N H., and Kirkaldy, W. H., ibid., 1965, 47B, 526.
[3] Baker, L. R. I., Brain, M. C., Miller, J. K., and Raphael, M. J., *Brit. med. J.*, 1967, 1, 722.

Thyrocalcitonin

Thyrocalcitonin, or simply calcitonin, is a hormone that lowers the concentration of calcium in the plasma. Though it was discovered four years ago,[1] its significance in clinical practice remains uncertain. However, its source is now clearly recognized to be in the thyroid gland.

In a number of species, including man, two distinct types of thyroid cell can be recognized. The thyroxine-producing epithelial cells, arranged in acini or follicles, are familiar, but in addition there are cells of a different histological and histochemical type lying adjacent to the follicles but within the basement membrane. These have been variously known as "light cells," "parafollicular cells," "mitochondrion-rich cells," and "C cells." From studies using histochemical[2] and immunofluorescent[3] techniques there seems little doubt that these cells are the site of production of calcitonin. The mode of action of the hormone has also been determined. Experiments in vitro[4 5] and in vivo[6 7] indicate that calcitonin lowers the calcium level in the plasma by a direct action on bone, inhibiting bone resorption. The hormone also lowers the inorganic phosphate level in plasma and causes phosphaturia.[8] Hypercalcaemia is the stimulus for secretion of the hormone, and hypocalcaemia inhibits secretion. It would appear, therefore, that secretion of calcitonin is controlled by a feedback mechanism operating through the plasma calcium level[9] in a manner similar to that for the control of the secretion of parathyroid hormone, but in the reverse direction.

Thus much is known of the physiology of this hormone from experimental work. It is known too that human thyroid contains thyrocalcitonin.[10 11] Nevertheless, the role of thyrocalcitonin in disease in man and its possible usefulness in therapeutics have not yet been defined. G. A. Williams and colleagues,[12] studying totally thyroidectomized patients maintained on exogenous thyroxine, found them to have normal resting levels of calcium but an impaired ability to restore the calcium level to normal after an infusion of calcium gluconate. This suggests that calcitonin is more necessary for the control of hypercalcaemia than for the maintenance of a normal level of calcium. The place, if any, of calcitonin in the disturbances of calcium metabolism in thyrotoxicosis is not known, but there is evidence to suggest that the occasional hypercalcaemia seen in this disease is not due to impaired secretion of calcitonin.[13] In the report of the Clinicopathological Conference this week at page 293 a remarkable case is described in which a medullary carcinoma of the thyroid was associated with persistent diarrhoea. The functions of the C cells and their possible relationship to this syndrome are the subject of expert discussion by Professor A. G. E. Pearse, Dr. E. D. Williams, and Professor I. McIntyre.

Syndromes of hypersecretion of thyrocalcitonin might be expected to occur, but so far only isolated cases have been reported in which the findings were consistent with that possibility. In one[14] the patient presented with tetany and a diffuse non-toxic goitre. The serum calcium was 8.1 mg./100 ml. and biopsy of the thyroid showed an increase in the "parafollicular" cells. Extraction of the biopsy material yielded about 14 times more calcitonin than normal thyroid tissue. The serum calcium levels rose after total thyroidectomy. In a second case[15] the patient presented with recurrent thyrotoxicosis after thyroidectomy, and a serum calcium level which never exceeded 4.6 mg./100 ml. despite treatment with dihydrotachysterol, calcium, and extract of parathyroid. A second thyroidectomy was performed and the calcium levels rose after operation, thereafter being maintained at normal by small doses of dihydrotachysterol. It has also been noted that in cases of pseudohypoparathyroidism the calcitonin content of the thyroid is greatly in excess of normal,[16] [17] but it is not certain whether this is a primary event in the disease or merely represents an accumulation of calcitonin in the thyroid owing to chronic hypocalcaemia, a possibility for which there is experimental support.[18]

The therapeutic possibilities of the hormone would appear to lie in two directions—the treatment of hypercalcaemia and the treatment of excessive bone resorption. G. V. Foster and colleagues,[19] using purified pig thyrocalcitonin, lowered the plasma levels of calcium in patients with hypercalcaemia associated with bony metastases from breast cancer. The plasma calcium was lowered for 6–18 hours by one injection of the purified preparation. Since in most cases of hypercalcaemia (other than that due to hyperparathyroidism) the raised plasma calcium is not itself the major problem, the therapeutic possibilities in this direction are limited. Thyrocalcitonin might, however, prove useful in averting a parathyroid crisis in cases of severe hyperparathyroidism while preparations for surgery were being made. It may be added in connexion with hyperparathyroidism that, since calcitonin has been shown to have a phosphaturic action and is secreted in response to hypercalcaemia, C. J. Robinson and colleagues[8] have suggested that tests for hyperparathyroidism depending on phosphate excretion should not be used clinically.

Foster and colleagues[19] postulate a therapeutic role for calcitonin in cases of osteoporosis. At present the peptide nature of the hormone necessitates its being given by injection, which limits its usefulness, but more potent or longer-acting synthetic analogues might be produced in future which could prove useful in promoting the remineralization of bones depleted of calcium.

[1] Hirsch, P. F., Gauthier, G. F., and Munson, P. L., *Endocrinology*, 1963, 73, 244.

[2] Foster, G. V., MacIntyre, I., and Pearse, A. G. E., *Nature (Lond.)*, 1964, 203, 1029.

[3] Bussolati, G., and Pearse, A. G. E., *J. Endocr.*, 1967, 37, 205.

[4] Friedman, J., and Raisz, L. G., *Science*, 1965, **150**, 1465.

[5] Aliapoulios, M. A., Goldhaber, P., and Munson, P. L., ibid., 1966, 151, 330.

[6] Wallach, S., Chausmer, A., Mittleman, R., and Dimich, A., *Endocrinology*, 1967, **80**, 61.

[7] Foster, G. V., Doyle, F. H., Bordier, P., and Matrajt., H., *Lancet*, 1966, **2**, 1428.

[8] Robinson, C. J., Martin, T. J., and MacIntyre, I., ibid., 1966, 2, 83.

[9] Care, A. D., Duncan, T., and Webster, D., *J. Endocr.*, 1967, 37, 155.

[10] Aliapoulios, M. A., and Munson, P. L., *Surg. Forum*, 1965, **16**, 55.

[11] Milhaud, G., Moukhtar, M. S., Bourichon, J., and Perault, A. M., *C.R. Acad. Sci. (Paris)*, 1965, **261**, 4513.

[12] Williams, G. A., Hargis, G. K., Galloway, W. B., and Henderson, W. J., *Proc. Soc. exp. Biol. (N.Y.)*, 1966, **122**, 1273.

[13] Duncan, T., and Care, A. D., *Brit. J. Surg.*, 1967, **54**, 196.

[14] Mazzuoli, G. F., Coen, G., and Baschieri, L., *Lancet*, 1966, 2, 1192.

[15] Chimènes, H., and Klotz, H. P., ibid., 1967, 1, 111.

[16] Aliapoulios, M. A., Voekel, E. F., and Munson, P. L., *J. clin. Endocr.*, 1966, **26**, 897.

[17] Tashjian, A. H., Frantz, A. G., and Lee, J. B., *Proc. nat. Acad. Sci. (Wash.)*, 1966, **56**, 1138

[18] Gittes, R. F., Munson, P. L., and Toverud, S. U., *Fed. Proc.*, 1966, 25, 496.

[19] Foster, G. V., Joplin, G. F., MacIntyre, I., Melvin, K. E. W., and Slack, E., *Lancet*, 1966, **1**, 107.

Problems of Transplantation

Extensive studies of the pathological changes that occur during the rejection of transplanted organs are still relatively few. One of the outstanding contributors to this field has been Professor K. A. Porter, of St. Mary's Hospital, so it is fitting that he should have edited the proceedings of a symposium held at the College of Pathologists[1] and now published as a supplement to the *Journal of Clinical Pathology.*[2]

Professor Porter's own contribution to the volume consists of a beautifully illustrated paper depicting the changes in transplanted kidneys when rejection occurs despite treatment of the recipient with immunosuppressive drugs. He describes four distinct patterns of rejection. First is an acute and immediate reaction within minutes of transplantation. Characteristic microscopical changes are glomerular microthrombi, with red-cell sludging. The lesion is thought to be due to circulating antibodies in pre-sensitized recipients or, when there has been severe blood-group incompatibility, between donor and host. The second form of rejection appears between two and ten days after transplantation. Cellular infiltration and rupture of peritubular capillaries are followed by tubular necrosis. This type of change is similar to that observed in experimental transplants in untreated animals. The third pattern of rejection occurs from 11 days onwards, and the main feature is vasculitis. Immunoglobulins and complement coat the arterioles and glomerular capillaries. Aggregates of platelets are found in the glomerular capillaries and fibrin thrombi in the walls of larger arteries. Organization of platelet thrombi results in narrowing of the interlobular arteries. The fourth type of rejection is insidious and can occur a long time after transplantation. There is subendothelial accumulation of immunoglobulin and complement on the glomerular capillary basement membrane, with progressive slow deterioration of renal function.

The two most promising recent advances in tissue transplantation—namely, the use of heterologous antilymphocyte serum and the application of tissue typing—were discussed by Professor M. F. A. Woodruff and Drs. J. J. Van Rood, A. Van Leeuwen, and J. W. Bruning. Professor Woodruff, who has pioneered the development of antilymphocyte serum, describes a serum prepared in the horse against human lymphocytes which has been used clinically by T. E. Starz and his colleagues. It would appear from preliminary result that this serum adds to the immunosuppressive action c azathioprine and prednisone without equivalent adde toxicity. Lower doses of prednisone can therefore be use with reduction in its unpleasant and even lethal side-effec when given in high dosage. Dr. Van Rood and his colleagu described two genetically independent leucocyte gro systems, one with ten and the other with two antigens. T antigens of the first leucocyte group system have been sho by skin-graft experiments to be transplantation antig Preliminary results suggest that matching of lymphoc groups of donor and recipient improves the chances successful kidney transplantation.

The remaining papers in this volume provide an excel background to the present state of knowledge of transpla tion immunity, particularly from the pathological poin view. Finally, in an authoritative summing up Prof Woodruff relates the experimental work to present cli results and future prospects in the field of transplantation. In addition to the problem of immunological rejection there are other difficulties, notably those in obtaining satisfactory numbers of donors, particularly from cadaver sources. Better methods of storing organs are also needed. Professor Woodruff ends with the hope that transplantation of organs from animals to man may eventually become successful.

---

[1] See *Brit. med. J.*, 1967, 1, 560.

[2] *Suppl. J. clin. Path.*, 1967, 20, ix–xv, 415–554. Published f College of Pathologists by the British Medical Association. 3

The College of Pathologists is to be congratulated on this symposium—the first it has held. The report of it provides an up-to-date account of tissue and organ transplantation which should be of help to all who are interested in this field, and particularly pathologists.

A Disease of Skin and Bowel

In the last 25 years occasional reports have appeared describing what is apparently a new disease affecting chiefly the skin and the intestines. The condition was first recognized in 1942 by R. Degos and his colleagues,[1] [2] who initially called it "atrophic papulosquamous dermatitis," and later[3] "malignant atrophic papulosis." An earlier report by W. Köhlmeier[4] which referred to a case of skin necrosis in a patient thought to have thromboangiitis obliterans clearly describes the same condition, and hence the name Köhlmeier–Degos disease has also been used.

The condition is rare. In a recent review W. E. Strole and others[5] found only 19 reported cases. The majority of these were from European countries, a few from the U.S.A., and one[6] from Great Britain. Seventeen of the patients were males, and of these 14 were aged under 40 years. The initial presentation is a papular skin lesion on the trunk and limbs. The papules are at first pink or grey, several millimetres in diameter, and appear in crops. They remain unchanged for some time, but later rapidly develop central umbilication and may coalesce to form larger lesions. With time they become less prominent and assume a rather mummified appearance, but they never disappear completely. At this stage the patient feels well, and, apart from the rash and transient burning or pruritus, has no symptoms. After a variable period, which may be weeks or years, abdominal pain, weakness, fatigue, loss of weight, and sometimes diarrhoea develop. Intestinal perforation then follows and in most cases it is fatal, because multiple perforations occur either simultaneously or at intervals. At laparotomy or necropsy the bowel wall is seen to be studded with multiple depressed white patches similar to the skin lesions. In three cases death was due to multiple cerebral infarcts.

Histologically the characteristic lesion is a change in the rterioles and small arteries. The affected vessels are occluded y relatively acellular fibrous thrombi, and the wall of the rtery at the site of occlusion shows a subendothelial fibrolasia. The elastic lamina remains intact and at this level ere is no inflammatory response either in the vessel wall in the periarterial tissues. Elsewhere in the artery, hower, an arteritis resembling that seen in polyarteritis nodosa ay be found. Though clinically the disease presents mainly th skin and intestinal lesions, the arterial changes are in fact widespread and may be in any organ. The skin lesion is a non-specific combination of epidermal atrophy and dermal sclerosis, and the histological diagnosis rests on finding the characteristic vascular lesion in the small arteries of the reticular dermis.

Laboratory investigations do not reveal any specific changes. The course of the disease appears to be uniformly fatal, and so far all the therapeutic regimens which have been tried have failed.

Is this a new disease ? From the published descriptions of the illness the clinical picture is apparently striking and it is unlikely that it would not have been recognized and reported by the astute clinicians of the early years of this century. The condition which it most closely resembles is polyarteritis nodosa. The clinical picture with the emphasis on the skin and the intestines is certainly unlike classical polyarteritis nodosa. Though the main lesion in the small arteries is apparently different from that of polyarteritis, yet some of the published photomicrographs do show a distinct arteritis in parts of the affected vessels. The time course of the illness and the lack of response to adrenal corticosteroids also suggest that though "malignant atrophic papulosis" is primarily a disease of small arteries and arterioles it may be distinct from polyarteritis nodosa. But it seems equally possible that, like Wegener's granulomatosis, it is a variant of a disease with protean manifestations.

---

egos, R., Delort, J., and Tricot, R., *Bull. Soc. franç. Derm. Syph.*, 1942, **49**, 148.

— Lortat-Jacob, E., Garnier, G., and Benoit, C., ibid., 1942, **49**, 281.

— *Brit. J. Derm.*, 1954, **66**, 304.

hlmeier, W., *Arch. Derm. Syph. (Berl.)*, 1941, **181**, 783.

ole, W. E., Clark, W. H., and Isselbacher, K. J., *New Engl. J. Med.*, 1967, **276**, 195.

ll-Smith, S. P., *Proc. roy. Soc. Med.*, 1964, **57**, 519.

A Case for Cannabis?

The full-page advertisement in *The Times*[1] signed by prominent scientists, doctors, and intellectuals, urging that "the law against marihuana is immoral in principle and unworkable in practice," is only one of many recent appeals[2] in Britain and the U.S.A. for a more permissive attitude.

Marihuana, "pot," and hashish are all forms of cannabis, and are obtained from the flowers or leaves of the female Indian hemp plant, *Cannabis sativa.* International legal control of cannabis came into being in 1925, when the League of Nations organized its second opium conference.[3] The Egyptian delegate stated that 30 to 60% of the patients suffering from insanity in Egypt were cases of chronic hashishism. The conference agreed that the use of Indian hemp and its products should be authorized for medical and scientific purposes only, and that international trade should be strictly controlled. In Britain the Dangerous Drugs Act of 1920 was amended to include cannabis, and it is still included in the 1965 Act.

Cannabis has no known therapeutic value,[4] and possibly as a result of this there has been little research into its pharmacology in man. Inhaled smoke produces initial effects within a few minutes and maximum response is obtained in half to one hour, persisting for some three to five hours. If the drug is taken in a conducive setting its effects commonly include tranquillity, apathy, and euphoria. Much less frequently fear, aggression, and hilarity are noted, these sometimes being seen when cannabis is used by an extrovert in a stimulating situation. With increasing doses changes in mood are followed by changes in perception including changes in perception of the passage of time and then by hallucinations. There is also an idiosyncratic reaction resembling a psychosis ; this is not dose-dependent, and the probability of its occurrence is apparently not related to the stability of the personality. Rarely hallucinations and fragmentation of thought processes occur and present as psychotic disturbances. The physical signs may include variations in blood pressure and pulse rate, bronchoconstriction, hypoglycaemia, and alimentary disturbances, though these features are not constant. More significant is the marked dilatation of conjunctival blood vessels which frequently occurs after first taking the drug.

---

[1] *The Times,* 24 July 1967.

[2] *Newsweek,* 24 July 1967.

[3] *Report of the International Conference on Opium and Dangerous Drugs,* Cmnd. 2461, 1925. H.M.S.O.

[4] *Brit. med. J.*, 1964, **2**, 1348.

[5] Eddy, N. B., Halbach, H., Isbell, H., and Seevers, M. H., *Bull. Wld Hlth Org.*, 1965, **38**, 721.

[6] *Ciba Foundation Study Group 21, Hashish; its Chemistry and Pharmacology,* 1965. London.

The World Health Organization has defined a state of drug dependence of the cannabis type.[5] There is a moderate to strong psychological dependence as a result of a desire for the subjective effects, but an absence of physical dependence—so no abstinence syndrome occurs—and there is no evidence of tolerance. Commenting on this, N. B. Eddy and his colleagues stated that individuals dependent on cannabis might suffer from " inertia, lethargy, self neglect, feelings of increased capability with consequent failure, and precipitation of psychotic episodes."

Research into the effects of cannabis in man is in progress in the U.S.A. and elsewhere.[6] No objective assessment of the effects of prolonged administration of the drug has yet been published. There is still disagreement whether or not cannabis users are likely to progress to heroin and other " hard " drugs. An answer to both these questions is urgent. But while the effects of prolonged exposure to cannabis remain speculative it is irresponsible to encourage a more permissive attitude to the drug.

Respiratory Burns

On 28 November 1942 a disastrous fire occurred at the Cocoanut Grove night club in Boston in which 491 people lost their lives. Of the 114 casualties taken to the Massachusetts General Hospital, 75 were either dead on arrival or died of anoxia within minutes. Of the 39 who survived long enough to be treated, only three were entirely without respiratory symptoms. The clinical picture,[1] *x*-ray appearances,[2] and pathology[3] of these pulmonary injuries were well recorded. Only a small proportion of the victims had extensive burns, and most of the deaths were attributed to anoxaemia and poisoning by carbon monoxide and traces of oxides of nitrogen.

In 1945 A. R. Moritz[4] and his co-workers published experimental work on dogs in which they showed that when hot air was blown into the larynx at 270° C. the temperature of the air fell to 50° C. in the trachea. Hot air and flame could burn the larynx and trachea but failed to produce pulmonary damage. On the other hand, inhaled steam produced severe pulmonary injury owing to its greater latent heat.

A review by A. W. Phillips and colleagues of cases treated at the Massachusetts General Hospital during 1939–57[5–7] showed that in 42% of fatal cases the patient died of damage to the respiratory tract, about half of these in the first three days. They stressed the significance of deep flame burns around the nose and mouth, burning in an enclosed environment, and the inhalation of smoke and the products of incomplete combustion as ominous warning signs of pulmonary damage even in the absence of respiratory signs and symptoms.

Recently H. H. Stone and his colleagues,[8] dissatisfied with the results of treating patients with pulmonary burns (mortality 89%), carried out experiments to evaluate present methods of therapy. They insufflated steam at 10 mm. Hg pressure through a chilled, plastic, intratracheal tube for one to five second in rats. Their studies showed that treatment with 40% oxygen or 80–100% humidity reduced the mortality of the animals. Antibiotics failed to decrease mortality, and treatment with adrenal steroids appeared to be contraindicated.

Respiratory tract damage in burned patients is less common in Britain than in the United States. In Britain extensive burns affecting the face are usually the result of clothes being set alight from unguarded coal fires, and not from people being trapped in burning buildings. The victims, usually children, run about breathing normal air till the flames are put out. In this country only about 5% of patients admitted to hospital with domestic burns have received them in conflagrations, and a pulmonary lesion, because it is uncommon, tends to be missed until a disaster like the Dellwood Maternity Home fire,[9] which killed 13 newborn babies, reminds us of the truism that " smoke is poison."

Clinically, the surgeon should suspect damage of the pulmonary tract from the circumstances in which the patient was burned. He must then assess the site of the damage. If the pharynx, larynx, and upper trachea alone are injured the patient will probably complain of a sore throat and hoarseness—possibly leading to stridor. He may also have a cough, with carbon particles in the sputum and perhaps flecks of blood. If pulmonary damage is present it may not be apparent for several hours, or it may kill the patient with anoxia in a matter of minutes.

Stone's classification of pulmonary damage into respiratory insufficiency, pulmonary oedema, and pulmonary infection is a practical one ; the first two stages may not be clinically obvious in a mild case.

Pulmonary insufficiency may last 24–36 hours. It is the result of narrowing of the smaller bronchi due to spasm, congestion, and oedema of the walls, and blocking with carbon particles, epithelium, fibrin, leucocytes, and mucus. This leads to laboured breathing with an expiratory wheeze. Anoxia is evident from restlessness and confusion, and it may lead to coma and permanent brain damage. Cyanosis is usual, but it may be masked by anaemia or the cherry-red of carbon monoxide poisoning. If rales are present within an hour the prognosis is grave, but even if they are absent the victim should be admitted to hospital overnight for observation like a case of concussion. A single normal chest radiograph is of no significance. Changing physical signs in the chest are probably due to transient atelectasis and filling of alveoli with exudate, epithelial debris, and white cells. Stone's work has shown the value of treating burned patients in this stage with 40% oxygen and 80–100% humidity. Positive-pressure ventilation did not appear to overcome hypoxia, and tracheostomy, except for associated laryngeal obstruction, may precipitate pulmonary oedema by reducing the intrapulmonary pressure produced by intermittent glottic obstruction to respiration. Aminophylline may help to relieve bronchospasm.

---

[1] Aub, J. C., Pittman, H., and Brues, A. M., *Ann. Surg.*, 1943, **117**, 834.
[2] Schatzki, R., ibid., 1943, **117**, 841.
[3] Mallory, T. B., and Brickley, W. J., ibid., 1943, **117**, 865.
[4] Moritz, A. R., Henriques, F. C., and McLean, R., *Amer. J. Path.*, 1945, **21**, 311.
[5] Phillips, A. W., and Cope, O., *Ann. Surg.*, 1962, **155**, 1.
[6] —— —— ibid., 1962, **156**, 759.
[7] —— Tanner, J. W., and Cope, O., ibid., 1963, **158**, 799.
[8] Stone, H. H., Rhame, D. W., Corbitt, J. D., Given, K. S., and Martin, J. D., ibid., 1967, **165**, 157.
[9] Cox, M. E., Heslop, B. F., Kempton, J. J., and Ratcliff, R. A., *Brit. med. J.*, 1955, **1**, 942.

Pulmonary oedema, which is uncommon within eight hours of the burn, usually follows resuscitation. Strictly aseptic positive-pressure ventilation is the only useful therapy[8] and may be given through a tracheostomy, cuffed tube, or face-piece. Pulmonary infection is the final condition through which all cases of pulmonary damage must pass, and it calls for antibiotics in high dosage controlled by daily cultures.

First aid for scalds has been in the public eye in recent months, particularly in the controversial matter of immediate cooling of the scalded skin. But there is no controversy about the value of a first-aid precaution against smoke and toxic fumes. The three survivors of the Cocoanut Grove disaster who sustained no damage to the respiratory tract had covered their mouths with wet clothes. Is this not a measure which television playwrights could teach by portrayal without comment ?

Sjögren's Syndrome

If a woman in her 40s complains of dry, smarting, burning, or itching eyes and a dry mouth, then the possibility of Sjögren's syndrome[1] should be considered. The other common component of the syndrome is rheumatoid arthritis, but this may be replaced or overshadowed by enlargement of the parotid or lacrimal gland, purpura, Raynaud's phenomenon, subcutaneous nodules, dry skin, scleroderma, splenomegaly, or peripheral lymphadenopathy.[2] Thus the patient may be seen in either the ophthalmic or the rheumatology clinic, thereby determining which set of investigations will be undertaken. The ophthalmologist will insert Schirmer filter paper inside the lower eyelid near the external canthus to demonstrate deficiency of lacrimal secretion ; a drop of rose-bengal dye to demonstrate obvious staining of the bulbar conjunctiva and cornea ; and he may find, by slit-lamp examination, punctate corneal staining with fluorescein. By these means the presence of kera-conjunctivitis sicca may be confirmed. The rheumatologist, on the other hand, will seek confirmation of the clinical diagnosis of rheumatoid arthritis by radiological and serological examinations. It is particularly the field of serology which has contributed richly to our knowledge of the disorder and extended the perspectives of its aetiology and pathogenesis. B. R. Jones[3] found that the sera of patients with Sjögren's syndrome contained specific precipitating antibodies reacting with extracts of salivary and lacrimal glands, while J. R. Anderson and his colleagues[4] detected non-organ-specific precipitating autoantibodies reacting with a variety of extracts of human and some animal tissues and thyroglobulin. Serological tests suggestive of systemic lupus erythematosus are also a feature of Sjögren's syndrome. J. M. Heaton[5] demonstrated the frequent occurrence of the lupus-erythematosus cell test, subsequently showing with D. Doniach that the antinuclear factor and thyroid autoantibodies occurred in about a half of patients with Sjögren's syndrome. The rheumatoid factor was found in 82% of cases ; it was present in the same proportion whether or not there was joint disease.[6] In a still wider clinicoserological survey in Bethesda in the United States evidence was found not only of distinct clinical but also of serological subgroups.[7] The presence of rheumatoid factors in almost every case of Sjögren's syndrome, even in the absence of rheumatoid arthritis, was an unexpected finding.

All the evidence points to the fact that Sjögren's disease is an autoimmune phenomenon, and the pathological findings support this view. Thus lacrimal and salivary glands are infiltrated by lymphocytes and plasma cells, with atrophy of the secreting acini and increased interstitial fibrosis. Similar infiltrative changes are widespread, as might be expected in a disorder which has a chameleon-like variety of clinical masquerades. Moreover, though the syndrome may present and be investigated in ophthalmic and rheumatology clinics, it may be found by diligent search in patients seen in psychiatric and gastroenterology clinics. Sjögren's syndrome is predominantly a disorder of menopausal women, many of whom are also suffering from endogenous or reactive depression. It may occur simultaneously with another autoimmune process—primary biliary cirrhosis—which is also common in women in their 40s. Under these circumstances depression and primary biliary cirrhosis may prove dominant and mask concomitant Sjögren's disease unless the serological abnormalities of the latter are specifically sought.

It remains a distressing affliction since treatment is so unsatisfactory. Local treatment to the eyes for relief of symptoms due to dryness includes 1% methylcellulose in saline (artificial tears) or sulphacetamide eye drops. The latter are bland and alkaline and minimize bacterial complications. The danger of corneal ulceration is always present, so that corticosteroid drops should incorporate an antibiotic. Sealing of the puncta by cautery helps to conserve what little moisture is present, and contact lenses may give relief if these are tolerated. Because of its similarities to rheumatoid arthritis and systemic lupus erythmatosus, J. M. Heaton[8] conducted a double-blind trial comparing the value of giving 800 mg. hydroxychloroquine daily for six months with a placebo. A significant difference was obtained, for 12 of 15 improved with hydroxychloroquine compared with 6 of 15 while on the placebo. Two patients developed toxicity owing to deposition of the drug in the cornea, which took two months to appear and about five months to disappear after the six-month course of hydroxychloroquine had ended. Antimalarial drugs are particularly indicated if an appreciable degree of rheumatoid arthritis is also present. Because of its putative autoimmune nature the syndrome has also been treated by immunosuppressive drugs. Thus corticosteroid drugs have been used both locally and by mouth, but relapses have followed cessation of treatment and the danger of corneal ulceration is a real one. Since it commonly occurs in menopausal women, oestrogens might be found to be helpful ; and this association is strengthened by the fact that excretion of hydroxyproline, which is greatly raised in Sjögren's syndrome, may be corrected by oestrogen administration. If the depression is endogenous rather than due to the distressing affliction itself, then a therapeutic trial of nortriptyline or imipramine is worthwhile.

---

[1] Sjögren, H., *Acta ophthal. (Kbh.)*, 1933, Suppl. No. 2.

[2] Vanselow, N. A., Dodson, V. N., Angell, D. C., and Duff, I. F., *Ann intern. Med.*, 1963, 58, 124.

[3] Jones, B. R., *Lancet*, 1958, 2, 773.

[4] Anderson, J. R., Gray, K. G., Beck, J. S., and Kinnear, W. F., ibid. 1961, 2, 456.

[5] Heaton, J. M., *Brit. med. J.*, 1959, 1, 466.

[6] —— *Proc. roy. Soc. Med.*, 1962, 55, 479.

[7] National Institutes of Health Staff Conference, *Ann. intern. Med.*, 1964, 61, 509.

[8] Heaton, J. M., *Amer. J. Ophthal.*, 1963, 55, 983.

Papers and Originals

Psychiatric Sequelae of Subarachnoid Haemorrhage

P. B. STOREY,* M.B., M.R.C.P., D.P.M.

Brit. med. J., 1967, 3, 261–266

This study is a report on the psychological and psychiatric morbidity of 261 cases of subarachnoid haemorrhage treated at Atkinson Morley's Hospital between January 1958 and June 1964. During this period approximately 2,750 patients with subarachnoid haemorrhage were admitted, in about 1,300 of whom aneurysms were demonstrated. Many of the latter were included in a trial of surgical versus nonsurgical treatment in patients with ruptured cerebral artery aneurysms, the organization and early results of which were described by McKissock, Richardson, and Walsh (1960). The background to the trial was that, although surgery of various types had been used for many years, there was no clear knowledge of the natural history of patients with ruptured aneurysms, so that the surgical results reported were possibly due to selection of cases already out of danger from rebleeding (McKissock and Walsh, 1956 ; Norlen and Barnum, 1953).

The trial was designed to allocate cases suitable for surgery randomly to operative or conservative treatment after stratification by site of aneurysm, blood pressure, age, clinical condition, and elapse of time since the haemorrhage. Sex was not originally used as a stratification factor, but it was realized later (McKissock, Richardson, and Walsh, 1962) that it was of great importance in middle cerebral aneurysms, as women fared worse with surgery than did men.

Conservative treatment in this trial means six weeks' rest in bed, with any necessary medical measures, including hypotensives, followed by gradual mobilization. Surgical treatment is of three main types: common carotid ligation (C.C.L.) ; direct attack on the aneurysm (D.A.) ; and proximal occlusion of the vessel from which the aneurysm arises, used only for anterior communicating aneurysm in this series. The operations used in the cases considered in the comparisons are described later.

The results of the trial of surgery so far have been published by McKissock, Richardson, and Walsh (1960, 1962, 1965) ; they indicate that surgery is of definite benefit in posterior communicating (P.C.) aneurysms and in men with middle cerebral (M.C.) aneurysms. No significant differences between operative and conservative treatment have been shown for women with M.C. aneurysms or for patients with anterior communicating (A.C.) aneurysms.

The risk of rebleeding from a ruptured cerebral artery aneurysm is greatest in the first few days, and is quite small after two weeks. Surgery to be of real value must therefore be used in the early stages.

There are many scattered references to various psychiatric complications in the literature, but no comprehensive study has been found. All who work in this field are aware that in a certain number of cases marked personality and intellectual deterioration may occur, and that anxiety and depression are not uncommon late results. Walton (1956) in his well-known book on subarachnoid haemorrhage said that mental symptoms proved to be an important cause of disability in his series of patients, both from organic brain damage and from anxiety symptoms ; and commented that such sequelae had received little attention in the literature.

Present Study

Material

Follow-up has been made of 261 patients with proved subarachnoid haemorrhage. All were seen between December 1963 and June 1965. Selection was made without knowledge of their clinical state ; but some patients with an aneurysm in a certain site were chosen in order to bring the groups up to approximately equal size. There was no other special selection.

The follow-up period varied between six years and six months: it was more than three years in 145, between three years and 18 months in 43, and less than 18 months in 73. In only 11 was the follow-up period less than one year ; two of these were at six months, and none was at less than six months.

The age of the patients varied from 19 to 67 years: 6% were under 30 years, 25% were from 30 to 44, 50% were from 45 to 59, and 20% 60 or more.

Of the 261 patients seen seven had multiple aneurysms and 30 had no aneurysms. None was believed to have had a primary intracerebral haematoma, nor had any had a head injury. None of the patients had been on M.A.O. inhibitor drugs at the time of haemorrhage, so far as is known. The remaining 224 had single aneurysms, 81 anterior communicating (A.C.), 72 posterior communicating (P.C.), and 71 middle cerebral (M.C.) aneurysms. Fifteen of those with single aneurysms were for technical reasons regarded as unsuitable for the trial or had an operation in order to evacuate a life-threatening haematoma. These and the seven patients with multiple aneurysms are not considered further here.

When the study was carried out all cases with A.C. aneurysms and women with M.C. aneurysms were still in the trial if they fulfilled the criteria, but those with P.C. aneurysms and men with M.C. aneurysms had been out of the trial, and therefore treated operatively, since 1959 and 1961 respectively. To increase the size of the groups under comparison all cases in the two latter categories have been included in the "trial comparisons" if they fulfilled the original trial criteria—even if they were admitted after the trial had been abandoned—and surgery recognized as the treatment of choice. Such cases are described as suitable for trial in this paper. Of the 224 patients with single aneurysms 163 were actually in the trial and a further 46 were suitable for trial (but all were treated surgically). There are consequently 209 patients who may be used to provide valid comparisons of the incidence of psychiatric and other sequelae—in 125 operatively and 84 non-operatively treated cases. Table I shows the sex and treatment distribution. Of the 30 cases with no aneurysm 14 were men and 16 women.

---

* Senior Lecturer in Psychiatry, St. George's Hospital Medical School, London S.W.1. Supported by grant number NB 03138-06 from N.I.H., Bethesda, Maryland, U.S.A., during course of the study.

In order to check the validity of the comparisons between the 125 operatively treated and 84 conservatively treated cases a series of χ^2 estimations was made on the incidence of the following 11 pretreatment factors in the two groups: sex; age; side of aneurysm; coma following the haemorrhage; level of consciousness on admission (alert or not alert); the incidence and severity of lateralizing neurological signs; blood pressure on admission (above 160/90 or not); incidence of haematomata and of cerebral arterial spasm on angiography; history of previous subarachnoid haemorrhage; and the results of carotid compression before angiography. No significant differences emerged, either between these two groups or in the distribution of the factors between operative and conservative subgroups for each type of aneurysm separately. They may therefore be justifiably compared for the results of treatment.

TABLE I.—*Material for Trial Comparisons* (209 *Cases*)

	A.C.		M.C.		P.C.		Totals
	M	F	M	F	M	F	
Op. ..	16	18	18	21	18	34	125
Cons. ..	25	17	10	19	3	10	84
Totals ..	41	35	28	40	21	44	209
	76		68		65		

Table II shows the type of operation used in the cases compared for the trial.

TABLE II.—*Operation Used in* 125 *Operatively Treated Cases* (*Trial and Suitable-for-trial Cases Only*)

	A.C.		M.C.		P.C.		Totals
	M	F	M	F	M	F	
C.C.L. ..	5	9	2	0	16	32	64
D.A. ..	3	5	16	21	2	2	49
Proximal occlusion	8	4	0	0	0	0	12
Totals ..	16	18	18	21	18	34	125
	34		39		52		

C.C.L. = Common carotid ligation. D.A. = Direct attack on aneurysm after craniotomy, with clipping or gauze wrapping of aneurysm. Proximal occlusion = Of the supplying vessel.

Methods

Of the 261 cases 260 were seen by me, all but eight in their own homes.[1] In 242 cases another informant was also seen, usually the spouse or other close relative.

Each interview lasted between one and a half and two hours, and consisted of an initial informal period with the patient, followed by history-taking and then by questions from a check list. Simple clinical tests of memory, grasp, and comprehension were used. Lastly, the Benton visual retention test and the Inglis paired-associate-learning test were given in most cases. The patient then laid down, and the relative was interviewed separately. The patient was finally examined physically, and blood pressure was measured at the beginning and end of the examination, the lower reading being accepted. Minor lateralizing neurological signs were carefully looked for as presumptive evidence of brain damage.

In addition to interview material letters from the patient in answer to earlier routine follow-up inquiries were studied, and in many cases letters from the patient's general practitioner were also available. A few general practitioners were seen personally—mainly in rural districts. With regard to patients who had had hospital psychiatric treatment the hospitals concerned were contacted, notes being forthcoming in most cases.

At the end of the interview ratings were made on four scales—physical disability, psychiatric symptoms, personality impairment, and intellectual impairment. These are described in the Appendix, and all were made within a few minutes of the end of the interview. (In some cases where other hospital notes were studied later the rating for psychiatric symptoms was changed.) Unfortunately no rating was made on overall mental disability at that time, but during analysis of the results it was realized that such a rating was necessary. As many patients were rated as impaired on more than one of the scales, a false impression could be gained by mentally summing the scores arithmetically. Rating scales of this type are not entirely suitable for such summing, as no truly mathematical relationships can be assumed. A five-point scale of overall mental disability was therefore constructed, the original notes were scrutinized again, and each patient was rated on the scale (see Appendix for details). This procedure has the advantage that more valid comparisons can be made on overall disability and, most importantly, each patient is being considered only once in the comparisons. It is obvious that these last ratings were made after the results were already clear, but every attempt was made to avoid bias.

Results

1. Overall Mental Disability

With the use of the five-point scale as a measure of overall mental disability (see Appendix), Table III shows the results in the 209 aneurysm cases used in the trial comparisons. Comparable figures for the 30 cases with no demonstrated aneurysm are also given.

TABLE III.—*Results in* 209 *Aneurysm Cases* (*Trial Comparisons*) *and* 30 *No-aneurysm Cases. Overall Mental Disability*

	Absent	Mild	Mod.	Severe	V. Severe	Totals
P.C. ..	33 (51)	15(23)	11 (17)	6 (9)	0 (0)	65 (100)
M.C. ..	26 (38)	14 (21)	12 (17)	11 (16)	5 (7)	68 (99)
A.C. ..	35 (46)	22 (29)	14 (18)	3 (4)	2 (3)	76 (100)
All an. ..	94 (45)	51 (24)	37 (18)	20 (10)	7 (3)	209 (100)
No an.	19 (63)	8 (27)	2 (7)	1 (3)	0 (0)	30 (100)

Percentages in parentheses.

Comparing all those with aneurysms with those without, and simplifying the results into absent/mild and moderate/severe/very severe, we find that morbidity is significantly greater in those with aneurysms ($\chi^2 = 5.593$ with 1 degree of freedom, $P < 0.02$).

Those with M.C. aneurysms do worse than those with A.C. or P.C. aneurysms. Again simplifying Table III as above, and considering only the aneurysm cases, then $\chi^2 = 5.345$, $P < 0.1$ with 2 degrees of freedom, not quite reaching conventional levels of significance. If, however, M.C. aneurysms are compared with the others as a whole, then $\chi^2 = 5.320$, $P < 0.05$ with one degree of freedom.

The distribution of central nervous system signs at follow-up is shown in Table IV, but the findings on admission are omitted to save space.

TABLE IV.—*C.N.S. Signs at Follow-up*

	Absent	Mild	Mod.	Severe	Totals
P.C. ..	40 (62)	12 (18)	6 (9)	7 (11)	65 (100)
M.C. ..	27 (39)	22 (32)	7 (10)	12 (18)	68 (99)
A.C. ..	49 (64)	20 (26)	3 (4)	4 (5)	76 (99)
All an. ..	116 (55)	54 (26)	16 (8)	23 (11)	209 (100)
No an. ..	24 (80)	5 (17)	1 (3)	0 (0)	30 (100)

---

[1] One case is included on the basis of detailed letters from the patient and his wife, and of a report from Wing Commander A. W. Black, R.A.F., who examined him, and to whom I am indebted. (The patient was rated unimpaired in all respects.)

In patients with aneurysms the neurological signs at follow-up were significantly more frequent and severe than on admission ($\chi^2=6.30$, $P<0.02$, with one degree of freedom). In those without aneurysms the incidence of the neurological signs was almost exactly as on admission. The fact that no increase occurs in the signs of the no-aneurysm cases indicates that the ratings are probably reliable, as these latter patients have very low rebleed rates, and no possibility of postoperative complications. (The ratings of C.N.S. signs on admission are derived from surgical notes made by a number of people over several years, whereas the follow-up examinations were all made by me.)

There is a significant difference in the incidence of neurological signs at follow-up in the three main aneurysm groups, being greatest in those with M.C. and least in those with A.C. aneurysms. (When grouped as absent/mild and moderate/severe $\chi^2=8.407$ with 2 degrees of freedom, $P<0.025$.)

The fact that those with M.C. aneurysms have a higher incidence of signs is at least a partial—and probably a complete—explanation for their increased overall mental morbidity, demonstrated in Table III. Equally, those with no aneurysms have the fewest neurological signs and the lowest mental disability, while those with A.C. and P.C. aneurysms have intermediate positions in these respects. The evidence is not set out fully in this paper, but, as would be expected, both personality and intellectual impairment are clearly associated with brain damage, of which neurological signs are unequivocal evidence. Psychiatric symptoms of anxiety and depression are not infrequent in those without neurological signs, but those with brain damage have a greater tendency to such symptoms than those without.

TABLE V.—*M.C. Aneurysms in Trial Comparisons. Overall Mental Disability*

	Absent	Mild	Mod.	Severe	V. Severe	Totals
			(a) Women			
R Op. ..	4	3	2	0	1	10
R Cons.	4	4	2	0	0	10
L Op. ..	1	2	2	4	2	11
L Cons.	4	2	1	1	1	9
Totals	13 (32)	11 (27)	7 (17)	5 (12)	4 (10)	40
			(b) Men			
R Op. ..	4	1	3	4	0	12
R Cons.	2	1	1	2	0	6
L Op. ..	3	1	1	0	1	6
L Cons.	4	0	0	0	0	4
Totals	13 (46)	3 (11)	5 (18)	6 (21)	1 (4)	28

There were no significant differences between the overall mental disability of the operatively and the conservatively treated groups, between men and women, nor between those with right-sided as opposed to left-sided aneurysms. A.C. aneurysms are essentially midline structures, although they may damage one side of the brain more than the other on rupture; they are therefore not included in this comparison.

Although when the trial material is considered as a whole there are no sizable differences between operative and conservative groups, between men and women, or between right- and left-sided aneurysms, this is not so when those with M.C. aneurysms are considered separately. Patients with M.C. aneurysms do worse overall than those with other aneurysms (Table III), and it can be seen from Table V that this is entirely because of the worse results with surgery in this group. The difference is most pronounced in the case of women with left-sided aneurysms, but men with right-sided aneurysms also fare worse with surgery than with conservative treatment.

Table V (*a*)—that is, for women with M.C. aneurysm—has been analysed using Cochrans's criterion, testing for the difference in mental disability when grouped as absent/mild and moderate/severe/very severe, and correcting for the differences between right- and left-sided lesions. The test is two-tailed, and the result is between the 7% and 8% levels of significance ($t=1.778$), not quite reaching conventional levels.

Table VI shows M.C. aneurysm cases of both sexes, divided by type of treatment for added clarity.

TABLE VI.—*M.C. Aneurysms in Trial Comparisons. Operative versus Conservative Treatment*

	Absent	Mild	Mod.	Severe	V. Severe	Totals
Op. ..	12 (31)	7 (18)	8 (21)	8 (21)	4 (10)	39 (101)
Cons. ..	14 (48)	7 (24)	4 (14)	3 (10)	1 (3)	29 (99)
Totals ..	26 (38)	14 (21)	12 (17)	11 (16)	5 (7)	68 (99)

Combining the results into two categories of absent/mild and moderate/severe/very severe, the latter contains 52% of the operative and only 27% of the conservative groups. The use of χ^2 test shows the difference to be significant at the 5% level. ($\chi^2=3.892$, $P<0.05$ with one degree of freedom.)

Comparable separate tables for A.C. and P.C. aneurysm groups are not given, but in fact those treated by surgery have a lower overall mental disability than the conservatively treated patients. The differences are not significant. They are, however, marked enough to even out the operative versus conservative comparisons when all aneurysms are considered together.

2. Using Separate Rating Scales

The results so far have been set out with the use of only the rating of overall mental disability. As was explained earlier, each patient was originally rated on four scales, each of four points, for personality impairment, psychiatric symptoms, intellectual impairment, and physical disability (see Appendix). These are set out as histograms in Figs. 1 and 2. It must be remembered that in the overall mental disability ratings psychiatric symptoms were given relatively less weight, as in

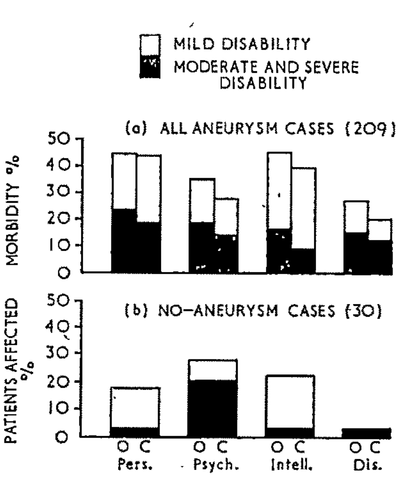


FIG. 1

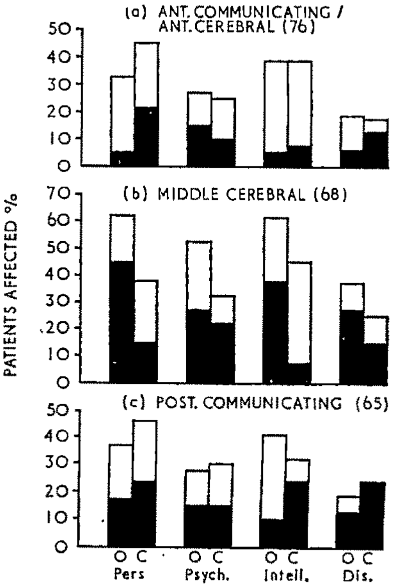


FIG. 2

FIG. 1.—All aneurysm cases in trial comparisons. O—Operated cases. C—Conservative. Pers.—Personality impairment. Psych.—Psychiatric symptoms. Intell.=Intellectual impairment. Dis.—Physical disability. FIG. 2.—Comparison of major aneurysm groups.

many cases they are transient, whereas personality and intellectual impairment are permanent. The histographic method, with four point-rating scales, makes differences between groups more apparent than did the overall rating method, but there are no major inconsistencies. The rating scales were also assessed statistically, using *t* tests, and the results of these will be mentioned where applicable. Fig. 1 shows that the aneurysm cases are more severely affected than those with no aneurysm, and also shows that in the latter group there is very little personality impairment, intellectual impairment, or physical disability rated as moderate or severe. One man, the only no-aneurysm case with C.N.S. signs rated moderately severe at follow-up, is responsible for the 3% shown in each of those categories. Patients with no aneurysms have, however, a similar incidence of psychiatric symptoms to patients with aneurysms. Seven of the 30 patients without aneurysms had clinically significant anxiety or anxiety/depressive states at the time of their haemorrhage, but only two out of seven are rated here as being worse than before the stroke. (This aspect will be dealt with in greater detail in a later publication.)

The columns representing the aneurysm cases in Fig. 1 show a slight worsening in the operative groups, which did not appear in the ratings of overall mental morbidity, but the differences are not significant.

Fig. 2 shows the results in the three main aneurysm groups, from which it can be seen that in the P.C. and A.C. cases those treated operatively do somewhat better than the others, but the differences are not significant. M.C. cases do considerably worse with surgery, however, particularly where moderate damage and severe damage are concerned. Using *t* tests, and considering the sexes and side of aneurysm separately (although the histograms do not show them separately), the significant differences are as follows: for personality impairment in women with left-sided aneurysms, operative cases do significantly worse than conservative cases at the 1% level ($t=2.9$, $n=17$, $P<0.01$); for intellectual symptoms in the same cases the difference is significant at the 2% level ($t=2.8$, $n=17$, $P<0.02$). None of the other differences reach conventional levels of significance.

3. "Improved Personality"

Details of the nature of the personality and intellectual impairment, and of the psychiatric symptoms, will be reported elsewhere, but there are some points which may suitably be mentioned here.

Depressive and anxiety states occurred in patients with and without brain damage, and in this study those with brain damage are rated as depressed even if there is no evidence of depressive illness, and if in my opinion the mood change was distinctive enough. In this way a number of those rated as having mild psychiatric symptoms showed a picture of shallow depression, easily lifted, in a setting of personality and intellectual impairment.

The personality changes which occurred were mainly those commonly recognized in brain damage, but 13 patients were regarded as having improved personalities. (They were rated unimpaired in the results already discussed.) Eight of the 13 had an A.C., four had a P.C., and one had an M.C. aneurysm. This description of "improved" depended essentially on the account of the patient's spouse, which was available in each case. Such a patient was typically described as being more pleasant to live with, a nicer person, less sarcastic and irritable, less tense and anxious, less fussy and overmeticulous, and often as more affectionate and tolerant. Two of the patients showed minor forgetfulness, but in none was there any loss of drive, any falling off in work ability, or any untoward development. None had experienced any depressive or anxiety symptoms, and most were aware of increased well-being subjectively. In seven cases there were no abnormal C.N.S. signs, and in six there were mild or moderate signs. There were no differences between operative and conservative groups in these cases. The previous personality of these patients was described in each case in such terms as "cold," "tense," "sarcastic and irritable," "unreasonably houseproud," or "timid and worrying." Naturally there were a good many patients in whom similar changes were associated with unfavourable changes, and who are therefore not described as having improved.

4. Epilepsy

In the whole case material of 261 patients there were 22 who had had epileptic disturbances. These all had either an M.C. aneurysm (17 cases out of 71, or 24%) or a P.C. aneurysm (five cases out of 72, or 7%). The overall incidence of epilepsy in those with single aneurysms was therefore 22 out of 224 cases, or approximately 10%. The epilepsy was easy to control in all except four patients, and in most there were only a few fits.

There are no significant differences between the operative and conservative groups, but epilepsy is significantly more common in men than in women ($\chi^2=8.556$, $P<0.01$ with one degree of freedom) and with M.C. aneurysm than with P.C. aneurysm ($\chi^2=5.685$, $P<0.025$ with 1 degree of freedom). None of the other differences is significant.

Epilepsy was in all but six cases associated with some abnormal neurological signs, mostly moderately severe or severe, and some other mental disability was present in all but five cases. Fourteen of the 19 patients with epilepsy had had a haematoma demonstrated by angiography—an incidence of 74%. Overall 40% of all patients with M.C. and P.C. aneurysms had haematomata.

Discussion

Subarachnoid haemorrhage from ruptured cerebral artery aneurysm is not uncommon, having been estimated at 6 per 100,000 of population in the area served by Atkinson Morley's Hospital (Crawford and Sarner, 1965). Among patients reaching hospital alive the subsequent mortality depends on various factors—particularly clinical condition, level of consciousness, site of aneurysm, age, blood pressure, and others—(McKissock *et al.*, 1960, 1962, 1965; Richardson, Jane, and Payne, 1964; Richardson, Jane, and Yashon, 1966). In this study the operative and conservative groups were shown to be comparable for the factors named, as well as for various others. The mortality after admission to hospital is high; in the studies mentioned the six-month survival rates of operatively and conservatively treated cases combined were approximately: P.C. aneurysms 69%, M.C. aneurysms 72%, and A.C. aneurysms 58%.

This study shows that the psychiatric morbidity of the survivors is also high. Only 45% of those in the trial comparisons were considered to be unimpaired and 24% as mildly affected. Eighteen per cent. were moderately, 10% severely, and 3% very severely damaged—these last being demented and inaccessible. M.C. aneurysm is associated with a significantly higher morbidity than either of the other main aneurysm types, and most of the serious mental disability was associated with neurological evidence of brain damage. Depressive and anxiety states, sometimes very severe, were quite commonly found in the absence of such damage, however. Those patients with no demonstrable aneurysm had a lower morbidity than the others, a finding which was clearly associated with a lower incidence of brain damage.

Depressive states did not show a more definite relationship to physical disability or to intellectual and personality impairment than they did to brain damage generally—that is, depression did not seem to be mainly a reaction to disability, although in many cases such an element was present. This aspect will be considered in more detail in a later publication.

The findings of 13 patients with improved personalities was unexpected, and seems to represent an effect of leucotomy. This is supported by the fact that most of the patients had A.C. aneurysms, which tend to damage the frontal lobes particularly. Vascular spasm, associated with subarachnoid haemorrhage from aneurysms at any site, may lead to patchy infarction anywhere in the brain, so that five cases that did not have A.C. aneurysms could still have had some frontal-lobe infarction.

The purely psychological reaction to a serious illness may lead a patient to reconsider his ways, change his attitudes to other people, etc., and this may have played a part. However, the nature of the changes and association with A.C. aneurysms make it more likely that this is indeed a leucotomy effect. Similar findings have been made by Logue *et al.* (1967, to be published).

The most important practical finding is that patients with M.C. aneurysms did worse with operative treatment than when treated conservatively. This was most noticeable in women, but it also occurred in men. Men, however, have a better chance of survival with surgery, and it is probable that their increased morbidity is because some of those more severely damaged, who might otherwise have died, have been saved by surgery ; and the findings here do not affect the policy of operating in these patients. In women, on the other hand, there is no increased survival rate with surgery, and it is probable that the cause lies in the morphological and neuropathological differences in M.C. aneurysms in women (Crompton, 1962). These aneurysms are more difficult to treat, and the added brain damage due to surgical exposure of the aneurysm is presumably responsible for the worse results after operation.

However, since the period during which many of the cases in this study were treated there has been a change in the preferred timing of operation, with a consequent improvement in mortality figures. These results have not yet been fully assessed or published, but it is our intention to follow up an adequate sample of women with M.C. aneurysms treated by operation on the fourth to sixth days, to see whether or not there has been a consequent lessening of psychiatric morbidity.

It is understandable that left-sided aneurysms should do worse with surgery, as is the case with women here, when the dominant hemisphere is involved. It is not clear why in men right-sided aneurysms should lead to a higher morbidity. Inspection of the original findings does not suggest a markedly different pattern of disability, although there is an overall tendency in M.C. aneurysms for right-sided lesions to be associated with a greater incidence of psychiatric symptoms and left-sided aneurysms with more intellectual impairment, and for there to be an equal incidence of personality impairment with right- and left-sided lesions.

The incidence of epilepsy, 10%, along with its distribution, is very similar to that found by Rose and Sarner (1965), who studied a larger material from the same neurosurgical department. There is a full discussion of the subject in their paper.

Employment status has not been considered separately as a measure of recovery, although always taken into account. Men in some occupations, mainly in large organizations, seemed often to be accepted by the management and carried by their workmates even when clearly incapable of full work. This was found in the case of a senior managerial executive who continued to draw full salary although suffering from marked intellectual and personality impairment ; but it was much commoner in lower employment levels. Self-employed people doing skilled or professional work seemed to suffer more from any given level of disability. Other patients were found who had retired or had changed their work, on medical grounds, unnecessarily—often because of exaggerated fears of exertion. The whole matter is closely linked with economic conditions and attitudes towards the handicapped, so that one would expect differences between various countries and various periods.

Appendix 1

Overall Mental Disability.—This is a five-point rating scale. Most weight is placed on permanent changes; transient anxiety and depression, even if severe, are considered to be less important than intellectual and personality damage.

Absent or Minimal Disability.—Includes those with only minor memory impairment (forgetfulness), and those with transient anxiety/depressive states not seeking or requiring treatment.

Mild Disability.—Comprises those with intellectual impairment which allows adequate functioning in nonintellectual occupations, those in whom personality change is not sufficient to lead to deterioration in family or other relationships, and those with depression or anxiety states responding to treatment —either as inpatients or as outpatients.

Moderate Disability.—Includes those with definite impairment of work status unless completely unskilled ; deterioration in personal relationships and subjective well-being ; severe and prolonged depression not responding fully to inpatient treatment even in the absence of other changes.

Severe Disability.—In this section are included those with personality and intellectual impairment, or both, severe enough to lead to unemployment or a pronounced fall in employment status ; marked deterioration in family relationships and subjective well-being, or both ; and severe prolonged depression not responding fully to inpatient treatment, in conjunction with otherwise moderate intellectual and personality damage. This category contains patients who are largely incapable of independent life and need institutional care or the protection of a tolerant family.

Very Severe Disability.—Includes those who are grossly demented, inaccessible, bedfast, and often grossly dysphasic. Two such cases were being nursed at home, the others were in institutions.

Appendix 2 : Rating Scales of Impairment and Disability

Each patient was initially rated on a four-point scale of impairment or disability (absent, slight, moderate, severe) on each of the following:

Personality Impairment.—In this rating the opinion of the other informants was regarded as most important. On the whole the changes were those commonly recognized as " organic personality change," with loss of drive and vitality, irritability, easily provoked anxiety, dependence, emotional lability, etc.

Psychiatric Symptoms.—These were almost entirely depressive states and anxiety symptoms, often together. Both lasting and limited illnesses are included, but symptoms restricted to the first three months of convalescence are excluded. In patients whose symptoms had cleared up before the follow-up examination it was sometimes difficult to assess severity, but most of these rated as severe cases had had inpatient or prolonged outpatient treatment ; most rated moderate had had outpatient treatment. However, several of those rated moderate, and who were also brain-damaged, had not had psychiatric treatment. In patients with pre-existing anxiety or depressive states, only a worsening is counted in the ratings. Epileptic syndromes are not included.

Intellectual Impairment.—In this rating the results of the Benton visual retention test and the Inglis paired associates test are ignored. The rating is based on accounts given by the patient and other informants, the results of simple clinical tests (orientation, digit span, remembering a name and address, simple calculations, serial seven subtraction, knowledge of current affairs, etc.), and the general impression made ; at the same time taking into account the patient's background and presumed previous intelligence. The rating of severe is equivalent to frank dementia ; mild rating to some impairment of recent memory and higher intellectual abilities, but compatible with no loss of employment status except in professional, executive, and similar occupations. Moderate impairment falls between the two above, and is usually associated with a drop in employment status.

Physical Disability.—This excludes purely ocular disabilities, and refers mainly to the consequences of weakness or other disturbances of the limbs. Those with C.N.S. signs are not included unless there is frank disability—which depends mainly on the severity of the signs and the nature of the patient's work.

Summary

Some results of a psychiatric study of 261 cases of subarachnoid haemorrhage are presented, dealing especially with comparisons between operative and conservative treatment of 209 patients with single aneurysms of the posterior communicating (P.C.), middle cerebral (M.C.), and anterior communicating (A.C.) arteries. The background and trial organization are briefly described.

Psychiatric morbidity is high. Of those with aneurysms in the trial comparisons 45% were regarded as unimpaired or nearly so ; 24% were mildly, 18% moderately, 10% severely, and 3% very severely affected. Patients with no demonstrable aneurysms (30) had lower morbidity rates.

Most of the psychiatric and psychological morbidity is due to brain damage, but anxiety and depressive states also occur in the absence of such damage, and may be very severe.

Patients with M.C. aneurysms have a significantly higher morbidity with surgical than with conservative treatment, especially women with left-sided lesions. Possible reasons for this are mentioned. Patients with aneurysms at other sites do slightly but not significantly better with surgery.

A group of 13 patients with apparently improved personalities is described. This improvement is regarded as a leucotomy effect.

The incidence of epilepsy is 10% overall in patients with single aneurysms. No case of epilepsy occurred in those with A.C. aneurysms or with no demonstrable aneurysm. The rate was 24% in those with M.C. and 7% in those with P.C. aneurysms. There was no difference between operative and conservative treatment in this respect.

Several tables have had to be omitted to save space. Details will be sent on request.

I wish to express my gratitude to all those who made this study possible. The patients examined were under the care of Mr. Wylie McKissock, who originally suggested the study, Mr. A. E. Richardson, and Mr. L. S. Walsh, all of whom gave every help and much valuable advice. Professor Desmond Curran provided me with facilities and gave me encouragement. I have had essential statistical advice from Mr. P. M. Payne and Mr. H. Gwynne Jones ; and there are many others, not named here, to whom I am also most grateful. Financial support for computer analysis was provided by St. George's Hospital Medical School.

REFERENCES

Crawford, M. D., and Sarner, M. (1965). *Lancet*, **2**, 1254.
Crompton, M. R. (1962). Ibid., **2**, 421.
Logue, V., Durward, M., Pratt, R. T. C., Piercy, M., and Nixon, W. B. L. (1967). *Brit. J. Psychiat.* In press.
McKissock, W., Richardson, A., and Walsh, L. (1960). *Lancet*, **1**, 1203.
—— —— —— (1962). Ibid., **2**, 417.
—— —— —— (1965). Ibid., **1**, 873.
—— and Walsh, L. (1956). *Brit. med. J.*, **2**, 559.
Norlen, G., and Barnum, H. S. (1953). *J. Neurosurg.*, **10**, 634.
Richardson, A. E., Jane, J. A., and Payne, P. M. (1964). Ibid., **21**, 266.
—— —— Yashon, D. (1966). *Arch. Neurol. (Chic.)*, **14**, 172.
Rose, F. C., and Sarner, M. (1965). *Brit. med. J.*, **1**, 18
Walton, J. N. (1956). *Subarachnoid Haemorrhage.* Edinburgh.

Psychiatric Aspects of Pernicious Anaemia: A Prospective Controlled Investigation

RALPH SHULMAN,* M.B., CH.B., M.R.C.P.ED., M.R.C.P.GLASG., D.P.M.

Brit. med. J., 1967, **3**, 266–270

Though a wide spectrum of psychiatric symptoms has been attributed to vitamin-B_{12} deficiency, the factors which predispose individuals to this form of illness rather than to haematological or neurological manifestations remain unknown. The frequency of mental symptoms in pernicious anaemia has not been established. Inquiries based on the retrospective analysis of general hospital case records have reported mental symptoms in only 2 to 4% of patients (Young, 1932 ; Cox, 1962), whereas in selected patients with chronic neurological disabilities the incidence of such symptoms has been as high as 60% (McAlpine, 1929 ; Holmes, 1956). No investigations to date have been carried out prospectively on unselected patients with pernicious anaemia admitted to general hospitals, and none have controlled the non-specific effects of physical illness and fatigue on the mental states of patients. Despite these uncertainties, interest in the psychiatric symptoms of pernicious anaemia has been renewed and routine screening tests to detect latent pernicious anaemia have been advocated for all psychiatric patients (Strachan and Henderson, 1965 ; Hunter and Matthews, 1965).

The present investigations were carried out, firstly, to determine the incidence of psychiatric symptoms in patients with pernicious anaemia and, secondly, to evaluate the importance of vitamin-B_{12} deficiency in their development. The method used was a comparison of the psychiatric symptoms in patients with pernicious anaemia and in a control series of patients with other types of anaemia, both groups being matched for age, sex, and haemoglobin level. It was predicted that if vitamin-B_{12} deficiency caused mental symptoms, their incidence would be higher in the pernicious anaemia group and their remission would not occur until after treatment with vitamin B_{12}.

Selection of Patients

Pernicious Anaemia.—Patients with suspected pernicious anaemia were seen through the co-operation of physicians and

---

* Lecturer in Psychological Medicine, University Department of Psychological Medicine and Southern General Hospital, Glasgow S.W.1.
Requests for reprints should be sent to Dr. R. Shulman, Riverview Hospital, Essondale, Vancouver, British Columbia, Canada.

haematologists, and treatment with vitamin B_{12} was withheld until the first psychiatric interview had been completed. In many of the patients a definitive haematological diagnosis had not been established, and several patients were later transferred to the control series when complete investigations had shown a normoblastic type of anaemia. In this way some of the interviews were carried out blindly. Between 1963 and 1966 38 patients were referred as possible cases of pernicious anaemia and interviewed before treatment had begun. Of the 38 patients, 27 are described in this report—25 with Addisonian pernicious anaemia and two with post-gastrectomy intrinsic factor deficiency. Of the remaining patients, two were excluded because of uncertainty in the final diagnosis. Six were transferred to the control series, and three were rejected because of difficulties in examining the mental state on account of deafness, mental subnormality, and advanced physical deterioration.

Control Patients.—The criterion for admission to the control group was a presentation with symptoms of anaemia with little evidence of disabling primary disease. To avoid possible bias in the frequency of psychiatric symptoms in the control group, patients with the following types of anaemia were excluded: (1) anaemia associated with chronic infective and toxic conditions such as renal disease, ulcerative colitis, etc.; (2) anaemia of carcinomatosis and reticuloses; (3) acute haemorrhagic anaemia; (4) pregnancy anaemia; and (5) folate deficiency megaloblastic anaemia. Twenty-one control patients were examined, 18 with chronic iron-deficiency anaemia, two with primary hypoplastic anaemia, and one with a benign haemolytic anaemia.

Methods of Examination

The examination consisted of an interview, a psychological test for organic brain damage, and a personality questionary.

Interview.—Two or more interviews were carried out, the first before treatment, and the second early in treatment at the time of the maximum reticulocyte response. The length and structure of the interviews varied with the physical state of the patients. At every interview the mental state was formally examined for changes in affect, orientation, and intellectual function and for the presence of obsessional symptoms, hallucinations, and delusions. Most patients were well enough to allow a comprehensive history to be taken and when possible the interview was conducted in a private room.

Psychological Test.—The synonym learning test (S.L.T.), an auditory word-learning test, was administered to patients before and after treatment with vitamin B_{12}. This test contains a factor of short-term memory and has been validated and standardized on an elderly psychiatric population (Kendrick *et al.*, 1965; Kendrick, 1965). Patients of low intelligence may be misclassified as brain damaged on this test (Kendrick, 1964), and for this reason all the patients had their verbal intelligence assessed on the synonym section of the Mill Hill vocabulary scale Form I Senior (Raven, 1958).

Questionary.—After their mental state had returned to normal, patients were given the Maudsley personality inventory to complete. This questionary measures two dimensions, neuroticism (N) and extroversion (E) by means of a self-rating scale of 48 questions (Eysenck, 1959).

Assessment of Psychiatric Symptoms and Method of Rating

Some of the symptoms which occur in the psychoneuroses and in depression may also be found in patients with anaemia who have no psychiatric illness. In the present investigations, for example, fatigue and loss of weight were regarded as physical and not psychogenic in origin. The severity of the psychiatric symptoms was measured by the degree to which *psychiatric* symptoms had interfered with the normal habitual activities of the patient. In terms of social disability three grades were defined: (1) mild, if disability occurred in one or more minor areas only—for example, recreation; (2) moderate, if working-time or efficiency had been appreciably diminished; and (3) severe, if unable to follow usual employment.

With this method of rating symptoms it was sometimes necessary to judge whether disability had been caused by psychiatric symptoms rather than by physical incapacity. In general it was possible to make this distinction, and when there was doubt the disability was not regarded as psychiatric.

Follow-up Study

Patients were asked to co-operate in a follow-up study after leaving hospital by a home visit, an outpatient appointment, or a postal questionary.

Results

Incidence and Severity of Psychiatric Symptoms

The psychiatric symptoms included depression, anxiety, loss of libido, irritability, poor concentration, and impaired memory. The only paranoid state encountered was in one of the control patients. Some psychiatric symptoms were present in 82% of the pernicious anaemia patients compared with 52% of the controls, the higher incidence in the former group reflecting symptoms rated as mild. Psychiatric symptoms rated as moderate or severe were present in approximately one-third of both groups of patients. Six of the patients with pernicious anaemia and three of the control patients had a moderate or severe depression.

Incidence and Severity of Psychiatric Symptoms

	Pernicious Anaemia Patients				Control Anaemic Patients			
	Mild	Mod.	Severe	Total	Mild	Mod.	Severe	Total
Normal ..				5				10
Depression..	7	4	2	13	4	2	1	7
Memory impaired ..	4	1	2	7	1	1	1	3
Irritable ..	2			2				
Paranoid state							1	1
Total ..	13	5	4	27	5	3	3	21

Factors Predisposing to Psychiatric Symptoms

Physical.—In pernicious anaemia the presence or severity of the psychiatric symptoms did not correlate with age, duration of illness, physical complications of the illness, loss of weight, neurological involvement, haemoglobin level, or serum vitamin-B_{12} levels.

Psychological.—The neuroticism score on the Maudsley personality inventory did not correlate with the presence of psychiatric symptoms. There was, however, a positive association between depressive symptoms in pernicious anaemia and a past history of depressive illness ($\chi^2=6.51$; $P<0.02$). Of the 13 depressed patients, seven had a personal or family history of depressive illness. Among the 14 patients who were not depressed, none had a history of previous depression.

Effect of Hospital Admission on Mental State of Patients

Early in this investigation it was observed that the psychiatric histories given by the pernicious anaemia patients did not correspond with their mental states shortly after admission to hospital. Eight of the patients reported that their mood had returned to normal shortly after or even before admission to hospital, and related this to the excellent prognosis received from their physicians. This tendency to spontaneous remission was well illustrated in the following case.

The patient, a 47-year-old policeman, had previously been in excellent physical and mental health. To siblings had a history of depression, treated with electric convulsion treatment. For six months the patient had become increasingly concerned by unexplained fatigue. He lost his confidence and became unable to control traffic or meet people. He became deeply depressed with ideas of unworthiness. Suicidal thoughts were present and he was referred for a psychiatric opinion. A blood count showed the presence of a macrocytic anaemia. He was told the result of the test and was referred to a physician. For the next two weeks while he was on the waiting-list for admission to a medical ward his depression remitted completely. "I was better as soon as I knew that it was my blood and not my nerves, doctor." At the first psychiatric interview his mental state was completely normal except for impaired memory on the synonym-learning test.

In most of the control patients the cause of anaemia was unknown on admission and the prognosis was uncertain. Not surprisingly, fewer of the control anaemic patients showed spontaneous improvement after hospital admission.

Memory Impairment: The Synonym-learning Test (Figs. 1 and 2)

Of 24 pernicious anaemia patients, 17 showed abnormal short-term memory on the synonym-learning test, with scores in the range (0–53) associated with brain damage. In pernicious anaemia a brain-damage score was not related either to age or to haemoglobin level. Of the 21 control patients, 16 also had brain-damage scores on this test, but in this group there was a positive correlation between advanced age and an increasingly abnormal score (+0.44; $P<0.01$ Kendall's τ; Siegel, 1956).

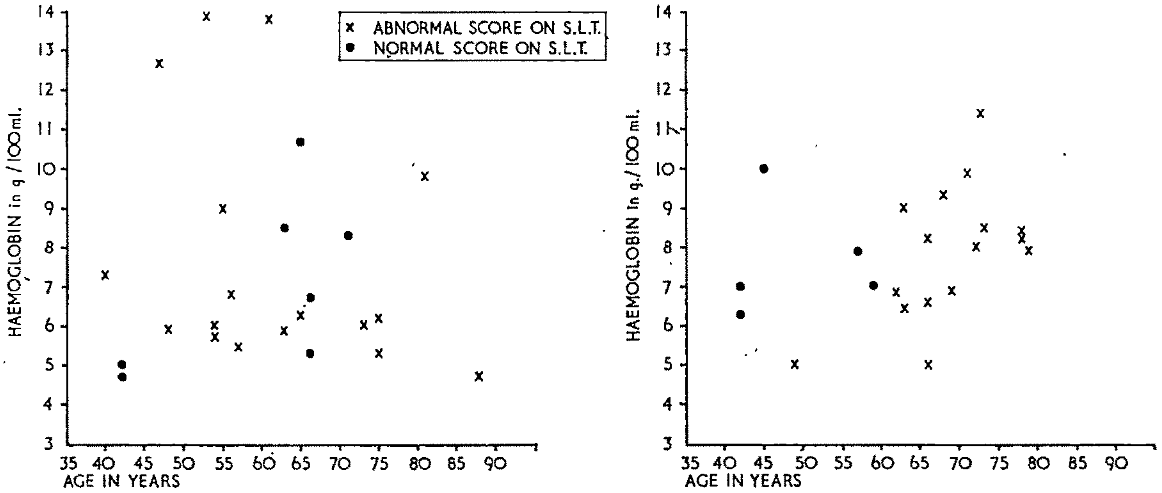


	Figure 1	Figure 2
S.L.T v. Age	+0·09 (N.S.)	+0·44 (P <·01)
S.L.T. v. Haemoglobin	+0·06 (N.S.)	+0·04 (N.S.)
Age v. Haemoglobin	−0·10 (N.S.)	+0·28 (P <·05)
S.L.T. v. Haemoglobin: Age constant	+0·05 (N.S.)	−0·12 (N.S.)
S.L.T. v. Age: Haemoglobin constant	+0·10 (N.S.)	+0·44 (P <·01)

Using Kendall's τ (Siegel, 1956)

FIG. 1.—Relation between age, haemoglobin level, and performance on the synonym-learning test in pernicious anaemia.
FIG. 2.—Relation between age, haemoglobin level, and performance on the synonym-learning test in control anaemic patients.

Effects of Vitamin B_{12}

On the Mental State.—At the second psychiatric interview 10 of the patients declared that they were more cheerful and were taking a new interest in ward activities and conversations. Confirmation of this improvement was sought whenever possible by an interview with the sister and resident doctor in charge of the ward. Nevertheless, it proved difficult to assess whether these changes in mood were the continuation of a previously noted spontaneous remission, the effects of the vitamin-B_{12} injections, or a combination of both. Fourteen patients reported an increased well-being and mental alertness which they had not experienced until after the vitamin-B_{12} treatment. None of the control patients, except two who had received large blood transfusions, were able to record a comparable feeling of well-being and alertness in the early phase of treatment.

On the Synonym-learning Test.—Twelve patients with brain-damage scores agreed to be retested, and nine of them were found to have a normal score early in treatment. After the first vitamin-B_{12} injection the time for the synonym-learning test score to return to normal varied between 10 and 27 days, with a mean interval of 16 days. Serial testing in two patients revealed a considerable improvement on their synonym-learning test scores as early as 20 hours after the first injection. Three patients with persistently abnormal scores had clinical evidence of senile and arteriosclerotic dementia; and during the follow-up study two of them were found to have died after a stroke.

Follow-up Study

The results of a follow-up study one year after leaving hospital are incomplete, since only nine of the pernicious anaemia patients returned a postal questionary or attended for interview. Of this small number, three have relapsed with depressive symptoms despite regular vitamin-B_{12} injections and the maintenance of normal blood values. One other patient has required admission to a psychiatric unit for management of his depression with electric convulsion treatment.

Discussion

In pernicious anaemia the accompanying psychiatric symptoms do not necessarily have a uniform relation to vitamin-B_{12} deficiency. The present investigation has suggested that the main syndromes encountered—depression and memory impairment—have a different origin and significance.

Depression in Pernicious Anaemia

Klerman (1966), in a review of antidepressant drugs, has commented on the frequency of depressive symptoms in conjunction with acute and chronic physical illness. Psychiatric studies in general medical wards have reported that 20% of the patients developed a clinical depression after the onset of an illness likely to be fatal or severely disabling (Helsborg, 1958 ; Stewart *et al.*, 1965). If minor neurotic symptoms had been included the frequency of depressive reactions would have been higher. The results of the present investigations in which 6 out of 27 pernicious anaemia patients and 3 out of 21 control patients developed a moderate or severe depression are consistent with these previous studies.

Patients attributed their depression to the consequences of their physical handicap. It is of interest that after they had received a favourable prognosis many of the pernicious anaemia patients showed a spontaneous remission of depressive symptoms before treatment with vitamin B_{12}. Had this investigation been carried out retrospectively these remissions might have been attributed to the effect of specific therapy with vitamin B_{12}. Because there were patients in both groups who did not develop psychiatric symptoms or in whom such symptoms were mild despite severe physical incapacity, personality characteristics and constitutional factors may have been decisive in determining the appearance of psychiatric sequelae. Evidence that those who developed depressive symptoms were constitutionally vulnerable was indicated by their high incidence of previous depressive reactions, and by a tendency to relapse after discharge from hospital.

In summary, the evidence relating to vitamin-B_{12} deficiency and depressive illness is tenuous. Depressive symptoms are not more common in pernicious anaemia than in other types of disabling physical illness. When depression accompanies pernicious anaemia it would appear to be related less to the direct effect of vitamin-B_{12} deficiency than to the uncovering of a constitutional predisposition to depressive illness precipitated by the anxiety of unexplained fatigue and physical incapacity.

Loss of Memory and Pernicious Anaemia

In pernicious anaemia a short-term loss of memory has been demonstrated on the synonym-learning test. In contrast with the control series this memory impairment was independent of age or anaemia. Memory changes may occur in depression, but few of the patients were clinically depressed at the time of testing. After receiving vitamin B_{12} many patients experienced a rapid sense of well-being and mental alertness. The cellular effects of vitamin B_{12} can be observed after a few hours without implicating placebo-responders. Cells in the bone marrow begin to revert to normoblastic type after nine hours, and in bone-marrow cultures the R.N.A./D.N.A. ratio in the cell returns completely to normal within 24 to 48 hours (Thomas and Lochte, 1958). After one week electroencephalographic abnormalities begin to improve (Samson *et al.*, 1952 ; Walton *et al.*, 1954) and cerebral oxygen consumption shows a moderate increase (Scheinberg, 1951). The earliest changes in the synonym-learning test were observed after 20 hours ; in nine patients a reversion to completely normal scores on this test took on average 16 days. Parallel electroencephalograms would have been interesting, but facilities for this were not available.

Did the nine patients with reversible synonym-learning test scores after vitamin B_{12} have a mild dysmnesic syndrome, and if untreated could this have proceeded to an established dementia ? Recent evidence suggests a hypothetical, biochemical, and pathological basis for memory disturbances in pernicious anaemia. Vitamin B_{12} has been implicated in the enzymatic incorporation of amino-acids into proteins (Neill and Weaver, 1958) and in the synthesis of R.N.A. (Nieweg *et al.*, 1952). Memory may be encoded and preserved in the molecular structure of certain nucleic acids, including R.N.A. (Dingman and Sporn, 1961). Intact hippocampal and mammillary zones are essential for the process of remembering (Brierley, 1961), and damage to those areas has been described in pernicious anaemia (Ferraro *et al.*, 1945).

Misdiagnosis of Psychiatric Illness in Pernicious Anaemia

In both the anaemic and vitamin-B_{12}-deficient patients physical fatigue was the most common symptom encountered, and was frequently the initial symptom. In several patients this unexplained fatigue had resulted in psychiatric referral as cases of neurosis or neurasthenia. One patient with an earlier history of difficulty in swallowing associated with a Plummer–Vinson syndrome had been referred as a case of hysteria.

Vitamin-B_{12} Deficiency as a Cause of Psychiatric Illness

Studies of serum vitamin-B_{12} levels in mental hospital patients have indicated some of the difficulties which exist in attributing the psychiatric illness to vitamin-B_{12} deficiency (Edwin *et al.*, 1965 ; Hansen *et al.*, 1966 ; Shulman, 1967a, 1967b). In a survey of 1,012 psychiatric patients 0.88% were found to have pernicious anaemia (Henderson *et al.*, 1966). This is no higher than the incidence of pernicious anaemia in a normal population. Latent pernicious anaemia is present in 5 to 6% of patients with iron-deficiency anaemia (Beveridge *et al.*, 1965 ; Dagg *et al.*, 1966). From epidemiological data on the incidence of iron-deficiency anaemia (Kilpatrick, 1961) the normal incidence of pernicious anaemia is 0.5%, rising to 1% over the age of 65. The results of the present investigation have suggested that except in the organic psychoses there is little evidence to support the mass screening of psychiatric patients for vitamin-B_{12} deficiency. Even when dementia occurs in pernicious anaemia it is often impossible to exclude a coincidental arteriosclerotic or senile dementia, as in three of the patients in the present report.

It is concluded that psychiatrists should be alert to the possibility of vitamin-B_{12} deficiency in three situations: patients thought to be at risk clinically—for example, anaemic or post-gastrectomy patients, patients with unexplained fatigue, and patients with confusional states or dementia of unknown origin.

Summary

The psychiatric status of 27 patients with pernicious anaemia and 21 control anaemic patients is described. Approximately one-third of both groups had psychiatric symptoms rated as moderate or severe.

Before treatment the most frequent symptoms were depression and memory impairment. Of the psychiatric symptoms encountered only memory impairment appeared to be related to vitamin-B_{12} deficiency. The role of vitamin-B_{12} deficiency in the production of mental symptoms is reviewed. Except for research purposes there is no evidence to support the routine screening of psychiatric patients for pernicious anaemia.

I am grateful to the many physicians and haematologists who co-operated in this investigation, and would especially like to thank Dr. L. Bernstock, consultant clinical pathologist, St. Helier Hospital, for continued interest and encouragement ; Dr. C. K. Kendrick for instruction in the use of the synonym-learning test ; and Mr. W. I. Hume for assistance with the statistical analysis.

Part of this investigation was submitted as a dissertation for the Academic Postgraduate Diploma in Psychological Medicine, University of London, 1964.

REFERENCES

Beveridge, B. R., Bannerman, R. M., Evanson, J. M., and Witts, L. J. (1965). *Quart. J. Med.*, **34**, 145.

Brierley, J. B. (1961). *Geront. clin. (Basel)*, **3**, 97.

Cox, E. V. (1962). In *Vitamin B_{12} and Intrinsic Factor*, edited by H. C. Heinrich, p. 590. Stuttgart.

Dagg, J. H., Goldberg, A., Gibbs, W. N., and Anderson, J. R. (1966). *Brit. med. J.*, **2**, 619.

Dingman, W., and Sporn, M. B. (1961). *J. psychiat. Res.*, **1**, 1.
Edwin, E., Holten, K., Norvum, K. R., Schrumpf, A., and Skaug, O. E. (1965). *Acta med. scand.*, **177**, 689.
Eysenck, H. J. (1959). *Manual of the Maudsley Personality Inventory.* London.
Ferraro, A., Arieti, S., and English, W. H. (1945). *J. Neuropath. exp. Neurol.*, **4**, 217.
Hansen, T., Rafaelsen, Ole J., and Rødbro, P. (1966). *Lancet*, **2**, 965.
Helsborg, H. C. (1958). *Acta psychiat. scand.*, **33**, 303.
Henderson, J. G., Strachan, R. W., Swanson Beck, J., Dawson, A. A., and Daniel, M. (1966). *Lancet*, **2**, 809.
Holmes, J. MacD. (1956). *Brit. med. J.*, **2**, 1394.
Hunter, R., and Matthews, D. M. (1965). *Lancet*, **2**, 738.
Kendrick, D. C. (1964). *Psychol. Rep.*, **15**, 188.
—— (1965). *Brit. J. Soc. clin. Psychol.*, **4**, 141.
—— Parboosingh, R., and Post, F. (1965). Ibid., **4**, 63.
Kilpatrick, G. S. (1961). *Brit. med. J.*, **2**, 1736.
Klerman, G. L. (1966). *Int. J. Psychiat.*, **2**, 73.
McAlpine, D. (1929). *Lancet*, **2**, 643.
Neill, D. W., and Weaver, J. A. (1958). *Brit. J. Haemat.*, **4**, 447.
Nieweg, H. O., Van Buchem, F. S. P., and Kroese, W. F. S. (1952). *Acta med. scand.*, **142**, 45.
Raven, J. C. (1958). *Guide to Using the Mill Hill Vocabulary Scale with the Progressive Matrices Scales.* London.
Samson, D. C., Swisher, S. N., Christian, R. M., and Engel, G. L. (1952). *Arch. intern. Med.*, **90**, 4.
Scheinberg, P. (1951). *Blood*, **6**, 213.
Shulman, R. (1967a). *Brit. J. Psychiat.*, **113**, 241.
—— (1967b). Ibid., **113**, 252.
Siegel, S. (1956). *Non-Parametric Statistics: For the Behavioural Sciences.* New York.
Stewart, M. A., Drake, F., and Winokur, G. (1965). *Dis. nerv. Syst.*, **26**, 479.
Strachan, R. W., and Henderson, J. G. (1965). *Quart. J. Med.*, **34**, 303.
Thomas, E. D., and Lochte, H. L. (1958). *J. clin. Invest.*, **37**, 166.
Walton, J. N., Kiloh, L. G., Osselton, J. W., and Farrall, J. (1954). *Electroenceph. clin. Neurophysiol.*, **6**, 45.
Young, R. H. (1932). *J. Amer. med. Ass.*, **99**, 612.

Stenosis and Occlusion of Vessels in Cerebral Infarction

S. K. BATTACHARJI,* M.B., CH.B., PH.D.; E. C. HUTCHINSON,* M.D., F.R.C.P.;
A. J. McCALL,* M.D., F.R.C.P., F.C.PATH.

Brit. med. J., 1967, 3, 270–274

The contribution of cerebral vascular disease to the morbidity and mortality of an ageing population has led to a notable increase in studies of the condition in many branches of medicine. Stenosis and occlusion of the extracranial part of the cerebral blood supply has been the subject of several pathological studies (Hutchinson and Yates, 1957; Duffy and Jacobs, 1958; Martin *et al.*, 1960; McGee *et al.*, 1962). Schwartz and Mitchell (1961) reported on the results of a study of the neck vessels in 93 unselected necropsies. They showed that atheroma of the neck vessels increased with age in all patients and that stenosis of severe degree may occur without evidence of cerebral infarction. On their findings they accepted a direct relation between thrombotic occlusion of neck vessels and cerebral infarction but felt that the significance of stenosis in this context was uncertain.

This communication concerns part of a study of the pathology of cerebral infarction and reports the prevalence of stenosis and occlusion of the cerebral arteries in a series of patients with cerebral infarction and compares these findings with an unselected series of patients who died of unrelated causes.

Material and Methods

The material for the study was obtained from 145 necropsies performed at the North Staffordshire Royal Infirmary. During the time of the investigation all 57 cases found to have a cerebral infarct were included in the infarct group. Cases of emboli obviously arising from the heart and cases of paradoxical embolism were excluded. The control group consisted of 88 cases where there was no evidence of cerebral infarction and the age at death was over 45. No deliberate selection was made, but as it was not always possible to remove the cervical spine in a particular case coming to necropsy the cases were not consecutive.

The brain was removed and fixed in 10% formalin in the routine manner. The arch of the aorta was divided above the aortic valve at the level of the third dorsal vertebra; the subclavian arteries were divided beyond the origin of the vertebral arteries and the major vessels were then mobilized. After sectioning the cervical spine at the level of the seventh cervical vertebra a saw cut was made through the base of the skull on a line which ran through the anterior, middle, and posterior fossae on both sides. This provided a specimen containing the aorta and the neck vessels throughout their entire course. The carotid arteries were then exposed in the carotid canal with bone forceps. After examination of the arch of the aorta, the innominate artery, the common and internal carotid arteries, the subclavian artery, and the extravertebral part of the vertebral artery were examined by transverse section at 1-cm. intervals throughout their course. The cervical spine was decalcified with 10% hydrochloric acid and after three weeks the vertebral portion of the vertebral artery was exposed and examined.

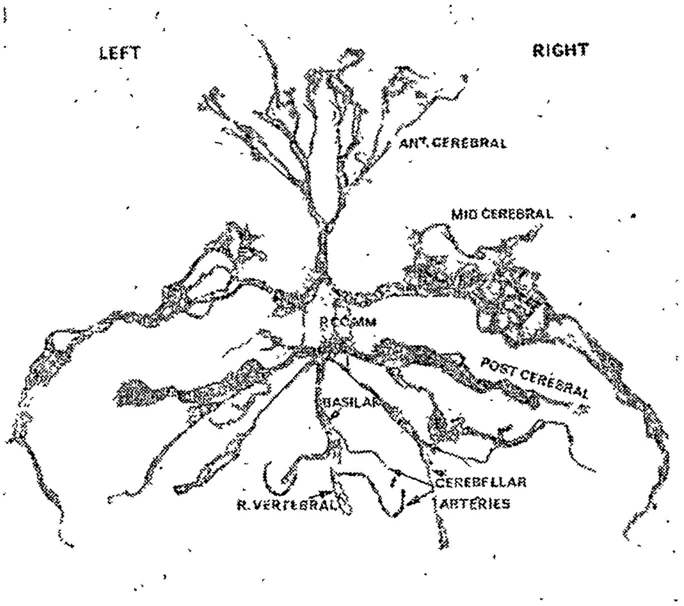


FIG. 1.—Specimen showing the intracranial vessels dissected from the brain preparatory to examination for stenosis and occlusion.

---

* North Staffordshire Royal Infirmary, Stoke-on-Trent.

Dr. Battacharji was awarded the Ph.D. at the University of Birmingham for a thesis entitled "The Role of Extracranial and Intracranial Arteries in Cerebral Infarction"

After fixation of the brain the remainder of the cerebral arteries were dissected free with blunt forceps. The circle of Willis, the basilar artery, and the arteries to the cerebellum and brain stem were first freed; the dissection was then continued and the major branches of the circle of Willis—the anterior, middle, and posterior cerebral arteries—were removed from the hemispheres (Fig. 1). The whole specimen was then floated in water for examination, and the extent of atheroma and degree of stenosis of vessels from their origin to their termination in the gyri were noted. The brain was examined by serial coronal sections 1 cm. thick and the extent of macroscopic infarction charted on a diagram.

In each specimen the vascular changes were classified in the following manner. The distribution of the arterial lesion was first noted on an outline diagram of the vascular supply. The nature of the vascular change was then recorded—that is, fatty streaks, fibrous plaques, plaques with softening, intramural haemorrhage, calcification—ulceration of the surface of the lesion and thrombus were noted separately. The degree of stenosis was classified as follows: grade 0, no encroachment on the lumen; grade 1, less than 25% reduction of lumen; grade 2, 25 to 50% reduction of lumen; grade 3, more than 50% reduction of lumen but no occlusion; grade 4, total occlusion.

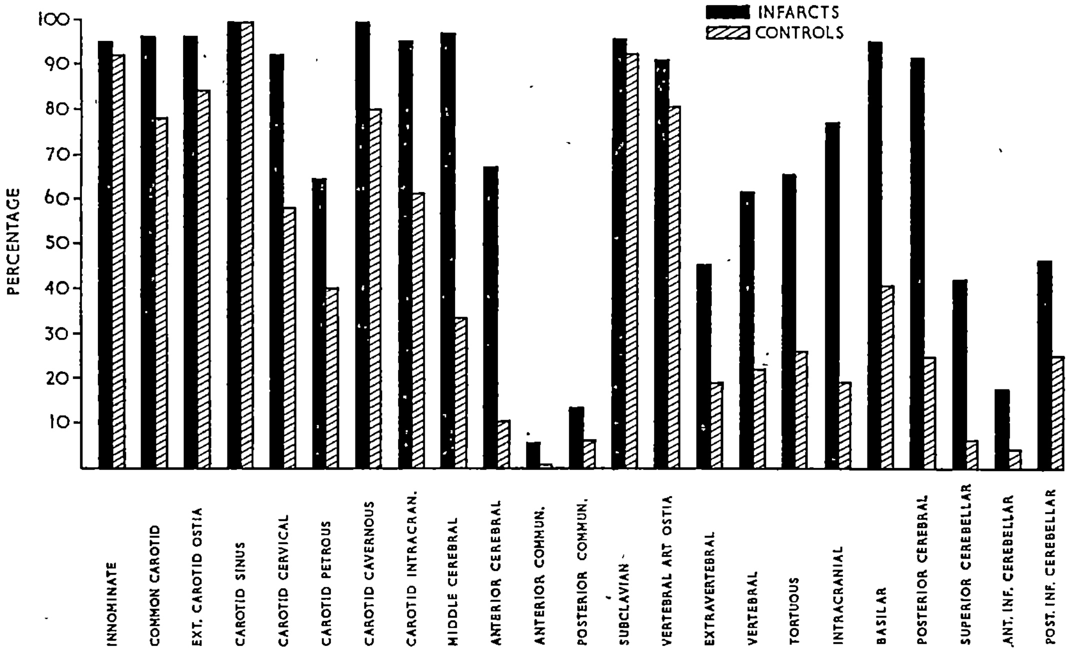


FIG. 2.—Distribution of all macroscopic vascular changes of the extracranial and intracranial vessels of the right side.

For each specimen the vascular change was recorded at multiple sites. In the carotid circulation the innominate artery, the common carotid, the external carotid ostia, the carotid sinus, and the cervical, cavernous, petrous, and intracranial portions of the carotid proximal to its primary division within the skull were assessed separately. In the vertebral circulation the subclavian, the vertebral artery ostia, the extravertebral portion of the artery, and the vertebral, tortuous, and intracranial parts of the vertebral artery were noted individually. The other intracranial arteries were scored according to the maximum degree of stenosis noted along the course of the individual vessel. For convenience, throughout the text the term "extracranial vessels" includes the terminal parts of the carotid and vertebral arteries within the skull. The term "intracranial vessels" refers to the branches of the carotid and vertebral arteries lying below the brain and within its substance.

All the dissections were done by one of us (S. K. B.); the vascular changes were assessed independently by the others (E. C. H. and A. J. M.), who were unaware of the state of the brain at the time of this assessment.

Results

Age and Sex Distribution

The age distribution in the infarct and control groups is shown in Table I. At death only 3 of the 57 with infarcts were below 60, whereas 22 of the 88 controls were between 40 and 60. In contrast, 15 with infarcts and only six controls were over 80 at death. The average age of the infarct group at death was 72.4 years, compared with 62 years in the control group. However, 68% of the patients in both the infarct and the control group were between 60 and 80 years of age at death.

TABLE I.—*Distribution by Age at Death and Sex of 57 Patients with Infarcts and of 88 Controls*

Age Group:	40–49	50–59	60–69	70–79	80–89	90+	Total
			Infarcts				
Male ..	—	2	10	12	6	1	31
Female ..	1	—	6	11	6	2	26
Total ..	1	2	16	23	12	3	57
			Controls				
Male ..	2	12	25	8	3	0	50
Female ..	3	5	13	14	2	1	38
Total ..	5	17	38	22	5	1	88

Cerebral Infarction

Because brain infarcts were frequently multiple, 130 separate areas of infarction were noted in the 57 specimens (Table II). In 12 cases (21%) the infarcts were cortical, in 29 (51%) they were subcortical, and in 16 (28%) both the cortical and the subcortical areas were affected. Table II shows the distribution of infarcts, and it will be seen that there were 107 in the

TABLE II.—*Distribution and Frequency of Cerebral Infarction in Individual Arterial Territories*

Artery	Arterial Territories Affected by Infarction		No. of Infarctions in Each Arterial Territory	
	Right	Left	Right	Left
Anterior cerebral ..	2	0	3	0
Middle cerebral ..	37	29	49	36
Posterior cerebral ..	8	9	10	9
Superior cerebellar ..	1	0	1	0
Anterior and posterior inferior cerebellar ..	6	5	6	5
Basilar	10		11	
Total	107		130	

carotid and 23 in the vertebro-basilar territories. The middle cerebral territories were most often affected, and accounted for all but four of the areas of multiple infarction.

Lesions in Cerebral Blood Supply

This communication is primarily concerned with the prevalence of stenosis or occlusion of the cerebral arteries, but for the sake of completeness we have included in one illustration (Fig. 2) all the macroscopic vascular lesions that were noted in the infarct and control groups. The figures are expressed as a percentage of the total in each group; the findings on the right and left sides are similar and, for the sake of brevity, the changes on the right side only are shown.

In the carotid circulation in the infarct and control groups the carotid sinus showed some change in all specimens. In the infarct group the innominate, the common carotid, and the cervical and cavernous portions of the carotid artery were also affected in over 90% of cases, and in the intracranial branches of the carotid artery the middle cerebral artery was affected to the same degree. In the control series there was a high incidence of vascular lesions at certain sites—for example, the innominate, the common carotid, the cavernous part of the carotid—but compared with the infarct group the changes in the cervical and petrous part of the carotid and in the anterior and middle cerebral vessels were considerably less.

The subclavian and vertebral artery ostia showed changes in over 80% of cases in both the infarct and control groups. In the infarct group the extravertebral portion of the vertebral artery was affected in 44%, compared with 21% of the controls. There was also a higher incidence of lesions within the vertebral canal and in the tortuous and intracranial portions of the vertebral artery in the infarct compared with the control group. In the intracranial branches the incidence of vascular change in the posterior cerebral artery was 91% in the infarct group compared with 25% in the control group.

The lowest incidence of vascular change in both the infarct and the control groups was found in the anterior and posterior communicating arteries and in the anterior inferior cerebellar artery.

Stenosis and Occlusion of Vessels

The incidence and distribution of stenosis (grades 1 to 3) and occlusion of vessels (grade 4) in the two groups are shown in Table III. For simplicity of presentation the numbers observed in each grade are expressed as a percentage of the total in the infarct and control groups. Statistical assessment was made on the numbers in each grade in both groups. It was often necessary to combine grades 3 and 4 and sometimes grades 2, 3, and 4 in order to provide groups of sufficient size. The χ^2 test was applied when three or more groups were combined, but for two groups the tables of Mainland *et al.* (1956) were used. The level of $P<0.05$ was accepted as significant.

When the extracranial vessels of the two groups were compared the innominate and subclavian arteries were the only vessels in the infarct group which failed to reach this level of significance when compared with the control group. Of the intracranial vessels the anterior inferior cerebellar and the communicating arteries were the only vessels in the infarct group which failed to show a significantly higher incidence of stenosis when compared with the controls.

If a severe degree of stenosis (grade 3) is considered in isolation certain points of interest arise. In the left carotid sinus the incidence of grade 3 stenosis is the same in the control and the infarct group (5%), and in the left cavernous sinus the incidence is slightly higher in the controls (3%) than in the infarcts (2%). Elsewhere the incidence of grade 3 stenosis is always higher in the extracranial vessels of the infarct group. The differences are more pronounced in certain intracranial vessels. The middle cerebral artery, for example, showed grade 3 stenosis in 33% of cases on the right side compared with an incidence of 5% in the controls. Less marked but still significant differences were found in the anterior and posterior cerebral arteries and in the posterior inferior cerebellar arteries. In spite of the higher incidence of stenosis in the infarct group it is worth emphasizing that grade 2 stenosis was frequently observed in the control group.

Occlusion of Vessels

One striking difference in vascular lesions between the two groups was that occlusion of vessels was confined to the infarct group. Occlusion of the carotid arteries was found on 64 occasions and occlusion of the vertebral arteries on 30. Of the 64 carotid occlusions, 42 were on the right and 22 on the left side; of the 30 vertebral occlusions, 16 were on the right and 14 on the left. In the intracerebral vessels occlusion was

TABLE III.—*Distribution of Occlusion and Different Grades of Stenosis in the Infarct and Control Groups. The Figures are Expressed as a Percentage of the Total Cases in the Infarct and Control Groups*

	Grade 1				Grade 2				Grade 3				Grade 4			
	Infarct		Control		Infarct		Control		Infarct		Control		Infarct		Control	
	R.	L.	R.	L.	R.	L.	R.	L.	R.	L.	R.	L.	R.	L.	R.	L.
Carotid Circulation																
Innominate artery	51		47		2		5		2		0		0		0	
Carotid artery:																
Common carotid artery	46	42	29	33	13	28	5	9	2	5	0	0	4	2	0	0
Ext. carotid art. ostia	65	58	48	37	11	14	6	10	4	5	1	3	2	1	0	0
Carotid sinus	67	63	70	64	16	21	10	6	5	5	0	5	7	4	0	0
Carotid Cervical part	33	33	23	28	12	18	12	11	18	14	5	7	19	5	0	0
Carotid Petrous „	18	16	15	12	5	11	1	2	0	4	0	0	9	4	0	0
Carotid Cavernous „	46	46	34	37	9	9	5	5	5	2	0	3	14	7	0	0
Carotid Intracranial „	58	58	36	32	7	13	3	1	7	2	1	0	7	4	0	0
Middle cerebral artery	23	23	19	24	26	39	8	7	33	25	5	2	11	9	0	0
Anterior cerebral „	16	19	8	3	19	23	2	5	21	18	0	1	2	4	0	0
Ant. communicating „	9		3		0		0		4		0		0		0	
Post. „ „	7	5	2	5	2	5	2	3	2	7	2	0	2	2	0	0
Vertebro-basilar Circulation																
Subclavian artery	67	60	61	62	9	14	5	9	0	4	1	1	0	0	0	0
Vertebral artery:																
Vertebral artery ostia	28	40	44	36	28	23	14	15	18	16	9	8	5	4	0	0
Extravertebral part	21	16	12	8	5	2	3	2	9	7	0	1	4	4	0	0
Vertebral „	18	19	8	10	11	18	3	2	14	13	0	1	0	4	0	0
Tortuous „	21	32	9	9	16	19	1	1	4	7	1	0	0	1	0	0
Intracranial „	26	33	9	8	13	23	2	1	18	5	1	0	4	4	0	0
Basilar artery	40		25		18		2		9		0		5		0	
Post. cerebral artery	13	19	12	18	35	30	8	9	32	32	3	3	7	4	0	0
Superior cerebellar artery	18	19	1	2	13	13	1	0	5	4	0	0	0	0	0	0
Ant. inf. cerebellar artery	9	11	0	1	4	4	0	0	2	2	0	0	2	0	0	0
Post. inf. cerebellar artery	13	16	8	6	18	16	2	2	13	19	0	0	0	0	0	0

found in 28 brains. The middle cerebral artery accounted for 11, the posterior cerebrals for 8; of the remainder the basilar and anterior cerebral were occluded three times, the communicating arteries twice, and the anterior inferior cerebellar once. In the paired intracranial vessels there was no predilection for either side.

"Stenosis Score"

A comparison of the extent of vascular disease in groups of vessels poses certain problems. A score of 0 to 4 may be allotted according to the maximum change noted along the course of a vessel. This uncomplicated system was adopted in the present series for the comparison of the intracranial vessels, as we felt that the difference between the two groups was so pronounced as to require no further examination. There is, however, a serious disadvantage in using this method to compare the larger cervical vessels in that a comparatively normal vessel occluded by embolus will score more than a vessel diffusely involved throughout its length. In order to avoid this emphasis on a localized site of disease the carotid and vertebral arteries in the two groups were compared by using a scoring system which took into account the findings at all sites examined. In each specimen scores from 0 to 4 were recorded at 27 sites distributed over the innominate, subclavian, carotid, and vertebral arteries, as previously described. In the extreme case of occlusion of all major vessels throughout their course a score of 108 (27 x 4) would be allotted. In order to minimize the effect of the difference in age distribution, the infarct and control series were divded into decades.

The stenosis score shown in Table IV is the total score for each decade expressed as a percentage of the maximum possible score for that decade. The results indicate that in the infarct group the stenosis score for the extracranial vessels was twice that observed in the controls. The only exception to this was in the over-90 age group, where only one patient was concerned in the controls. It should be noted that there were only three patients below the age of 60 in the infarct group compared with 22 controls, and therefore direct comparison between the two groups in these decades is not valid. However, 68% of the patients in both groups lie in the 60–80 age range, and the stenosis score for the extracranial vessels of the infarct group was over twice that of the controls. In these two decades the intracranial stenosis score for the infarct group was between three and six times more than that noted in the control group.

TABLE IV.—*Comparison of the "Stenosis Score" (see Text for Definition) in the Major Neck Vessels and the Intracranial Vessels of the Infarct and Control Groups. The Figures in Parentheses are the Number of Patients in Each Decade*

Age:	40–49	50–59	60–69	70–79	80–89	90+
			Extracranial Vessels			
Infarct ..	(1) 27·8%	(2) 36·2%	(16) 29·4%	(23) 24·2%	(12) 18·0%	(3) 25·6%
Control	(5) 8·7%	(17) 12·5%	(38) 12·5%	(22) 10·8%	(5) 5·6%	(1) 24·0%
			Intracranial Vessels			
Infarct ..	20·3%	33·5%	28·9%	21·6%	22·8%	29%
Control	1%	3·8%	4·3%	5·9%	5·7%	10%

Multiple Involvement of Cervical Vessels

It is now generally appreciated that when one of the four major cervical vessels is affected by atheroma it is highly probable that one or more of the remaining three vessels will show similar changes. In our material we examined this point in relation to severe stenosis (grade 3) and occlusion in both the control and the infarct series and compared the two groups. Table V shows the incidence in both groups, and the results are tabulated on the presence of grade 3 stenosis or occlusion in one, two, three, or four of the major vessels. It will be seen that in 17 of the 57 infarcts grade 3 stenosis or occlusion was found in all four vessels, whereas only 2 of the 88 controls showed grade 3 stenosis in all four vessels. In spite of this marked difference it is worth emphasizing that grade 3 stenosis was noted in one or more of the four vessels in 29 of the 88 controls.

TABLE V.—*Incidence of "Multiple" Involvement of Carotid and Vertebral Arteries by Grade 3 Stenosis or Total Occlusion in the Infarct and Control Groups*

	4 Vessels	3 Vessels	2 Vessels	1 Vessel	Total
			Infarct		
Male .. Female ..	8 9 } 17	14 5 } 19	5 5 } 10	3 5 } 8	54
			Control		
Male .. Female ..	1 1 } 2	2 0 } 2	4 2 } 6	5 14 } 19	29

Correlation of Extracranial and Intracranial Vascular Disease

An attempt was made to examine quantitatively the relation between extracranial and intracranial stenosis. For this purpose attention was paid only to the maximum stenosis in a particular vessel, and the intracranial and extracranial vessels were scored from 0 to 4 according to the degree of stenosis.

Product/moment correlation coefficients (r) were calculated as follows: control group (88 cases), $r=0.2246$; infarct group (57 cases), $r=0.139$.

The coefficients are statistically significant in the control group ($P<0.05$) but not in the infarct group (Fisher, 1946).

Discussion

The frequency of multiple involvement by atheroma of the carotid and vertebral arteries and the high incidence of stenosis at the carotid sinus and in the cavernous part of the carotid artery observed in the present study have been noted by previous observers. There are minor differences in the distribution of the arterial lesions as compared with previous work. McGee *et al.* (1962), for example, found that the vertebral artery within the vertebral canal was the commonest site for stenosis in the vertebral circulation, whereas in the present series the vertebral artery ostia showed the highest incidence. Schwartz and Mitchell (1961) found a higher incidence of stenosis at the carotid sinus relative to the cervical part of the carotid artery than we observed. Nevertheless the pattern of vascular disease in the carotid and vertebral arteries is in broad agreement with the findings of previous observers (Hutchinson and Yates, 1957; Martin *et al.*, 1960; Schwartz and Mitchell, 1961; McGee *et al.*, 1962).

In this paper we have not attempted to analyse the mechanism of infarcts as we are preparing a further communication on this subject, but thrombosis or embolic occlusion of neck vessels is clearly of crucial importance. The speed with which occlusion occurs may leave no time for the development of an adequate collateral circulation, and the lesion itself provides a possible source of emboli that may occlude the cerebral vessels.

Fisher (1954), in a clinical and pathological study of carotid artery disease, emphasized the importance of thrombi arising at the carotid bifurcation as a cause of embolic infarction. More recently attention has been focused on episodes of cerebral ischaemia due to platelet emboli arising from the carotid artery. Millikan and Siekert (1955) first suggested that a cerebral embolus may fragment, and pass through the cerebral circulation, causing only transient cerebral ischaemia. Clinical observations on the optic fundi, where small emboli were seen to pass through the retinal circulation without causing permanent retinal damage, supported this suggestion (Fisher, 1959; Russell, 1961; Ashby *et al.*, 1963). The suggestion that these emboli may be a small aggregation of platelets (Denny-Brown, 1960) was confirmed by the pathological study of McBrien *et al.* (1963). It is uncertain how frequently emboli of this type may be responsible for transient ischaemic episodes, but Gunning *et al.* (1964) suggested that these microemboli, composed largely of platelets and leucocytes and arising from an atheromatous internal carotid artery, were a common cause of repeated attacks of monocular blindness and contralateral hemiparesis.

The significance of stenosis alone—uncomplicated by thrombosis—as a cause of cerebral infarction has been increasingly questioned. The high incidence of neck-vessel stenosis in persons with infarct-free brains was pointed out by Schwartz and Mitchell (1961) and is apparent in our material. Hypotensive episodes may produce cerebral infarction (Adams *et al.*, 1966), and it is very probable that vascular stenosis may, on occasion, increase the likelihood of infarction from hypotension. The importance of episodic hypotension associated with cerebral vascular disease in causing transient cerebral ischaemia has been convincingly argued by Denny-Brown (1951) and supported by Williams and Wilson (1962). Millikan (1965), however, questioned the importance of both episodic hypotension and neck-vessel stenoses as a frequent cause of transient cerebral ischaemia. It is relevant that Vost *et al.* (1964) found no evidence that hypotensive episodes contribute in any of the 255 cases of cerebral infarction they examined at necropsy.

The observations of Brice *et al.* (1964) have also discouraged the suggestion that uncomplicated carotid stenosis may determine infarction. They carried out in-vivo experiments on 13 patients and also made observations using an excised carotid artery in a constant-flow perfusion circuit. They found that the lumen had to be reduced to 2 sq. mm. before significant reduction in flow occurred. They concluded that with a residual cross-section of 5 sq. mm. or more a reduction in flow was very unlikely, even when there were stenoses in series. Our results and those of other observers (Martin *et al.*, 1960 ; Schwartz and Mitchell, 1961 ; McGee *et al.*, 1962) all indicate that multiple severe stenoses of the cerebral blood supply may be present in the absence of cerebral infarction. Confirmatory observations were made during life by Faris *et al.* (1963), who studied 43 volunteers who had no clinical or historical evidence of cerebral vascular disease. Arch aortograms were carried out and in half the subjects some form of arterial lesion was shown in the carotid or the vertebral arteries and more than one vessel was affected in 10% of the subjects.

Not only may there be lack of association between extracranial stenosis and cerebral infarction, but there may also be a lack of correlation between the symptomatology and the site of arterial disease. This point was made by Sutton and Davies (1966), who reported their findings in 330 patients who were referred to them with a clinical diagnosis of cerebral vascular insufficiency and who were examined by arch aortography. They found that in patients with symptoms of basilar artery insufficiency radiological abnormalities were found in only 52%, and that lesions were noted as frequently in the carotid as in the vertebral circulation.

In our material the method we adopted for examining the intracranial arteries enabled us to define precisely the degree of stenosis in each of these vessels, and our analysis throws further light on the significance—or lack of significance—of arterial stenosis in relation to infarction. We found that cerebral infarction was most common in the middle cerebral artery territory and a severe degree (grade 3) of stenosis occurred in over 30% of these vessels. However, the posterior cerebral arteries showed grade 3 stenosis in a similar number of cases, whereas the incidence of infarction in the posterior cerebral territory was considerably less than that noted in the middle cerebral territories. The anterior cerebral artery also showed an appreciable incidence of grade 3 stenosis, for, on the right side, it was noted in one in five subjects in the infarct group and yet infarction was observed only three times in this arterial territory.

Cerebral infarction is a dynamic process with several possible contributory causes, and therefore a pathological study of the type reported will do no more than permit a partial appraisal of the pathogenesis. However, we believe that our findings—particularly those in relation to the intracranial vessels—do not support the view that stenosis alone plays a decisive part in the pathogenesis of cerebral infarction. The high incidence of infarction in the middle cerebral territories, together with an appreciable incidence of vascular change in other intracranial vessels, suggests that emboli may have an even more important part to play than has been recognized previously. We intend to examine our material further with this point in mind.

Summary

The necropsy findings in 57 patients with cerebral infarction and 88 controls are compared.

In the 57 brains, 130 separate areas of infarction were found.

The distribution of vascular disease in the cerebral blood supply is described in both the infarct and the control group. Occlusion of the cerebral arteries was confined to the infarct group and the incidence of stenosis in this group is significantly higher than in the controls.

The results suggest that uncomplicated stenosis is not a decisive factor in the development of cerebral infarction.

We wish to acknowledge the encouragement and advice of Professor J. W. Orr and the generous financial support of the Research Subcommittee of the Birmingham Regional Hospital Board throughout this investigation. We are grateful to H.M. Coroners, Mr. F. G. Hails and Mr. J. S. Marshall, for permission to make use of certain material.

References

Adams, J. H., Brierley, J. B., Connor, R. C. R., and Treip, C. S. (1966). *Brain*, **89**, 235.
Ashby, M., Oakley, N., Lorentz, I., and Scott, D. (1963). *Brit. med. J.*, **2**, 894.
Brice, J. G., Dowsett, D. J., and Lowe, R. D. (1964). Ibid., **2**, 1363.
Denny-Brown, D. (1951). *Med. Clin. N. Amer.*, **35**, 1457.
—— (1960). *Arch Neurol. (Chic.)*, **2**, 194.
Duffy, P. E., and Jacobs, G. B. (1958). *Neurology (Minneap.)*, **8**, 862.
Faris, A. A., Poser, C. M., Wilmore, D. W., and Agnew, C. H. (1963). Ibid., **13**, 386.
Fisher, C. M. (1954). *Arch. Neurol. Psychiat.*, **72**, 187.
—— (1959). *Neurology (Minneap.)*, **9**, 333.
Fisher, R. A. (1946). *Statistical Methods for Research Workers*, 10th ed., p. 209. Edinburgh.
Gunning, A. J., Pickering, G. W., Robb-Smith, A. H. T., and Russell, R. R. (1964). *Quart. J. Med.*, **33**, 155.
Hutchinson, E. C., and Yates, P. O. (1957). *Lancet*, **1**, 2.
McBrien, D. J., Bradley, R. D., and Ashton, N. (1963). Ibid., **1**, 697.
McGee, D. A., McPhedran, R. S., and Hoffman, H. J. (1962). *Neurology (Minneap.)*, **12**, 848.
Mainland, D., Herrara, L., and Sutcliffe, H. I. (1956). *Tables for Use with Binomial Samples*. New York.
Martin, M. J., Whisnant, J. P., and Sayre, G. P. (1960). *Arch. Neurol. (Chic.)*, **3**, 530
Millikan, C. H. (1965). *Circulation*, **32**, 438.
—— and Siekert, R. G. (1955). *Proc. Mayo Clin.* **30**, 61.
Russell, R. W. R. (1961). *Lancet*, **2**, 1422.
Schwartz, C. J., and Mitchell, J. R. A. (1961). *Brit. med. J.*, **2**, 1057.
Sutton, D., and Davies, E. R. (1966). *Clin. Radiol.*, **17**, 330.
Vost, A., Wolochow, D. A., and Howell, D. A. (1964). *J. Path. Bact.*, **88**, 463.
Williams, D., and Wilson, T. G. (1962). *Brain*, 85, 741.

Mechanism of Bronchoconstriction Caused by Cigarette Smoking

G. M. STERLING,[*] M.B., B.CHIR., M.R.C.P.

Brit. med. J., 1967, **3**, 275–277

Inhalation of the smoke of a single cigarette causes brief bronchoconstriction in man (Zamel *et al.*, 1963 ; Pelzer and Thomson, 1966), and it has been suggested that this is due to the irritant action of smoke particles on receptors in the tracheobronchial tree. Other possible mechanisms are the pharmacological activity of nicotine or gaseous products of combustion such as oxides of nitrogen, but it has been shown that neither varying the nicotine content of cigarettes nor removal of nitrous oxide from the smoke alters the bronchoconstrictor effect (Nadel and Comroe, 1961). Moreover, Widdicombe *et al.* (1962) have found that chemically inert carbon particles can cause bronchoconstriction in man and cats and that this effect can be blocked by atropine or by cooling the vagi, indicating that it is a reflex reaction mediated through the vagus. By analogy it has been assumed and stated that smoking in man works in the same way, but there is little direct evidence on this point, and the present study has been designed to investigate this assumption further, through observation of the effect of atropine on the bronchial reaction to cigarette smoke.

Methods

Cigarette smoke causes only slight bronchoconstriction, which is not usually detectable by standard spirometry, and a more sensitive method has therefore been used.

Airway resistance and lung volume were measured by means of a constant-volume whole-body plethysmograph of about 450 litres capacity, as described by DuBois *et al.* (1956). After waiting two or three minutes to allow the air in the plethysmograph to warm to a constant temperature, the subject panted shallowly through a heated flowmeter at two breaths a second, and the flow signal was fed into the vertical axis of a cathode-ray oscilloscope, while a simultaneous plethysmograph pressure signal was fed into the horizontal axis to produce a flat vector loop. A shutter attached to the flowmeter and mouthpiece was then closed by a remotely controlled solenoid and the subject continued to make shallow panting movements against this obstruction, which enabled the lung volume at the natural panting level to be measured plethysmographically. This was called the thoracic gas volume (T.G.V.) and was used to correct airway resistance, since the latter normally varies inversely with lung volume (Briscoe and DuBois, 1958). Functional residual capacity (F.R.C.) was measured by instructing the subject to make panting movements after the shutter had been closed at the end of a normal slow expiration. The angles of the vector loops produced by these manœuvres were measured by alignment against a ruled Perspex disc which rotated within a fixed protractor scale in front of the oscilloscope screen. This method was initially checked against simultaneous photographic traces, and, after close agreement had been found, the latter more laborious method was abandoned.

Each test consisted of six or seven consecutive measurements of airway resistance and thoracic gas volume, of which the last five were used in the calculation of mean airway resistance in cm. H_2O/litre/second. From this value 0.45 cm. H_2O/l./sec. was subtracted for the resistance of the flowmeter and mouthpiece, and the result was then converted to its reciprocal, airway conductance (C.A.), which has a more linear relation with lung volume. Results were expressed as the ratio of airway conductance to thoracic gas volume (C.A./T.G.V.) to allow for changes in lung volume when comparing changes in airway resistance (Nadel and Comroe, 1961).

Subjects

Eleven normal adults, of whom three were non-smokers, were each tested on two occasions. On the first, C.A./T.G.V. was measured at rest and again two to three minutes after 15 inhalations over five minutes of a filter-tipped cigarette. On the second, C.A./T.G.V. was measured at rest, then 25 minutes after the subcutaneous injection of 1.2 mg. of atropine sulphate, and finally after inhalation of a cigarette as before. The two studies were carried out at the same time of day, within a few days of one another, and care was taken to ensure that none of the subjects had smoked within two hours of the experiment, since the bronchoconstrictor effect of a cigarette may last up to 80 minutes (Nadel and Comroe, 1961).

Results

Lung Volumes

Lung volume was measured at both F.R.C. and natural panting volume (T.G.V.), and the results, with the one female subject excluded, are shown in Table I. It can be seen that T.G.V. is generally larger than F.R.C., as has been found previously (Nadel and Comroe, 1961), and this fact is illustrated by the specimen spirometer tracing (Fig. 1). This shows three normal

TABLE I.—*Lung Volumes (Litres) at Rest on Two Occasions in 10 Male Subjects*

Subject	Functional Residual Capacity			Thoracic Gas Volume (= Panting Volume)		
	1	2	Mean	1	2	Mean
G.M.S.	4·69	3·83	4·26	4·88	4·19	4·54
R.H.	2·90	3·11	3·00	3·54	3·64	3 59
P.R.	4·64	4·40	4·52	4·91	4·40	4·66
J.H.	3·10	2·94	3·02	4·12	4·26	4·19
J.B.	4·92	5·02	4·97	5·55	5·33	5 44
P.L.	4·16	4·24	4·20	4·67	4·74	4·71
T.D.	4·02	3·88	3·95	4·75	5·35	5·05
J.C.B.	4·05	3·91	3·98	4·80	4·61	4·71
R.B.	4·58	4·54	4·56	5·25	5·42	5·34
C.L.	3·44	3·16	3·30	4·19	3·51	3·85
Mean			3·98*			4·61*

* Difference = 0·63 l.

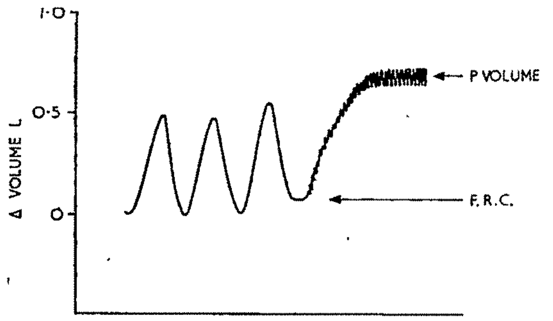


FIG. 1.—Lung volume change with onset of rapid shallow panting after three normal tidal breaths. (P.volume ≡ T.G.V.)

---

[*] Research Registrar, Respiratory Department, St. George's Hospital, London S.W.1.

breaths of 500 ml. tidal volume followed by a period of rapid shallow panting similar to that performed during measurements in the plethysmograph. At the start of panting there is a rapid increase in lung volume for a few breaths, after which lung volume stabilizes for a time though further fluctuations may occur if panting is prolonged. Though this point has been noted before, it has not been emphasized, and in the past there has sometimes been doubt about whether F.R.C. or T.G.V. has been used in the correction of airway conductance for lung volume.

The mean values of 3.98 and 4.61 litres for F.R.C. and T.G.V. respectively are a little high, but this probably represents the selection of fit young men as subjects, and the figures fall within the range of other series (Table II).

TABLE II.—*Present Lung Volumes Compared with Values for Normal Males in Other Studies*

Authors	Year	Male Subjects	F.R.C.	T.G.V.	T.G.V.–F.R.C.
Nadel and Comroe ..	1961	17	3·28	3·96	0·68
McDermott and Collins..	1965	32	—	4·81	—
Pelzer and Thomson ..	1966	53	—	4·32	—
Present results	1966	10	3·98	4·61	0·63

Airway Resistance

The mean C.A./T.G.V. of the 11 subjects was 0.205 ± 0.033 [S.D.] at rest before smoking, and 0.21 ± 0.035 at rest before atropine and smoking, showing that there was no overall difference in "bronchial tone" on the two occasions. These values agree well with those of 0.22 and 0.23 obtained from normal resting subjects in previous series (Nadel and Comroe, 1961; Pelzer and Thomson, 1966). However, there was some day-to-day variation within individuals, and anyone who showed a change in C.A./T.G.V. of more than 25% at rest was excluded from the trial.

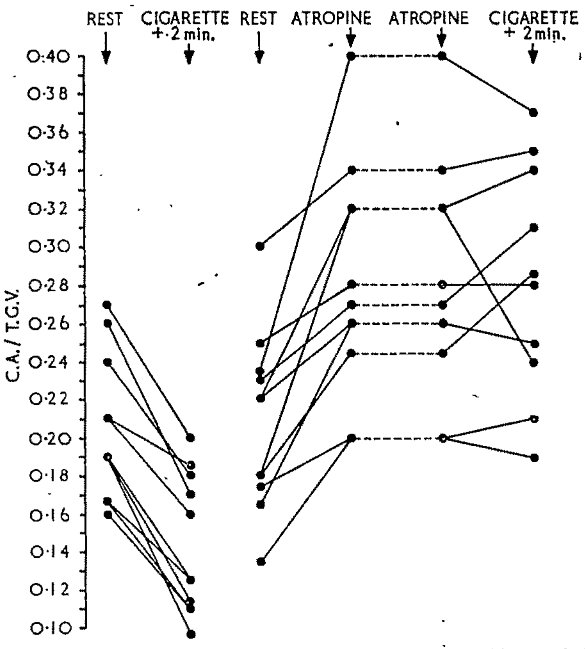


FIG. 2.—Change in C.A./T.G.V. after smoking (left-hand column) and after atropine followed by smoking (right-hand column).

In all the subjects there was a fall in C.A./T.G.V. two minutes after finishing a cigarette, to a mean of 0.14 ± 0.028, which is a highly significant change ($P<0.005$ by Student's *t* test). There was considerable individual variation in this response, with a range of −12% to −53%, but the average change of −31% is very close to that found in an earlier study (Nadel and Comroe, 1961) (Fig. 2). The bronchoconstriction diminished rapidly, and in those subjects in whom it was followed serially C.A./T.G.V. had returned to resting values in 20 to 30 minutes.

After the injection of atropine there was a consistent rise in C.A./T.G.V., from a mean of 0.21 ± 0.035 to one of 0.28 ± 0.63, an average increase of 38%, which confirmed previous findings of resting bronchial tone (Widdicombe *et al.*, 1962). Inhalation of a cigarette after atropine failed to cause any consistent change in C.A./T.G.V., which showed only an insignificant mean fall of 0.6%.

Discussion

These results confirm that the inhalation of cigarette smoke causes an increase in airway resistance, which is maximal within two or three minutes of smoking and usually declines to its resting value over about 20 minutes. It has been shown that this effect is unaltered by extraction of volatile substances from the smoke (Nadel and Comroe, 1961) or by varying the nicotine content of the cigarette smoked, and it has therefore been suggested that the tiny particles that constitute smoke are irritant to receptors in the airways. A similar response has been described in men and cats given chemically inert carbon particles to inhale, and the mechanism has been shown to be a vagal reflex, since in animals it can be blocked both by atropine and by vagal cooling, and since increased activity can be demonstrated in afferent vagal fibres (Widdicombe *et al.*, 1962). Vagal reflexes are also the pathways for production of bronchoconstriction due to mechanical irritation of the larynx (Nadel and Widdicombe, 1962), or to inhalation of low concentrations of sulphur dioxide (Nadel *et al.*, 1965). The prevention of bronchoconstriction by atropine in the present study therefore suggests that the same mechanism is involved, though the afferent side of the reflex arc has not been investigated.

It has generally been assumed that any increase in airway resistance is due to narrowing of the bronchi and bronchioles, but another possible explanation is that irritant particles might alter overall airway resistance by causing laryngeal obstruction through mucosal swelling or muscular contraction, particularly as extrathoracic resistance may comprise as much as 50% of total airway resistance during mouth breathing in normal subjects (Hyatt and Wilcox, 1961). However, it is difficult to see how atropine could prevent such a change except, possibly, by its drying action on the epithelium of the vocal cords. Moreover, in animal experiments, carbon particles inhaled through a tracheostomy, thus by-passing the larynx, still cause constriction of the lower airways, indicating that the latter are the site of at least part of the increased airway resistance.

The fall in resting airway resistance after atropine seen in normal subjects has been described before, and, like the prevention of a provoked rise in airway resistance, is generally attributed to blockade of vagal bronchomotor activity. This is certainly the most obvious and likely explanation, but there is some doubt on whether it is the only one, since the action of atropine in drying up bronchial secretions might be expected to cause some increase in the calibre of the airways. Differentiation of these mechanisms is difficult, but isoprenaline causes a comparable fall in airway resistance without affecting secretions significantly, which suggests that muscular relaxation could account for the major part of the dilator action of atropine.

Summary

Inhalation of cigarette smoke causes bronchoconstriction in both smokers and non-smokers.

This effect is almost certainly due to the irritant action of smoke particles.

It can be blocked by atropine, suggesting that it is brought about by the vagus, probably through the action of the latter on bronchial smooth muscle.

I would like to thank Dr. J. C. Batten for his advice and encouragement, and Miss F. A. Boother for her frequent technical help.

This study was supported by a research grant from the Board of Governors, St. George's Hospital, London S.W.1.

REFERENCES

Briscoe, W. A., and DuBois, A. B. (1958). *J. clin. Invest.*, **37**, 1279.
DuBois, A. B., Botelho, S. Y., and Comroe, J. H. (1956). Ibid., **35**, 327.
Hyatt, R. E., and Wilcox, R. E. (1961). *J. appl. Physiol.*, **16**, 326.
McDermott, M., and Collins, M. M. (1965). *Thorax*, **20**, 562.
Nadel, J. A., and Comroe, J. H., jun. (1961). *J. appl. Physiol.*, **16**, 713.
—— Salem, H., Tamplin, B., and Tokiwa, Y. (1965). Ibid., **20**, 164.
—— and Widdicombe, J. G. (1962). Ibid., **17**, 861.
Pelzer, A. M., and Thomson, M. L. (1966). Ibid., **21**, 469.
Widdicombe, J. G., Kent, D. C., and Nadel, J. A. (1962). Ibid., **17**, 613.
Zamel, N., Youssef, H. H., and Prime, F. J. (1963). *Lancet*, **1**, 1237.

Is the Woulfe Bottle an Efficient Humidifier for Oxygen?

BERNARD J. FREEDMAN,* M.B., B.S., M.R.C.P.

Brit. med. J., 1967, 3, 277–279

Oxygen from cylinders is dry. The need for adequate humidity of inhaled gases in oxygen therapy is generally recognized. There is, however, no unanimity regarding the desirable level of humidity, nor regarding the best means of achieving it. Bubbling oxygen through water in a Woulfe bottle has been the most widely used method of humidifying oxygen since the early days of oxygen therapy. This method has been the object of adverse criticism. It has been alleged that it "does not result in adequate humidification" and that "this method should be abandoned" (*Brit. med. J.*, 1964). Cadman (1961) was of similar opinion. The Woulfe bottle is a widely used apparatus for this purpose, and in many hospitals it is the only one. Before urging the widespread abandonment of a cheap, simple, and easily replaceable apparatus in favour of something complex and expensive, or of giving it up altogether, it seemed desirable to test the efficiency of the Woulfe bottle as a humidifier, since no record could be found of this having been previously done.

There are three questions to answer. What level of humidification does this method achieve within the range of working conditions likely to be encountered? What level of humidification is desirable? Does this method meet clinical requirements? Experiments are described which give an answer to the first question, and an attempt is made to answer the second and third in the discussion which follows.

Material and Methods

Conventional bedside apparatus was used. Oxygen from a cylinder was bubbled through water in a Woulfe bottle and conveyed thence by 1.5 m. (4 ft. 9 in.) of rubber tubing to a hair hygrometer which occupied the position of a face-mask. Oxygen flow-rates were measured with a bobbin flow-meter calibrated against a Parkinson-Cowan gas-meter. The Woulfe bottle measured 14 cm. high and 5.8 cm. internal diameter, and it was filled to a depth of 4.5 cm. (about 160 ml.) with tap-water, the inlet tube reaching to 0.5 cm. above the floor of the bottle. The tube conveying oxygen from the bottle was connected to an opening in one end of a transparent polyvinyl chloride bag. The hygrometer lay within the bag. It fitted fairly snugly so as to ensure adequate entry of humidified oxygen into its casing (Fig. 1). Oxygen left the bag through tubes inserted into the two distal corners. This prevented retrograde entry of ambient air. The hair hygrometer was calibrated against a wet-and-dry bulb whirling hygrometer.

Dry oxygen was passed through water in the Woulfe bottle at a constant rate. At intervals of two minutes or less the following were measured: (1) relative humidity in the bag, and (2) temperature of the water, of the gas in the bag reaching the hygrometer, and of the ambient air. Gas flow continued until stable readings were obtained. Duplicate experiments were performed at flow-rates of 3, 5, and 8 litres per minute in cool, temperate, and hot environments. The hot environment was in the hospital basement alongside the steam-pipes, the temperate was in the laboratory, and the cool was on a ward balcony. Day-to-day variations in weather conditions and in boiler temperatures rendered it impossible to achieve identical ambient temperatures in the experiments carried out within each of the three temperature ranges. Ambient temperatures were as follows:

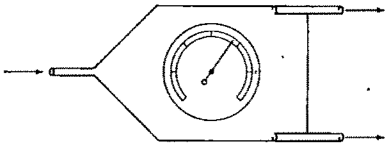


FIG. 1.—Humidified oxygen is passed through the plastic bag containing the hygrometer.

Cool ...	... 11.0–13.4° C.	(51.8–56.1° F.)
Temperate	... 18.5–19.8° C.	(65.3–67.6° F.)
Hot ...	... 27.6–31.6° C.	(81.7–88.9° F.)

Results

After the oxygen was turned on, the humidity rose rapidly. Progressive cooling of the water then led to a corresponding fall in humidity. Eventually the water temperature and the relative humidity were steady. A high flow-rate and a high ambient temperature were associated with much cooling of the water (Table I), and a big drop in final humidity. For example, at 8 l./min. and 31.5° C. (88.7° F.), the water temperature fell as much as 11.6° C. (20° F.).

TABLE I.—*Depression of Temperature of Water in Woulfe's Bottle Below Ambient Temperature*

Ambient Temperature	Oxygen Flow-rate (l./min.)		
	3	5	8
Cool	2·6° C.	3·3° C.	4·7° C.
Temperate ..	3·3° C.	4·2° C.	5·5° C.
Hot	4·7° C.	8·7° C.	11·6° C.

---

* Dulwich Hospital, King's College Hospital Group, London.

Despite the cooling of oxygen that must have occurred, it was always rewarmed to within a degree of ambient temperature in the course of its passage along the tube to the hygrometer. The results shown in Table II are the levels of humidity which were eventually reached after the initial rise and fall when conditions were stable, and are the means of closely agreeing duplicates.

Table II.—*Humidity of Oxygen After Bubbling Through Water in a Woulfe Bottle at Three Flow-rates and Three Ambient Temperatures*

		Oxygen Flow-rate (litres/min.)		
		3	5	8
A. Water-vapour concentration (grammes water per cubic metre oxygen)	Cool ..	8·34	8·75	7·95
	Temperate	13·40	13·03	11·50
	Hot ..	22·74	22·57	19·42
B. Relative humidity (%)	Cool ..	70	70·5	75
	Temperate	79	80	70
	Hot	81·5	68	60
C. Evaporation rate (mg. water evaporated per minute)	Cool	25·0	43·7	63·6
	Temperate	40·2	65·2	92·0
	Hot	68·2	112·8	155·4

Water-vapour concentrations achieved in these experiments (Table II A) ranged from 7.95 g./cu. m. (at low ambient temperature and high flow-rate) to 22.74 g./cu. m. (at high ambient and low flow-rate). A rise in temperature yielded a striking increase in water-vapour content. A rise in flow-rate made little difference. The figures were obtained by calculation from the relative humidity (Table II B), the temperature, and values for water-vapour concentrations in saturated air at various temperatures (Hygrometric Table, 1940).

Table II B shows relative humidities, measured as described in the experiments, which ranged from 60 to 81.5%.

Table II C shows weight of water vaporized per minute, which ranged from 25 to 155 mg., the quantity varying as temperature and flow-rate. The figures were obtained by calculation from concentrations (Table II A) and flow-rates.

The effectiveness of humidification must be judged by the water-vapour *concentration* (expressed here in g./cu. m.) and not by relative humidity or the amount of water vaporized in one minute. Table II A therefore shows the essential results in this connexion. It cannot be too strongly emphasized that relative humidity readings are of limited value and must lead to fallacious conclusions unless taken in conjunction with temperature and expressed as water-vapour concentration. Air or oxygen which is saturated with water vapour at body temperature contains 44 g. of water per cubic metre. The drying power of inspired gases is proportional to the amount by which their water content falls short of this amount. Fig. 2 shows the water-vapour concentration at various relative humidities and temperatures, and has been drawn from values calculated from the Hygrometric Table (1940). Comparison of Table II A and II B shows some of the differences between water-vapour concentration and relative humidity in identical circumstances, and demonstrates the fallacy of accepting the latter in preference to the former. For example, at a flow-rate of 8 l./min. the relative humidity is 75% in a cool environment and 60% in a hot one (Table II B), yet the corresponding water-vapour concentrations are 7.95 and 19.42 g./cu. m. respectively (Table II A). The hot environment thus yields a higher water-vapour concentration, despite the lower relative humidity, than the cool one. Fig. 3 shows water-vapour concentrations occurring during the course of the experiments, strikingly showing the effect of ambient temperature.

Discussion

What level of humidification is desirable? In extreme atmospheric conditions, as in Himalayan mountaineering, there is evidence that during a stay of several weeks under conditions involving strenuous physical activity there is some liability to bronchitis (Pugh and Ward, 1953; Ward, 1953). In these circumstances the cold air at low pressure has an exceedingly low water-vapour content. However, in the range of atmospheric conditions likely to be encountered in clinical practice, air inhaled through the nose is warmed to within a degree or two of body temperature and saturated with water vapour. Perwitzschky (1927) showed that air at 25° C. (77° F.) and relative humidity 24% inhaled through the nose acquires a relative humidity of 99% at 35–36° C. (95–97° F.) by the time it reaches the trachea. Even with mouth-breathing it acquires

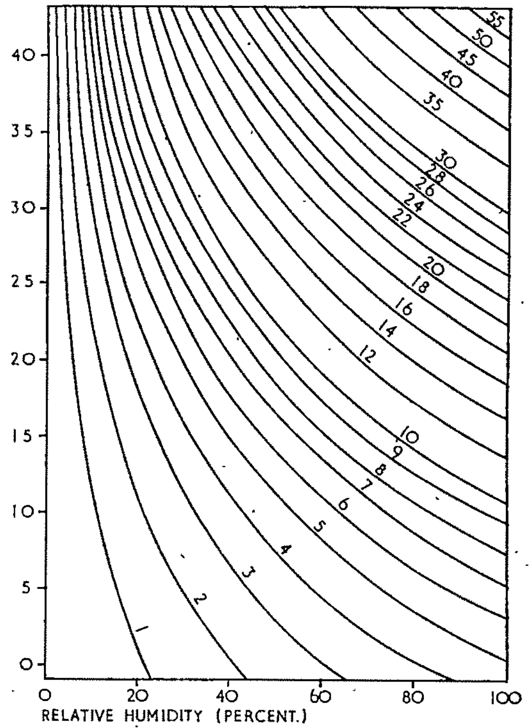


Fig. 2.—Given relative humidity and temperature, the absolute humidity, or water-vapour concentration in grammes per cubic metre of gas, can be derived from these curves. Each curve represents the number of grammes per cubic metre.

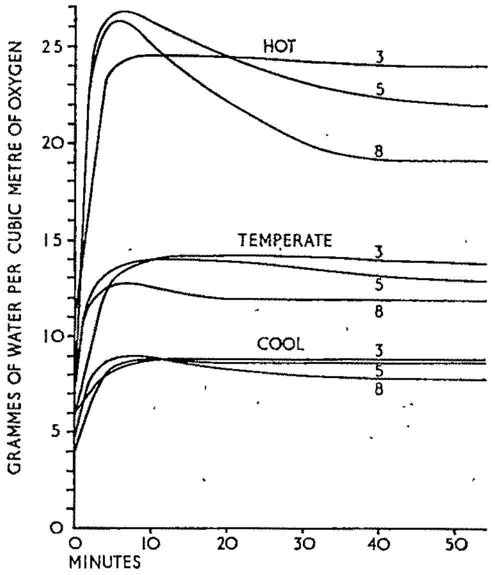


Fig. 3.—Examples of the sequence of changes that occur in absolute humidity (grammes of water per cubic metre) in oxygen when it is bubbled through water in a Woulfe bottle at three flow-rates (3, 5, and 8 litres per minute) and at three ambient temperatures.

a relative humidity of 93% at a temperature of 34.5° C. (94° F.). At the ambient temperature and relative humidity of his experiment air contains 5.52 g. of water vapour per cubic metre.

In the experiments described here the water-vapour content of the humidified oxygen was in the range of 7.95 to 22.74 g./cu. m. This is above the amount which Perwitzschky has shown will rise to almost saturation level at body temperature in the trachea. His experiments were carried out on healthy subjects and lasted five minutes each. It is possible that prolonged mouth-breathing would have led eventually to a lower relative humidity in the trachea.

There seem to have been no comparable experiments in patients. One is therefore obliged to consider the varying circumstances that affect patients, and to speculate on their influence on humidity in the airways and the state of the bronchi. The purpose of humidification of oxygen for inhalation is the reduction of its capacity to dry the mucosa of the airways and of the mucus lying thereon. What constitutes a desirable level of humidification depends on factors that vary from patient to patient. A high level of humidity is required in the following circumstances: sticky mucus, a weak cough, a partially obstructed nose, prolonged mouth-breathing, a tracheostomy, and the use of masks involving admixture with ambient air when the latter is excessively dry.

My experience of many cases of acute chest infection over a number of years suggests that cases of moderate severity receive adequate humidification by the Woulfe bottle method. The indications of inadequate humidification are a dry mouth, strings of sticky mucus in the fauces, a rattly but unproductive cough with an adequately expulsive blast, or the expectoration of small amounts of very tenacious mucus with undue effort. These signs are especially likely to occur in gravely ill patients whose infections are complicated by emphysema or asthma, and in whom the maximal expiratory flow-rate and expulsive blast are much reduced. Patients with acute chest infections who have undergone tracheostomy are in similar plight. These patients require inspired gases which are saturated at body temperature.

Summary

The method of humidifying oxygen by bubbling it through water in a Woulfe bottle has been criticized. This method was tested by bubbling oxygen at three flow-rates (3, 5, and 8 l./min.) and at three ambient temperatures (approximately 12°, 20°, and 32° C.). The relative humidities ranged from 60 to 82%, and water-vapour concentrations from 7.95 to 22.74 g./cu. m. During the first few minutes of bubbling, before appreciable cooling had occurred in the water in the Woulfe bottle, the humidities were still higher. It is thought that humidification of oxygen by this method is adequate for the treatment of most chest infections and for non-respiratory disorders requiring oxygen.

Attention is again drawn to the fallacy of accepting relative humidity alone as a measure of the humidification of gases for inhalation. The need to use measurements of water-vapour concentrations for this purpose is emphasized.

A family of curves has been drawn to facilitate calculation of water-vapour concentration when the relative humidity and temperature are known.

I wish to thank Mr. C. Hinkel, of the Meteorological Office, for advice, and the South-east Metropolitan Regional Hospital Board and King's College Hospital for the grant of equipment and technical assistance.

REFERENCES

Brit. med. J., 1964, **2**, 1580.
Cadman, E. F. B. (1961). *Brit. med. J.*, **1**, 591
Hygrometric Tables, Meteorological Office, MO.265, 4th ed., 1940 (reprinted 1956). Appendix IIIB, p. 44.
Perwitzschky, R. (1927). *Arch. Ohr.-, Nas.-, u. Kehlk.-Heilk.*, **117**, 1.
Pugh, J., and Ward, M. (1953) *The Ascent of Everest*, by J. Hunt, p. 278. London.
Ward, M. (1953). "The Medical Aspects of Mountaineering." Report on R.C.P. meeting, p. 14.

Heparin as an Analgesic in Myocardial Infarction: A Double-blind Trial

C. J. BULPITT,* M.B., M.R.C.P.

Brit. med. J., 1967, **3**, 279–281

Nichol *et al.* (1959) reported that heparin usually relieves anginal pain, but no controls were employed. This impression has been repeated (*British Medical Journal*, 1966) but never proved. Heparin does not increase forearm blood flow (Lambert, 1958) and there is no evidence of a vasodilator effect. It was decided, therefore, to perform a double-blind study on the effects of intravenous heparin on myocardial pain, blood pressure, pulse rate, and electrocardiographic tracings. Twenty-eight patients with "myocardial infarction" took part in the trial.

Method

The patients had been admitted to a general medical ward, usually in the Medway Hospital. To enter the trial a patient had to satisfy the following criteria: he should have cardiac ischaemic pain but not show more than slight distress; he should not have received an anticoagulant within the preceding few days, nor an opiate or drug of similar analgesic potency within the preceding six hours.

When the patient was first seen by a doctor a quick assessment was made. If the patient was not unduly distressed, and it was thought that no analgesic therapy would be required for 30 minutes, he was requested to enter the trial. He was told that he would receive an intravenous injection of a well-known drug, to discover whether or not it would relieve his pain. One patient who showed distress during this trial was given morphine and withdrawn.

Each patient verbally answered the first of three questionaries. An intravenous injection of either 2 ml. of normal saline or 2 ml. of a solution containing 10,000 units of heparin was then given. The solutions, which were identical in appearance, were prepared in numbered phials and used in numerical order. The code was held by the pharmacist, who had randomly allocated the solutions.

The blood pressure and pulse rate were recorded, and nine patients had an electrocardiogram taken before and after the

---

* Medical Registrar, Medway Hospital, Gillingham, Kent. Present address: Whipps Cross Hospital, London.

The Questionary

QUESTIONARY 1 (0 MINUTES) Please tick (✓) or cross ( ) to indicate whether question is correct or incorrect. Please ensure that every space is filled.

Time ....

1. Is the pain severe, moderate mild, or has it disappeared?	Severe?	
	Moderate?	
	Mild?	
	Disappeared?	
2. Does the pain radiate into the left arm or shoulder, right arm or shoulder, jaw, back, or into the abdomen?	Left arm or shoulder?	
	Right arm or shoulder?	
	Jaw?	
	Back?	
	Abdomen?	
3. Is the pain improving, worsening, or the same over the last 30 minutes?*	Improving?	
	Worsening?	
	Same?	

4. Have you any other complaints? List these ....

Pulse /min.

B.P. /

E.C.G. done/not done

....

* 10 minutes in Questionary 2 and 20 minutes in Questionary 3.

trial. After 10 and 30 minutes an identical questionary was answered and the blood pressure and pulse were again recorded.

The questionaries were devised to calculate the degree of pain present and thereby to assess any improvement. A points system provided a numerical basis. Severe pain rated six points, moderate pain four points, mild pain two points, and a "disappeared" pain counted nil. "Improving" counted minus two points, "worsening" plus two points, and "the same" counted nil. A radiating pain is probably more severe than one confined to the anterior chest wall, and plus one point was given for every site of radiation.

Results

Tables I and II show the patients' initial pain score and subsequent improvement or deterioration. The improvement is calculated from the difference between two pain ratings, a positive sign indicating a fall in pain rating and therefore improvement. Also shown are changes in pulse rate and diastolic blood pressure.

The 28 patients investigated had the characteristic pain plus typical electrocardiographic changes (Table I). Twenty-three of them had significantly raised transaminase levels. The patients were divided into two groups. The first group received heparin and the second saline. The heparin group included 12 men and three women, with an average age of 55 years. Two patients subsequently died during that hospital admission. The saline group included 12 men and one woman, with an average age of 58 years; three subsequently died. The only disparity between the groups is that the saline group showed higher transaminase levels. The mean aspartate aminotransferase level of the heparin group was 72 units and that of the saline group 103 units. The mean lactic dehydrogenase of the heparin group was 740 units and of the saline group 1,030 units.

Both groups showed pain relief 10 minutes after the injection. The difference between the two means is not significant (P>0.5). There was no further reduction in pain between 10 and 30 minutes in either group. The analgesic effect of intravenous heparin in myocardial infarction was no greater than that of normal saline.

The changes in pulse rate are of interest. At 10 minutes there was a reduction in rate in the saline group. As indicated in Table I, one patient (Case 35) had atrial fibrillation. The reduction in radial pulse rate was possibly due to the fall in diastolic blood pressure of 20 mm. Hg, the vertex rate not necessarily being altered to such an extent. This finding was included in calculations, and the results are still not significant. (P>0.1).

Between 10 and 30 minutes there was a reduction in pulse rate only in the heparin group. This remains unexplained and is probably not significant (P>0.05). The changes in diastolic blood pressure were minimal in both groups.

The six patients with "coronary insufficiency" had the characteristic prolonged pain at rest without typical electrocardiographic changes or marked elevation of the transaminase levels. The results in this section follow the pattern found in myocardial infarction (Table II). There is a similar degree of pain relief at 10 minutes and minimal improvement thereafter. Again heparin shows no advantage over saline in these patients.

Nine patients had an electrocardiographic tracing taken before the injection and after 30 minutes. Six had received heparin and three saline. Six patients showed no change in their electrocardiographic tracings. A minor increase in ischaemic change was observed in one patient receiving saline and in one receiving heparin. One patient receiving heparin showed a minor improvement in his tracing: an ST elevation of 1 mm. in lead II reverted to the isoelectric line at 30 minutes.

TABLE I.—*Patients with Myocardial Infarction*

Case No.	Initial Pain Assessment	Numerical Improvement		Pulse Change Beats/minute		Change in Diastolic B.P. in mm. Hg	
		At 10 Mins.	Between 10 and 30 Mins.	At 10 Mins.	Between 10 and 30 Mins.	At 10 Mins.	Between 10 and 30 Mins.
			Heparin Group				
4	4	+1	+3	−2	+4	+16	+8
5	5	+5	0	0	−4	−10	0
8	7	+2	−4	+12	−8	0	0
14	1	0	+2	−16	−4	+10	0
19	1	+1	0	−2	0	0	0
20	3	+2	+1	−12	+4	+5	+5
22	6	0	+6	−4	−6	−5	+15
23	1	+1	−2	+4	−13	+20	−20
28	2	−4	0	−12	−16	0	−20
30	6	+4	−2	+20	−20	−10	0
31	8	+2	−4	−4	−8	−5	0
33	9	+8	0	0	+8	0	0
37	4	+4	+2	+8	−8	−5	−5
41	7	+4	−2	+6	−2	−3	−2
81	3	+4	−1	0	0	—	—
Mean	4·5	2·3	0	0	−5	+1	−1
			Saline Group				
2	1	−3	+2	−6	−2	0	0
9	2	−2	−4	−8	+4	—	—
12	2	0	0	0	0	0	0
15	7	+4	−4	−4	−6	−10	−10
21	6	+3	+3	0	−10	+4	0
29	4	0	0	−4	+12	0	−5
35*	5	+3	+4	−56	0	−20	+10
42	0	0	−2	−12	−4	−6	+12
43	9	+4	−1	0	−3	0	+10
61	2	+4	−2	−4	0	—	—
77	9	0	0	−2	0	0	0
80	8	+7	0	0	+18	0	−10
82	6	+4	+4	+4	−4	0	0
Mean	4·7	1·8	0	−7	0	−3	+1

* Atrial fibrillation.

TABLE II.—*Patients with "Coronary Insufficiency"*

Case No.	Initial Pain Assessment	Numerical Improvement		Pulse Change Beats/minute		Change in Diastolic B.P. in mm. Hg	
		At 10 Mins.	Between 10 and 30 Mins.	At 10 Mins.	Between 10 and 30 Mins.	At 10 Mins.	Between 10 and 30 Mins.
			Heparin				
1	7	+2	+2	+4	−2	−20	0
16	0	+2	0	0	−12	+5	−5
79	4	+1	—	+2	—	+5	—
			Saline				
6	3	+3	0	+12	−8	0	+10
13	4	+2	−2	−4	−8	0	0
27	0	0	+1	−8	0	0	+10

Conclusions

Under the conditions of this trial heparin did not exert an analgesic effect in myocardial infarction greater than that of a placebo, nor did it affect the pulse rate or diastolic blood pressure. There was no significant alteration in the electrocardiographic tracings of six patients who received heparin.

Summary

A double-blind trial was performed to determine the effect of intravenous heparin on myocardial pain, pulse rate, diastolic blood pressure, and the electrocardiographic tracing.

No significant differences were found from the placebo effects of intravenous saline.

I am indebted to Drs. F. A. Richards, R. A. Moir, J. D. Craig, and M. Sadiq for encouragement, criticism, and permission to study patients under their care. The chief pharmacist, Mr. H. Duckett, kindly prepared the drugs and held the code. My thanks are also due to the resident medical staff for their assistance and to Miss D. Rose for secretarial work.

References

Brit. med. J., 1966, 2, 3.
Lambert, H. P. (1958). *Clin. Sci.*, 17, 621.
Nichol, E. S., Phillips, W. C., and Casten, G. G. (1959). *Ann. intern. Med.*, 50, 1158

Calcium Infusion Test in Osteomalacia: an Appraisal

J. V. LEVER,* M.B., B.SC.; C. R. PATERSON,* M.A., B.M., B.SC.; D. B. MORGAN,† M.B.

Brit. med. J., 1967, 3, 281-282

Nordin and Fraser (1956), as well as many other authors, have reported that patients with osteomalacia retain more of an infused dose of calcium than normal persons. A high retention of infused calcium by itself has been taken as diagnostic of osteomalacia (Harvald *et al.*, 1962; Deller *et al.*, 1963; Thompson *et al.*, 1966). Nordin and Fraser suggested that the calcium retained in osteomalacia was taken up by the uncalcified bone matrix—that is, osteoid tissue. If this was so then the amount of calcium retained should be related to the amount of osteoid.

We report here the relation between calcium retention and the amount of osteoid in trabecular bone in 15 patients.

Patients

Eleven patients had had a partial gastrectomy, but only four had typical osteomalacia with bone pains and a large increase in serum alkaline phosphatase which responded to vitamin D (Morgan *et al.*, 1965). The other seven were investigated because at that time we thought that a small increase in serum alkaline phosphatase, which they were shown to have, meant that they had a symptomless osteomalacia. Four further patients had typical osteomalacia which was not the result of gastric surgery. Three of these had proved gluten-induced enteropathy; the fourth is still being investigated.

Methods

The protocol for the infusion of calcium was that given by Nordin and Fraser (1956) except that calcium gluconate was infused in a 5% solution of dextrose and not in saline. Calcium in the urine was estimated by flame photometry (MacIntyre, 1961).

The proportion of the dose excreted was calculated from the difference between the calcium excreted in the urine in the 12 hours from the beginning of the infusion and the calcium excreted during the corresponding period on the previous day. The results were expressed as the percentage of the infused calcium retained in the body in the 12 hours.

The bone biopsy specimens were obtained from the iliac crest under local anaesthesia (Williams and Nicholson, 1963). The specimens were fixed in barbitone-buffered formalin (Ball, 1957) and sections cut without decalcification by Russell's (1956) technique. The area of osteoid in the section was expressed as a percentage of the total area of bone in the section. These measurements were made by Dr. C. G. Woods and will be reported by him elsewhere.

Results and Discussion

Fig. 1 shows that while all eight patients with typical osteomalacia retained most of the infused calcium so did four of the seven patients without an excess of osteoid in the bone. There was no relation between the amount of calcium retained and the area of osteoid.

Thus an excessive retention of calcium does not depend on an excess of osteoid. A similar conclusion could be drawn from the data of Thompson *et al.* (1966) and of Deller *et al.* (1963). The results in these two series have been plotted in Fig. 2, which includes our results for comparison. The histological criteria for the diagnosis of osteomalacia have been those of the respective authors.

The high retention of calcium in patients without osteoid is not limited to patients who have had a gastrectomy. Lindahl (1959) reported that a third of 70 patients with senile osteoporosis retained excessive amounts of infused calcium, though none of them had histological evidence of osteomalacia. Atkinson *et al.* (1956) reported an increased calcium retention in 7 out of 14 patients with chronic jaundice. Three of these seven had no osteoid on bone biopsy.

Apart from osteomalacia, high retention of calcium has been reported in other disorders of bone where osteoid is found. Thompson *et al.* reported, and we have confirmed, that in Paget's disease of bone there is an increased calcium retention after calcium infusion. Nordin and Fraser (1956) showed this in hypoparathyroidism, and also in a number of other diseases such as diabetes, rheumatoid arthritis, and renal failure.

The interpretation of calcium infusion tests may be questioned because normal persons retain as much as 73% of an infused dose, yet the retention of a further 10% is regarded as highly abnormal. The fate of the retained calcium is not

---

* Research Assistant, Clinical Investigation Unit, University of Leeds.
† Lecturer, Clinical Investigation Unit, University of Leeds.

known even in normal people. The extra calcium may be accommodated by the growth of immature crystals in bone; or the calcium may be deposited in the soft tissues of the body and not the bone. It would be interesting to know the effect of age on the retention of calcium; it is reasonable to postulate that the calcified soft tissues found in elderly persons have an increased affinity for calcium (Bürger, 1960) and, in addition, many of them have some impairment of renal function. But we do not think such an investigation is justified, and we report these results in the hope of sparing many patients an unnecessary infusion of calcium.

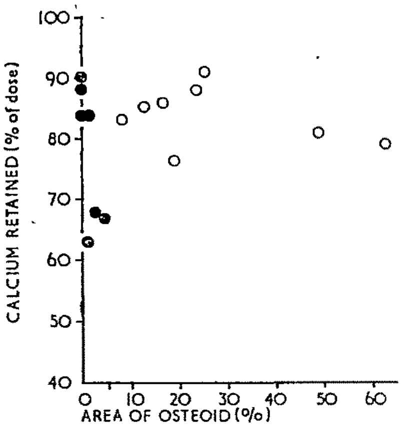


FIG. 1

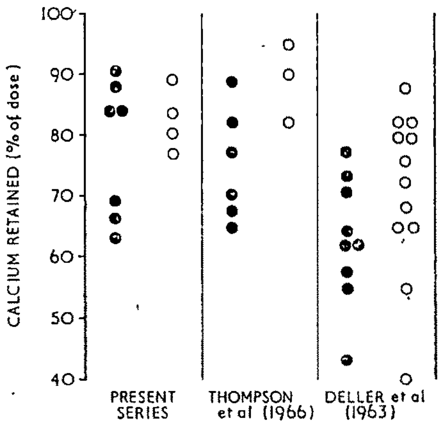


FIG. 2

FIG. 1.—Relation between retention of infused calcium and amount of osteoid (by area) in the bone biopsy specimen in eight patients with osteomalacia (open circles) and seven patients with a partial gastrectomy but without osteomalacia (closed circles). FIG. 2.—Retention of infused calcium in patients after gastrectomy. The open circles represent patients with osteomalacia and the closed circles patients who did not have osteomalacia. The histological definition of osteomalacia was that given by the respective authors.

We feel that it is impossible to interpret an "abnormal" calcium infusion test and that the only possible value of the test is that a normal result may exclude osteomalacia.

Summary

A high retention of infused calcium has been regarded as evidence of osteomalacia. This extra retention has been attributed to the excess of uncalcified bone (osteoid). In 15 patients the calcium retention and the amount of osteoid were compared. Although eight patients with osteomalacia did have a high retention of infused calcium, so did four out of seven patients with a gastrectomy but without osteomalacia. There was no relation between the amount of calcium retained and the amount of osteoid. These findings, together with the reports of high retentions of infused calcium in bone disorders other than osteomalacia, make it impossible to interpret an "abnormal" calcium infusion test. It is suggested that the only possible value of this test is that a normal result may exclude osteomalacia.

We thank Miss Judith Metcalfe for technical help and the sisters and nursing staff of the Leeds General Infirmary for their willing co-operation.

The study owes much to the guidance of our chief, Professor Paul Fourman. The work was supported in part by a grant from the Medical Research Council to Professor Fourman.

REFERENCES

Atkinson, M., Nordin, B. E. C., and Sherlock, S. (1956). *Quart. J. Med.*, **25**, 299.
Ball, J. (1957). *J. clin. Path.*, **10**, 281.
Bürger, M. (1960). *Dtsch. med. Wschr.*, **85**, 1493.
Deller, D. J., Edwards, R. G., and Addison, M. (1963). *Aust. Ann. Med.*, **12**, 295.
Harvald, B., Krogsgaard, A. R., and Lous, P. (1962). *Acta med. scand.*, **172**, 497.
Lindahl, O. (1959). *Acta orthop. scand.*, **29**, 160.
MacIntyre, I. (1961). *Advanc. clin. Chem.*, **4**, 1.
Morgan, D. B., Paterson, C. R., Woods, C. G., Pulvertaft, C. N., and Fourman, P. (1965). *Lancet*, **2**, 1089.
Nordin, B. E. C., and Fraser, R. (1956). Ibid., **1**, 823.
Russell, N. L. (1956). *J. med. Lab. Technol.*, **13**, 484.
Thompson, G. R., Neale, G., Watts, J. M., and Booth, C. C. (1966). *Lancet*, **1**, 623.
Williams, J. A., and Nicholson, G. I. (1963). Ibid., **1**, 1408.

Renal Papillary Necrosis in Sickle-cell Haemoglobinopathy

O. O. AKINKUGBE,* D.PHIL., M.B., M.R.C.P.ED.

Brit. med. J., 1967, 3, 283–284

Abel and Brown (1948) first drew attention to profuse haematuria in sickle-cell anaemia. Subsequent reports have confirmed that this association is more than fortuitous (Harrison and Harrison, 1952; Chapman *et al.*, 1955; Sharpe *et al.*, 1959). Haematuria is also known to occur in sickle-cell trait, sickle-cell haemoglobin C disease, sickle-cell thalassaemia, and a variety of combinations of haemoglobin S with other abnormal haemoglobins. The present report of four cases of haematuria in sickle-cell haemoglobinopathies is prompted for two reasons. Firstly, detection of blood in the urine of young adults in an environment endemic for schistosomiasis need not always indicate the presence of the infection. Of more practical importance is the surgical diagnostic problem sometimes posed by gross haematuria simulating renal neoplasm. Awareness of the possibility that this symptom may exist in sickle-cell haemoglobinopathy makes careful appraisal necessary, to avoid the inadvertent sacrifice of an apparently normal-functioning kidney.

Case 1

A 30-year-old female trader had had persistent haematuria for five weeks, at first mild, but later gross and alarming. There were no associated urinary findings. Her blood pressure (B.P.) was 120/85 mm. Hg. Both kidneys were easily felt. Her blood group was O-positive, sickling was present, and her genotype AS. The clotting-time (Biggs and Macfarlane, 1957) was 8 minutes and bleeding-time (Duke, 1910) 3 minutes. Haemoglobin (Hb) 7.3 g./100 ml.; packed-cell volume (P.C.V.) 22%; mean corpuscular haemoglobin concentration (M.C.H.C.) 33%; white blood count (W.B.C.) 6,600/cu. mm.; platelets 138,000/cu. mm. Her blood urea, electrolytes, and liver-function tests were all normal. Total serum proteins were 7.8 g./100 ml., and on electrophoresis showed a diffuse increase in the globulin fraction. Urinary specific gravity (S.G.) was 1008 and the specimen contained many red cells. At cystoscopy bleeding was observed from the left ureteric orifice. Intravenous pyelography (I.V.P.) showed good function bilaterally, but extending from three calices on the left was some contrast in small medullary cavities (Fig. 1). Her haematuria cleared gradually within a fortnight and she has since remained well and active.

Case 2

A tailor aged 47 was subject to recurrent episodes of painless haematuria for two months. Examination revealed severe anaemia (Hb 3.0 g./100 ml.). His urine contained a trace of albumin and its S.G. was 1006; red blood cells were detected at microscopy, but there were no casts. Blood group was O-positive, sickling was present, and his genotype AS. His blood urea was 16 mg./100 ml. Cystoscopy showed blood spurting from the left ureteric orifice. Left ureteric catheterization was followed by a retrograde pyelogram, after which a nephrectomy was performed. Naked-eye appearance of the kidney showed marked congestion of the vessels close to the papillae, with softening of the central and apical portions of the pyramid; there were blood clots in the renal pelvis. Microscopy did not reveal any abnormalities in either glomerular or tubular morphology. He remained well for five years, but has lately developed proteinuria and hypertension. The latter event has been complicated by congestive heart failure, but this has responded well to digoxin, thiazides, and reserpine. At the time of writing he remained practically symptom-free.

Case 3

A 37-year-old housewife gave a three-year history of recurrent attacks of haematuria, each episode lasting a few days. She had been so impressed by the transient nature of her symptom that she had not thought it necessary to seek medical attention. Indeed, all her previous admissions into hospital were for obstetric reasons, and during her last admission her ankles were noticed to be swollen, she had proteinuria and microscopic haematuria, and her B.P. was 140/100 mm. Hg. She was eventually delivered of a full-term live foetus, but at postnatal attendances these features persisted. Her red cells showed sickling, genotype AS. Blood-clotting and bleeding times were normal. Hb 11 g./100 ml.; P.C.V. 33%; M.C.H.C. 33%; W.B.C. 3,500/cu. mm. Her blood urea was 23 mg./100 ml. and total serum proteins were 8.0 g./100 ml. Urine: S.G. 1010; midstream sample contained a few red cells but numerous white cells. Culture of this yielded a mixed growth of coliform organisms, and a week's course of nitrofurantoin cleared her urinary infection. I.V.P. showed evidence of cavitation involving the central and apical parts of the right upper calicine configuration extending into the medulla.

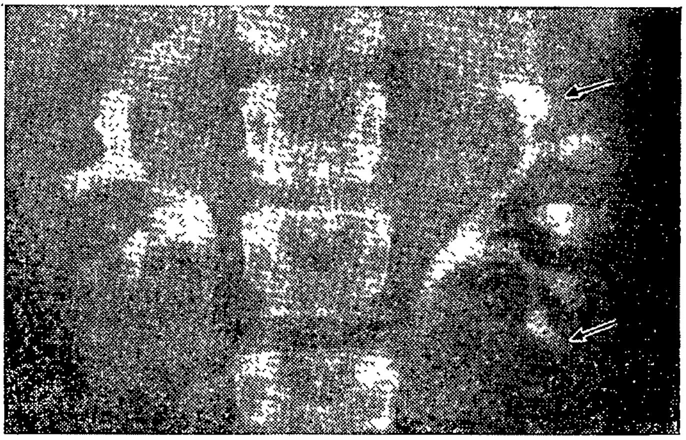


FIG. 1.—Case 1. Intravenous pyelogram (sickle-cell trait). On the left side dye extends from calices into small medullary cavities.

Case 4

A steward aged 37 had haematuria for two days. This was associated with frequency of micturition (three times at night), but there was no dysuria. Examination showed a well-built man with minimal pallor of his mucous membrane and tenderness in the right loin. B.P. 125/80 mm. Hg. Urine S.G. 1010, and midstream specimen contained many red cells and a trace of protein. His blood group was O-negative and genotype SS. I.V.P. showed changes in the right upper group of calices consistent with the medullary form of papillary necrosis (Fig. 2). Within a week his haematuria cleared completely and he has remained well for five years.

Discussion

Ischaemic infarction of the medullary pyramids has been known to occur since Friedreich's (1877) original description in a man with hydronephrosis due to an enlarged prostate. It was not until many decades afterwards (Günther, 1937) that its association with diabetes mellitus was recognized, becoming familiar to latter-day pathologists as necrotizing papillitis. In the past decade there have been widespread reports, notably from Switzerland and Scandinavia, of a great increase in the numbers of cases of renal papillary necrosis after excessive use of phenacetin compounds (Lindeneg *et al.*, 1959; Harvald, 1963).

---

* Lecturer in Medicine, University College Hospital, Ibadan, Nigeria.

It is estimated that about 4% of those individuals possessing the S gene suffer from haematuria at some time during their lives (Allen, 1964). Harrow *et al.* (1963) described renal papillary necrosis in five patients with sickle-cell trait. The true incidence of renal papillary necrosis in each of the various types of haemoglobinopathy is unknown. The scant reference in the literature to haematuria in patients homozygous for the S gene seems paradoxical, since the disorder is thought to be brought about by the presence of S haemoglobin. However, the relative frequency of this symptom in the trait may be more apparent than real. Firstly, the trait is far more common in the general population than the anaemia, and, secondly, the presence of haematuria as a lone symptom in the most innocuous of the genotypes naturally attracts more attention. The incidence of haematuria in haemoglobin SC disease is somewhere between these two extremes (River *et al.*, 1961).

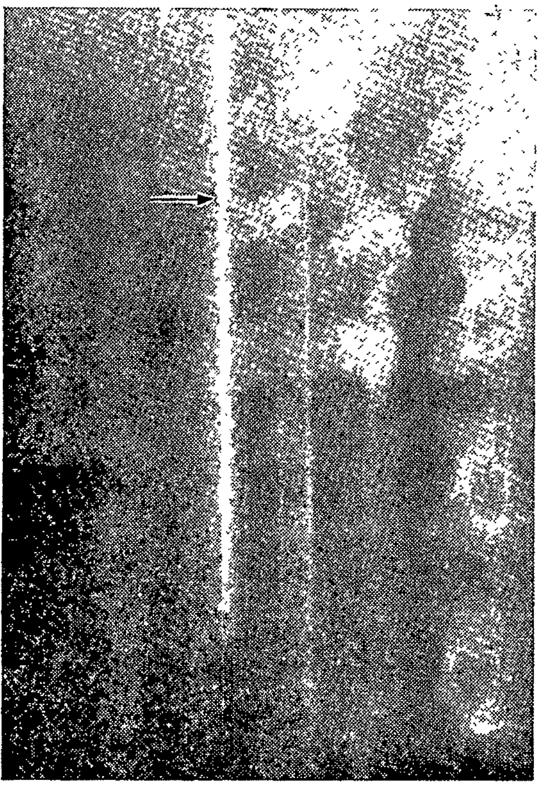


FIG. 2.—Case 4. Intravenous pyelogram (sickle-cell anaemia). On the right side the upper group of calices show changes consistent with papillary necrosis.

In more than half of all cases of papillary necrosis so far reported diagnosis was made during life by histological examination of papillae voided in the urine. Examination of renal biopsy specimens has not been rewarding. In three of the four cases reported above radiological investigation involving the use of contrast medium in I.V.P. revealed definitive ring changes in the renal papillae, formation of cavities in the pyramids or at the papillae, or an outline of concretions formed around necrotic fragments.

The pathogenesis of renal papillary necrosis in these states remains obscure. Its early association with diabetes and chronic obstructive renal disease suggested antecedent pyelonephritis. Support for this view was strengthened by the observation that phenacetin itself would cause an interstitial nephritis. The blood supply to the renal papillae derives from two sources: the vasa recta from the juxtamedullary region, and branches from the plexus of spiral vessels in the calix. Baker (1959) has shown how vulnerable these vessels are in diabetic arterial disease, infection, or back pressure on the calices. Whether primary vascular spasm occurs, as suggested by Kimmelstiel (1948), to account for ischaemic infarcts in sickle-cell crises is unknown. Perillie and Epstein (1961) found that sickling occurred in SS and AS subjects if the red blood cells were exposed to a hypertonic medium. It is well known that the counter-current system responsible for the concentration of urine produces a graded increase in osmolarity and lowering of oxygen tension from the base of the medulla to the tips of the papillae. It thus seems likely that increased viscosity and stasis would more readily affect the vasa recta supplying the papillary tips, leading to local ischaemia and tissue destruction.

Summary

Four cases of haematuria of varying severity associated with a sickling tendency are reported. Of these, three had sickle-cell trait and one sickle-cell anaemia. In three patients the radiological changes observed in the kidneys were those of renal papillary necrosis; in the remaining case the macroscopic appearance of the kidney from which the bleeding arose was suggestive of this lesion.

The conditions associated with renal papillary necrosis are reviewed. Hyperosmolarity in the region of the papillary tips is thought to predispose to sickling of red cells in neighbouring small vessels with subsequent ischaemic necrosis.

REFERENCES

Abel, M. S., and Brown, C. R. (1948). *J. Amer. med. Ass.*, **136**, 624.
Allen, T. D. (1964). *J. Urol. (Baltimore)*, **91**, 177.
Baker, S. B. de C. (1959). *Brit. J. Urol.*, **31**, 53.
Biggs, R., and Macfarlane, R. G. (1957). *Human Blood Coagulation and its Disorders*, 2nd ed. Oxford.
Chapman, A. Z., Reeder, P. S., Friedman, I. A., and Baker, L. A. (1955). *Amer. J. Med.*, **19**, 773.
Duke, W. W. (1910). *J. Amer. med. Ass.*, **55**, 1185.
Friedreich, N. (1877). *Virchows Arch. path. Anat.*, **69**, 308.
Günther, G. W. (1937). *Münch. med. Wschr.*, **84**, 1695.
Harrison, F. G., and Harrison, F. G., jun. (1952). *J. Urol. (Baltimore)*, **68**, 943.
Harrow, B. R., Sloane, J. A., and Liebman, N. C. (1963). *New Engl. J. Med.*, **268**, 969.
Harvald, B. (1963). *Amer. J. Med.*, **35**, 481.
Kimmelstiel, P. (1948). *Amer. J. med. Sci.*, **216**, 11.
Lindeneg, O., Fischer, S., Pedersen, J., and Nissen, N. I. (1959). *Acta med. scand.*, **165**, 321.
Perillie, P. E., and Epstein, F. H. (1961). *Clin. Res.*, **9**, 332.
River, G. L., Robbins, A. B., and Schwartz, S. O. (1961). *Blood*, **18**, 385.
Sharpe, A. R., jun., Fox, P. G., jun., and Dodson, A. I. (1959). *J. Urol. (Baltimore)*, **81**, 780.

Preliminary Communications

A Serological Method for Demonstrating Recent Infection by Rubella Virus

Brit. med. J., 1967, 3, 285–286

Serological evidence of infection by rubella virus may be obtained by neutralization (Parkman *et al.*, 1964), complement-fixation (Sever *et al.*, 1965), or haemagglutination-inhibition tests (Steward *et al.*, 1967). As rubella often presents atypically or even inapparently, diagnosis on clinical grounds alone is liable to error. Because of the risk of subsequent congenital malformations (Gregg, 1941), serological tests are particularly valuable in the assessment of mothers exposed to or acquiring rubella early in pregnancy. Both neutralizing and haemagglutination-inhibiting (H.I.) antibodies often rise sharply to a high level early in the disease, a significant level of H.I. antibody sometimes being present on the first day of rash (Stewart *et al.*, 1967 ; A. Field, personal communication). In our experience many patients with rubella, particularly those who are pregnant, may be five to seven days or more from the onset of symptoms by the time they are referred for investigation. In these circumstances there may not be a significant rise in antibody titre between an acute phase sample of serum and a subsequent one taken two to three weeks later, both having equally elevated titres. This makes it impossible to say whether their antibody results from recent or from past infection. Although a rising or high complement-fixing antibody titre is useful, since it suggests relatively recent infection (Sever *et al.*, 1965 ; Schmidt and Lennette, 1966), a significant rise in antibody titre may not become detectable until four to six weeks after onset of symptoms (Sever *et al.*, 1966 ; Banatvala, unpublished observations), peak titres sometimes being achieved as late as three to six months after infection (Veronelli and Eckert, 1966).

The first immunoglobulins (IgM) to be detected after primary antigenic stimulus are of high molecular weight (Smith, 1960 ; Uhr and Finkelstein, 1963 ; Svehag and Mandel, 1964). These are almost entirely replaced within a few weeks by those of lower molecular weight (IgG and IgA). This paper describes a method of detecting the presence of recently acquired rubella antibody by H.I. tests, titrating early and late convalescent sera in parallel before and after treatment with 2-mercaptoethanol (2ME) ; this being a sulphydryl-reducing compound which breaks down IgM immunoglobulins.

MATERIALS AND METHODS

Serial serum samples were obtained from patients with rubella at variable intervals from the day of onset (day 1), to 14 months after illness. Sera showing elevated H.I. titres in acute (day 1–5), early convalescent (day 7–30), or late convalescent (6 weeks to 14 months) were pretreated with 25% kaolin and 50% day-old chick red blood cells according to the method described by Stewart *et al.*, 1967. Sulphydryl reduction was demonstrated by treating sera with 1/10 volume 0.5 *M* 2ME for one hour at 37° C. An equal volume of phosphate-buffered saline was added to untreated sera. Antibody titres were measured by H.I. tests (Stewart *et al.*, 1967), employing 8 HA units of ether-tween split virus antigen with a micro-titre apparatus and plastic disposable " V " plates (Linbro Ltd.). Treated and untreated sera were titrated in parallel. The results of most of these tests were confirmed with a double blind technique. Complement-fixing tests were performed with microtitre apparatus, employing overnight fixation at 4° C. with 1 unit of antigen (Flow Laboratories Ltd.) and 1.5 units of complement.

RESULTS

Eighteen (85.7%) of 21 sera obtained during the acute or early convalescent phase of illness showed consistent reductions in antibody titre after treatment with 2ME (Table I). The most marked reductions occurred in five sera (Cases 1–5) obtained during the first few days of illness (4 to 32-fold reductions) ; these included two sera obtained on the first day of rash. This suggests that even at this early stage true antibody consisting principally of IgM immunoglobulin is present. Thirteen (76.5%) of the 17 sera obtained in the early convalescent phase of illness showed consistent reductions in antibody titre, mostly twofold, but on two occasions fourfold in magnitude. However, of nine sera containing antibody to rubella virus collected during the first 14 days after the onset of illness, all showed reductions in antibody titre. The four early convalescent sera which were not reduced were obtained later, on days 16, 21, 23, and 27 respectively. A fourfold or greater rise in complement-fixing antibody between acute and early convalescent sera occurred in only 7 of 16 (43.7%) sera tested (Table I), although a twofold or greater rise was present in 14. Repeated tests on 14 late convalescent sera obtained from 11 patients failed to show reduction in antibody titre between treated and untreated sera (Table II), although complement-fixing antibody titres persisted or increased. Thus reductions in antibody titre after treatment with 2ME indicated that infec-

TABLE I

Case	Acute Sera					Early Convalescent Sera				C.F.
	*Day	H.I.			C.F.	Day	H.I.			
		Un-treated	2ME	Fold Redn.			Un-treated	2ME	Fold Redn.	
1	1	256	8	32	< 4	17	2,048	512	2	8
2	1	16	< 4	4	4	22	2,048	1,024	2	32
3	2	16	< 4	> 4	< 4	16	1,024	1,024	—	8
4	3	32	< 4	> 8	8	23	512	512	—	16
5	5	256	64	4	NT	16	4,096	2,048	2	NT
6	1	< 4	—	—	< 4	7	4,096	2,048	2	16
7	1	< 8	—	—	< 8	14	512	256	2	16
8	2	< 4	—	—	< 4	14	8,192	4,096	2	32
9	1	4	—	—	4	14	2,048	512	4	16
10	1	< 4	—	—	4	16	1,024	512	2	16
11	2	4	—	—	4	18	2,048	1,024	2	8
12	2	< 4	—	—	< 4	19	16,384	8,192	2	16
13	1	< 4	—	—	4	19	1,024	512	2	8
14	2	4	—	—	< 4	23	4,096	1,024	4	4
15	1	< 4	—	—	< 4	30	16,384	8,192	2	32
16	2	32	NT	NT	4	21	8,192	8,192	—	4
17	3	< 4	—	—	< 4	27	1,024	1,024	—	8

* Onset of rash = day 1. NT = not tested.

TABLE II.—*Late Convalescent Sera*

Case	Months from Onset	HI			C.F.
		Untreated	2ME	Fold Reduction	
1	1½	1,024	1,024	—	64
2	3	4,096	4,096	—	32
	7	4,096	4,096	—	32
3	3	4,096	4,096	—	32
4	3	2,048	2,048	—	8
	9	1,024	1,024	—	8
5	4	2,048	2,048	—	32
6	5	2,048	2,048	—	8
7	6	1,024	1,024	—	> 64
8	6	4,096	4,096	—	4
9	6	1,024	1,024	—	32
	11	4,096	4,096	—	8
10	12	128	128	—	NT
11	14	4,096	4,096	—	8

tion had occurred recently, whereas no reduction in antibody titre was suggestive, but was not conclusive evidence of less recent infection.

DISCUSSION

These results are similar to those obtained by Schluederberg (1965), who found consistent twofold to fourfold reductions in antibody titre after treatment with 2ME in serum obtained at 12-day to 21-day intervals after measles vaccination and natural infection with mumps virus, but no reduction in those obtained two months or more after infection. Lindquist *et al.* (1965), employing neutralization tests, observed fourfold or greater reductions in rubella antibody titre in seven of nine infants aged 10 weeks or less with the rubella syndrome, suggesting that, in addition to maternal IgG immunoglobulins, infants were synthesizing their own antibody, consisting principally of IgM components either before birth or in the neonatal period. Although treatment with 2ME provides a considerably less precise estimate of the presence of IgM immunoglobulins than, for example, analyses of antibody components by means of sucrose density gradients or gel filtration on Sephadex, the technique is simpler and can be used more readily if many sera have to be tested routinely. Even though the action of 2ME may not be entirely selective in breaking down only IgM immunoglobulins, both this and Schluederberg's series (1965) demonstrate that reduction in antibody titre after virus infection in early but not late convalescent sera, even though sometimes of small magnitude, is consistent. Reductions in antibody titre after treatment with 2ME compared favourably with complement-fixing tests as an index of recent infection by rubella virus. However, treatment with 2ME may be especially useful in assessing the duration of antibody in single serum samples obtained in the early stages of illness, a period at which greatest reductions in antibody titres are to be expected, or in obtaining evidence of recent infection in a proportion of patients who might present in early convalescence before complement-fixing antibody has fully developed. These preliminary results suggest that this test, since it can be both simply and rapidly performed, may, in conjunction with virus isolation and other serological tests, be of additional value in the assessment of patients who have been contacts of or who gave a history of rubella during pregnancy.

SUMMARY

Eighteen of 21 (85.7%) acute and early convalescent sera from patients with rubella showed reduction in haemagglutination-inhibiting antibody titre after treatment with 2ME, whereas all late convalescent sera showed no reduction. This test provided a method for recognizing recent infection by rubella virus that may be particularly useful in the serological assessment of mothers contracting rubella during pregnancy.

J. E. BANATVALA, M.A., M.D., M.C.PATH., D.P.H., D.C.H.
JENNIFER M. BEST, B.SC.
ELIZABETH A. KENNEDY, B.A.
ELIZABETH E. SMITH, R.T.(CAN.).
MARJORIE E. SPENCE.

Clinical Virology Laboratory, Department of Medical Microbiology, St. Thomas's Hospital, London S.E.1.

REFERENCES

Gregg, N. M. (1941). *Trans. ophthal. Soc. Aust.*, **3**, 35.
Lindquist, J. M., Plotkin, S. A., Shaw, L., Gilden, R. V., and Williams, M. L. (1965). *Brit. med. J.*, **2**, 1401.
Parkman, P. D., Mundon, F. K., McCown, J. M., and Buescher, E. L. (1964). *J. Immunol.*, **93**, 608.
Schluederberg, A. (1965). *Nature (Lond.)*, **205**, 1232.
Schmidt, N. J., and Lennette, E. H. (1966). *Proc. Soc. exp. Biol. (N.Y.)*, **121**, 243.
Sever, J. L., Huebner, R. J., Castellano, G. A., Sarma, P. S., Fabiyi, A., Schiff, G. M., and Cusumano, C. L. (1965). *Science*, **148**, 385.
—— —— Fabiyi, A., Monif, G. R., Castellano, G., Cusumano, C. L., Traub, R. G., Ley, A. C., Gilkeson, M. R., and Roberts, J. M. (1966). *Proc. Soc. exp. Biol. (N.Y.)*, **122**, 513.
Smith, R. T. (1960). Ciba Foundation Symposium, Cellular Aspects of Immunity, p. 384, edited by G. E. W. Wolstenholme and M. O'Connor. London.
Stewart, G. L., Parkman, P. D., Hopps, H. E., Douglas, R. D., Hamilton, J. P., and Meyer, H. M. (1967). *New Engl. J. Med.*, **276**, 554.
Svehag, S., and Mandel, B. (1964). *J. exp. Med.*, **119**, 21.
Uhr, J. W., and Finkelstein, M. S. (1963). Ibid., **117**, 457.
Veronelli, J. A., and Eckert, E. A. (1966). *Proc. Soc. exp. Biol. (N.Y.)*, **121**, 1223.

Medical Memoranda

Guillain-Barré Syndrome Associated with Chronic Lymphatic Leukaemia

Brit. med. J., 1967, **3**, 286–287

The occurrence of the Guillain–Barré syndrome in patients with chronic lymphatic leukaemia is rare. There seem to be no previous reports of this association, and it has been seen in only two instances in our series of more than 500 patients with chronic lymphatic leukaemia.

CASE 1

A man aged 60 was admitted to hospital at the end of November 1965 with a history of pain in the region of the right hip, radiating into the right thigh, accompanied by increasing weakness of the arms and legs. A diagnosis of chronic lymphatic leukaemia had been made in July 1965 after the examination of a peripheral blood smear and bone-marrow biopsy. He had been treated with chlorambucil.

On admission he was hardly able to walk. Fine movements with his hands were impossible. He was not anaemic, and there was no lymphadenopathy. His spleen was palpable 1 cm. below the left costal margin. He had generalized muscle weakness of his limbs and trunk. The muscles were flaccid ; there was no fasciculation but some tenderness, particularly of the leg muscles. All the tendon jerks were absent. The plantar reflexes were flexor. There was loss of appreciation of painful stimuli in a stocking and glove distribution. After admission he developed cranial nerve involvement, with a bilaterally symmetrical facial nerve weakness and some difficulty in swallowing.

Investigations.—The haemoglobin was 14.2 g. ; W.B.C. 15,200/cu. mm., with 11,400 lymphocytes ; E.S.R. 2 mm./hour (Westergren). The cerebrospinal fluid contained 58 mg. of protein per 100 ml. Porphyrins were not detected in the urine. Electromyography showed changes compatible with a widespread peripheral neuropathy, and a suggestion of primary muscle disease in the forearm muscles. The creatine kinase level was 0.3 unit. The serum protein contained a low level of gammaglobulin. The IgG was 720 mg./100 ml. IgM was 63% and IgA 23% of a reference normal serum.

Large doses of corticosteroid (60 mg. of prednisolone daily) brought slow but steady improvement. He was able to walk, and fine movements of his hands were possible. Electromyographic changes, still present, were compatible with a diagnosis of Guillain–Barré syndrome.

CASE 2

A woman aged 59 was admitted to hospital in October 1960 with a three-weeks history of pain in the back and left shoulder, and a steadily increasing weakness of her arms and legs. Four days before admission she had developed a bilateral facial weakness and difficulty in swallowing. A diagnosis of chronic lymphatic leukaemia had been made two years previously, in January 1958, as the result of examination of a blood film and bone-marrow biopsy. Some ten months before her present illness she had herpes zoster affecting the D 12 and L 1 dermatomes on the right side. She had been treated with a small dose of prednisolone for six months before the present illness.

On examination she was pale with scarring on her trunk following the attack of herpes zoster. There was no lymphadenopathy, but her spleen was palpable 1 cm. below the left costal margin. She had a bilaterally symmetrical facial palsy. Her arms were not weak, though her muscle tone was diminished and the tendon reflexes were much reduced. Her legs were weak, the muscles flaccid, and the tendon jerks much reduced. The plantar responses were flexor. Though she complained of subjective disturbances in sensation in the limbs there were no objective signs.

Investigations.—Haemoglobin was 10.7 g.; W.B.C. 84,000/cu. mm. (73,080 lymphocytes); E.S.R. 13 mm./hour (Westergren); platelets 140,000. Cerebrospinal fluid contained protein in a concentration of 320 mg./100 ml. with increased globulin and 66 lymphocytes/cu. mm. Diminished nerve conduction was demonstrated in the branches of the facial nerve. The serum proteins showed a low level of IgG, 720 mg./100 ml., and low levels of IgM and IgA, 23% and 6% of a reference normal serum respectively.

The patient was treated with 40 mg. of prednisolone daily and made a slow but steady recovery. Eight months later she was completely free from symptoms, and a year after her illness she had no abnormal neurological signs.

DISCUSSION

These cases show the usual clinical course of acute polyneuritis described by Guillain *et al.* (1916). Their progress contrasts with previous reports of polyneuritis complicating tumours of lymphoid tissue in which there has either been no recovery or only transient improvement. Williams *et al.* (1959) noted that peripheral neuropathy of some form occurred in only 2.25% of their series of 5,778 patients with lymphomas or leukaemias. The combination of chronic lymphatic leukaemia and peripheral neuropathy was seen in only three patients, and in none of these did it take the form of acute polyneuritis. The neuropathies described in their cases of lymphoma, and in single cases of reticulum-cell sarcoma (Blanchard, 1962) and lymphofollicular reticulosis (Shafar, 1965), resembled those seen in other malignant conditions, particularly carcinoma.

The association of diseases of the nervous system and those of lymphoid tissue occurs in such conditions as idiopathic autoimmune haemolytic anaemia, which may be complicated by peripheral neuritis, or in Hodgkin's disease and chronic lymphatic leukaemia where demyelinization occurs in the central nervous system (Åström *et al.*, 1958; Cavanagh *et al.*, 1959). In these instances it would seem likely that there was an immunological basis for the pathological changes. Widespread involvement of lymphatic tissue in infection may rarely be associated with peripheral nerve lesions. Infectious mononucleosis may sometimes be complicated in this way.

The cause of Guillain–Barré syndrome is uncertain—it may be immunological or infective in nature. The benefit that steroid therapy has on the course of the condition would suggest that there is an autoimmune process directed at damaging nervous tissue. Melnick and Flewett (1964), in reviewing the theories of causation, did not find evidence of a specific viral cause. They were, however, able to show, in a carefully controlled clinical study, that common viral infections were significantly more common in patients with Guillain–Barré syndrome than in a matched control population.

Heath *et al.* (1964) showed that the level of resting antibodies in a wide variety of virus infections was reduced in chronic lymphatic leukaemia, and the ability to form antibodies against influenza viruses grossly impaired. The level of globulin concerned with response to infection, IgG, was reduced in the two cases reported here, and this may have rendered them more susceptible to virus infections. If the polyneuritis is precipitated by a virus infection, then it would appear from these cases that the prognosis of the neurological lesion is not made worse by the chronic lymphatic leukaemia and associated hypogammaglobulinaemia. This would support the concept that the perpetuation is an autoimmune phenomenon.

We are grateful to Sir Ronald Bodley Scott for allowing us to publish these case reports, and for his helpful criticism and advice. Dr. Ann Beardwell kindly carried out the electromyographic studies, and the serum protein estimations were made with the helpful co-operation of Dr. D. S. Rowe.

R. L. POWLES, M.B., B.S., B.SC.,
House-physician, St. Bartholomew's Hospital, London.
J. S. MALPAS, M.B., D.PHIL., M.R.C.P.,
Registrar, St. Bartholomew's Hospital, London.

REFERENCES

Åström, K. E., Mancall, E. L., and Richardson, E. P. (1958). *Brain*, **81**, 93.
Blanchard, B. M. (1962). *Ann. intern. Med.*, **56**, 774.
Cavanagh, J. B., Greenbaum, D., Marshall, A. H. E., and Rubinstein, L. J. (1959). *Lancet*, **2**, 524.
Guillain, G., Barré, J. A., and Strohl, A. (1916). *Bull. Soc. méd. Hôp. Paris*, **40**, 1462.
Heath, R. B., Fairley, G. H., and Malpas, J. S. (1964). *Brit. J. Haemat.*, **10**, 365.
Melnick, S. C., and Flewett, T. H. (1964). *J. Neurol. Neurosurg. Psychiat.*, **27**, 395.
Shafar, J. (1965). *Lancet*, **2**, 470.
Williams, H. M., Diamond, H. D., Craver, L. F., and Parsons, H. (1959). *Neurological Complications of Lymphomas and Leukaemias.* Illinois.

Gas in the Portal Vein in Association with a Pelvic Abscess

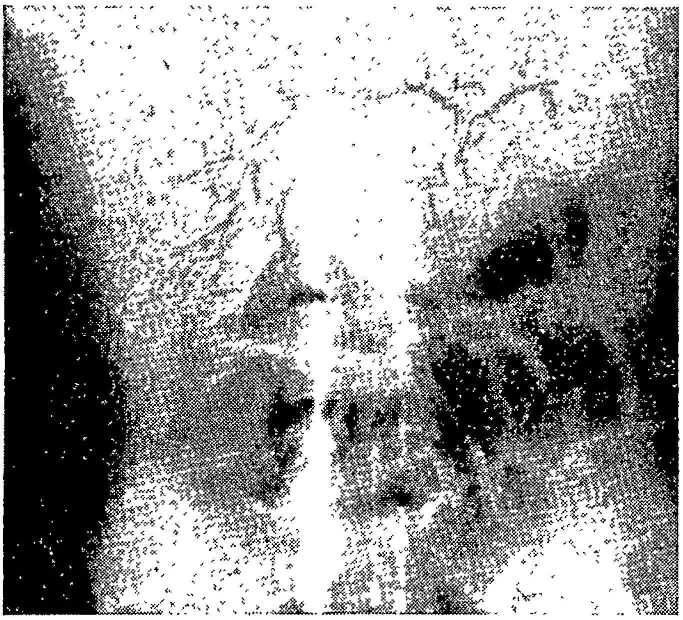
Brit. med. J., 1967, 3, 288

The radiological demonstration of gas in the portal vein was first reported by Wolfe and Evans (1955), and since then there have been nine further papers on this subject in the English language (Susman and Senturia, 1960 ; Sisk, 1961 ; Wiot and Felson, 1961 ; Barrett, 1962 ; Stewart, 1963 ; Guyer and Grainger, 1963 ; McCandless, 1964 ; Lazar, 1965 ; Fink and Boyden, 1966). The purpose of this communication is to record a further example of this apparently rare finding, which occurred in association with a pelvic abscess, and briefly to review the literature.

CASE REPORT

A 49-year-old woman was referred in 1964 with a rectovaginal fistula complicating radium therapy for carcinoma of the cervix in 1950. A loop sigmoid colostomy had been constructed in 1951 and was working satisfactorily, but the patient wished to be rid of it. Accordingly, it was decided to resect the fistula and the affected segment of rectum by an abdomino-anal pull-through excision. This was done in November 1964 under cover of the existing colostomy. Her postoperative course was complicated by pulmonary atelectasis and infection, which responded only slowly to physiotherapy and antibiotics, and delayed the closure of the sigmoid colostomy until 29 March 1965. After this procedure atelectasis recurred with infection and she was given a course of penicillin and streptomycin, which may well have masked the development of a pelvic abscess. However, she seemed to make good progress and was discharged home on the fourteenth postoperative day. She was readmitted three days later with abdominal distension and cardiovascular shock due to a bowel obstruction. After resuscitation plain abdominal *x*-ray examination was carried out in the erect and supine positions, and showed the following features: (1) moderate small-bowel distension with fluid levels ; (2) a fluid level in the pelvis, apparently in a well-defined cavity, suggesting a high pelvic abscess ; and (3) linear gas shadows in the liver extending to within 2 cm. of the liver margin, as occurs when gas is present in the portal vein and its branches (see Fig.).

Laparotomy was performed on the day of admission and confirmed the diagnosis of a small-bowel obstruction, this being due to adhesions between the small bowel and the wall of a pelvic abscess closely related to the site of colostomy closure. The bowel was only moderately distended and there was no evidence of ischaemia. The adhesions were freed and the abscess was drained. At the conclusion of the operation a tracheostomy was performed because of the previous episodes of postoperative pulmonary collapse and infection. Bacteriological culture of the pus obtained from the pelvic abscess gave a heavy growth of a coliform organism. During the operation the patient was given tetracycline, because, despite apparently adequate fluid and electrolyte replacement, her general condition deteriorated and it seemed likely that the abdominal condition was complicated by a Gram-negative septicaemia, though we were not able to prove this by positive blood culture. Her condition improved and she was subsequently treated in the intensive-care ward. Her initial progress was satisfactory and bowel function was re-established. Antibiotic therapy was changed from tetracycline to ampicillin on the basis of sensitivity tests. A pulmonary infarct was revealed radiologically on the seventh postoperative day, and this was complicated by a pyopneumothorax on the ninth day. Intercostal suction-tube drainage was instituted and chloramphenicol added to the antibiotic regimen, but she slowly deteriorated and died on the eighteenth postoperative day. Permission for necropsy was refused.



Supine abdominal *x*-ray plate of patient, showing moderate small-bowel distension and the portal veins outlined by gas. Note the gas shadows approach to within 2 cm. of the liver margin, a feature which serves to distinguish this variety of intrahepatic gas from the more commonly occurring condition of gas in the bile-duct system.

Throughout the postoperative period daily *x*-ray plates of her chest and abdomen were obtained, but in none of these was gas demonstrated within the hepatic shadow.

COMMENT

Gas in the portal vein is a rare finding, probably owing to its transient nature and to difficulty in obtaining good quality *x*-ray films in severely ill patients. When obtainable, however, the radiological features are characteristic (see Fig.). An analysis of the pathology in 29 reported cases (see Table) emphasizes the combination of gross distension and impaired viability of the bowel. These features were noted in no fewer than 26 of the 29 cases. Susman and Senturia (1960) suggested three possible sources of gas in the portal vein: (1) gas within the distended bowel ; (2) gas-forming organisms within the bowel wall ; and (3) gas from an abscess cavity within the drainage area of the portal vein. In most reported cases the first two of these factors seem to be implicated in that the bowel was distended and ischaemic. Portal septicaemia may well be an accompanying feature, and in one reported case (Barrett, 1962) a positive blood culture for gas-gangrene organisms was obtained at operation from the portal vein.

Pathological Lesions Present in 29 Recorded Cases of Gas in the Portal Vein

Vascular occlusions:	
(*a*) Thrombosis or embolism of superior mesenteric artery or vein	10
(*b*) Strangulation of bowel	3
Necrotizing inflammations of intestine	7
Inflammation with less definite necrosis	6
Severe mediastinitis with septicaemia	1
Diabetic acidosis with bowel distension	1
Pelvic abscess with intestinal obstruction	1

Bowel distension was present in 27 patients, this distension often being described as gross or very marked. Impairment of the viability or actual necrosis of the intestinal wall was present in 26 patients.

The present case is unique in that gas in the portal vein was associated with a proved intra-abdominal abscess containing gas, which may well have been forced into the portal venous system. However, even in this patient portal septicaemia has not been excluded as a contributory factor.

I am grateful to Professor J. C. Goligher for permission to publish this report and for his helpful advice in the preparation of the paper.

N. G. GRAHAM,* M.B., F.R.A.C.S., F.R.C.S.

* From the Professorial Surgical Unit, the General Infirmary at Leeds.

REFERENCES

Barrett, A. F. (1962). *Clin. Radiol.*, **13**, 92.
Fink, D. W., and Boyden, F. M. (1966). *Radiology*, **87**, 741.
Guyer, P. B., and Grainger, K. (1963). *Brit. J. Radiol.*, **36**, 379.
Lazar, H. P. (1965). *Amer J. dig. Dis.*, **10**, 259.
McCandless, R. G. (1964). *Amer. J. Roentgenol.*, **92**, 1162.
Sisk, P. B. (1961). *Radiology*, **77**, 103.
Stewart, J. O. R. (1963). *Brit. med. J.*, **1**, 1328.
Susman, N., and Senturia, H. R. (1960). *Amer. J. Roentgenol.*, **83**, 847.
Wiot, J. F., and Felson, B. (1961). Ibid., **86**, 920.
Wolfe, J. N., and Evans, W. A. (1955). Ibid., **74**, 486.

Current Practice

ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Mechanism of Leuco-erythroblastosis

Q.—*What is the mechanism of leuco-erythroblastosis in the bone-marrow replacement syndrome?*

A.—The term "leuco-erythroblastic anaemia" was defined by Janet Vaughan[1] as a condition characterized by the presence in the peripheral blood of immature red cells and a few immature white cells of the myeloid series. She noted its association with infiltrative bone marrow disease. Subsequently the term "leuco-erythroblastosis" came into use in recognition of the fact that anaemia may be disproportionately slight or even absent.

The most common cause is infiltration of bone marrow by carcinoma, and it also occurs when the bone marrow is infiltrated by other foreign cells, such as in myelomatosis, myelosclerosis, and xanthomatosis, and also when there is overgrowth of the bony tissue itself, as in osteopetrosis. It should not be forgotten, however, that leuco-erythroblastosis does not necessarily imply marrow infiltration. It also occurs in association with haemolytic anaemias, severe bacterial infections, and a group of miscellaneous conditions including liver disease.[2]

With such a wide range of causes the mechanism of the leuco-erythroblastosis is unlikely to be due to a single factor. The question refers especially to the bone-marrow replacement syndrome, but even here the problem is a complex one. The traditional explanation is that the infiltrating foreign material causes "irritation" or "stimulation" of adjacent marrow leading to excessive myeloid and erythroid activity. This is a facile explanation, which does not really clarify the problem. When there is an infiltrative tumour the presence of leuco-erythroblastic anaemia does not mean that the bone marrow has been crowded out by the tumour tissue.

There seems no quantitative relationship between the extent of infiltration and the leuco-erythroblastic reaction.[3] It is possible that tumour cells produce some chemical factor which leads to marrow hypofunction and premature release of some cells into the circulation, or they may have an effect by diverting some haematinic factor necessary for normal maturation. Erythropoietin promotes differentiation of the erythroid stem cell into the erythroblast with subsequent release of newly formed mature cells into circulation. A block in the production of erythropoietin and the equivalent leucocyte factor or interference with their sites of action by neoplastic disease, either in the bone marrow or at the primary site of the tumour, have been postulated.[3]

Another suggestion has been that stress or damage to bone marrow as a result of the infiltration leads to the evolution of areas of extramedullary haematopoiesis, and that the immature circulating cells are derived from these sites where the barriers which restrain the release of immature cells are not as effective as in the bone marrow.[4] However, the mechanism by which the foci might develop is not clear, especially when anaemia is slight, and it is again necessary to postulate tumour stimulus on the haematopoietic regulators.

The short answer to the question is that the mechanism is unknown.

REFERENCES

[1] Vaughan, J. M., *J. Path. Bact.*, 1936, 42, 541.
[2] Retief, F. P., *Lancet*, 1964, 1, 639.
[3] Hyman, G. A., *J. chron. Dis.*, 1963, 16, 645.
[4] Clifford, G. O., *Med. Clin. N. Amer.*, 1966, 50, 779.

Oral Contraceptives and Fertility

Q.—*For how long should a course of oral contraceptives be given to try to increase fertility, and which preparation would be best for this purpose?*

A.—Though there is some evidence that a "rebound phenomenon" occurs after discontinuing oral contraception and that some women are more likely to conceive, I know of no way of predicting in which patient it is likely to happen.

I assume that both partners have had full-scale infertility investigations and no abnormalities have been discovered in either. I would not, under these circumstances, use oral contraception to initiate a rebound phenomenon. If however anovulation has been demonstrated, treatment is best effected in suitable cases by the use of either clomiphene citrate or human pituitary gonadotrophin.

Subarachnoid Haemorrhage

Q.—*Is there any firm evidence of an association between subarachnoid haemorrhage and a chronic cough?*

A.—There is no evidence of any association in terms of pathology or aetiology between subarachnoid haemorrhage on the one hand and conditions causing chronic cough on the other.

It is plain that coughing causes increased pressure in the venous system which is in turn communicated to the intracranial venous sinuses, so that each cough causes a transient rise in intracranial pressure. This increased pressure is, however, venous, though it is communicated to the cerebrospinal fluid, and there is no convincing evidence that intra-arterial pressure is significantly raised during the act of coughing. In fact, repeated coughing may cause it to fall sharply, as in the syndrome of cough syncope.

These points are raised since it is apparent that there are many recorded instances in which subarachnoid haemorrhage has followed physical exertion or trauma of many kinds, but almost invariably the mechanism implicated has been one which would be expected to raise intra-arterial pressure. Despite this common association, most authors now believe that exertion simply precipitates rupture of an aneurysm or vascular malformation which was about to rupture spontaneously, since most subarachnoid haemorrhages occur during rest and many have been observed to begin during sleep.

There is no statistical relationship between intracranial aneurysm and angioma on the one hand and any lung disease on the other, though very rare instances of subarachnoid haemorrhage have been described as a complication of tuberculous meningitis resulting presumably from tuberculous arteritis in intracranial vessels, and equally rarely subarachnoid haemorrhage has been shown pathologically to be due to the presence of cerebral metastases from bronchial carcinoma.

Salk Vaccine as Booster

Q.—*Is oral poliomyelitis vaccine the best to give as a booster immunization in adolescents who were immunized with Salk vaccine in childhood?*

A.—Yes, it is the best. Whereas another injection of Salk vaccine would boost the poliomyelitis antibody titres, a similar effect is obtained by the administration of the oral vaccine. The oral vaccine also produces intestinal immunity to polioviruses and provides a more durable protection.

The main disadvantages of oral vaccine as a booster after a primary immunization course with Salk vaccine is that a single administration may not always be effective against all the three types of polioviruses. It is therefore desirable to give a second dose of oral vaccine not less than four weeks after the first.

Current Practice Books

"Treatment of Common Skin Diseases."—A paper-back book containing this series of articles, first published in the Current Practice section, is available from the Publishing Manager, B.M.A. House, Tavistock Square, London W.C.1. Price 10s.

Copies of *Obstetrics in General Practice*, price 30s., *Child Care*, price 30s., and *Health Centres and Group Practices*, price 3s. 6d., are still available through the Publishing Manager.

Book Reviews

Medical Virology

Modern Trends in Medical Virology—1. Edited by R. B. Heath, M.D., and A. P. Waterson, M.D., M.R.C.P. (Pp. 231+viii; illustrated. 65s.) London: Butterworth. 1967.

The "Modern Trends" series have been bringing us articles on recent developments in microbiology for some years, but this is the first of the series to be devoted to medical virology. The editors have chosen well in their ten authors from Great Britain, the United States, Sweden, and Germany, who have reviewed developments of the greatest interest in the subject.

Though many chapters and books have been written on the nucleic acids of viruses, few are as concise and well documented as Burke's contribution to this volume. Rott and Scholtissek have used the work on myxoviruses to review many of the concepts of virus cell interaction. In the chapters by Bauer on antiviral chemotherapy and Baron on host defences during virus infection it is significant that a quarter of the book is devoted to body defence by humoral and cellular mechanisms. Dudgeon has given a clear and up-to-the-minute review of the recent knowledge of rubella at the clinical and laboratory levels, and Morley has discussed the medical and economic aspects of measles immunization, especially in the developing countries.

In the last three or four years we have heard much about the 31 serotypes of adenoviruses, and it is useful to have their importance in diseases of the intestinal tract reviewed by Potter. It is equally important to read such an authoritative opinion on the relationship between cytomegaloviruses and herpes viruses as that of Plummer. The final chapter, on immunology of virus-induced tumours, covers a rapidly changing field and has been well summarized by Sjögren.

This is a very readable book that will have an interest to both the senior student and research worker. Though at the price few will consider it a necessary addition to their personal collection, no science library can afford to be without it.

F. T. PERKINS.

Growth of Thought

The Art of the Soluble. By P. B. Medawar, F.R.S. (Pp. 160. 25s.) London: Methuen. 1967.

This collection of six essays and addresses and two book reviews centres round the nature of scientific discoveries and the kind of men who make them. They are beautifully written in lucid, lively prose and display the penetrating insight and immense learning we should expect from their distinguished author.

The first, *D'Arcy Thompson and Growth and Form,* is a deeply appreciative and critical appraisal of a man and his work. It begins: "D'Arcy Wentworth Thompson was an aristocrat of learning whose intellectual endowments are not likely ever again to be combined within one man. He was a classicist of sufficient distinction to have become President of the Classical Associations of England and Wales and of Scotland; a mathematician good enough to have had an entirely mathematical paper accepted for publication by the Royal Society; and a naturalist who held important chairs for sixty-four years, that is, for all but the length of time into which we must nowadays squeeze the whole of our lives from birth until professional retirement. He was a famous conversationalist and lecturer (the two are often thought to go together, but seldom do), and the author of a work which, considered as literature, is the equal of anything of Pater's or Logan Pearsall Smith's in its complete mastery of the *bel canto* style. Add to all this that he was over six feet tall, with the build and carriage of a Viking and with the pride of bearing that comes from good looks known to be possessed."

The second, *Herbert Spencer and the Law of General Evolution,* contains this: "In our moods of abstract theorization we tend to forget how great and how diverse are the functional commitments of biological macromolecules. They insulate, they fill out; they fetch and carry; they prevent the Organism as a whole from falling apart or from dissolving in water; they prop up, they protect; they attack and defend; they store energy and catalyze its transfer; they store information and convey messages, and sometimes they themselves *are* messages. The successful prosecution of all these activities depends upon properties more complex, various and particular than can be written down in the language of energetics or information theory." It ends: "But for all that, I for one can still see Spencer's System as a great adventure, and now that I know my way about those thick, square volumes I do not feel I am taking leave of them for good."

Darwin's Illness. "Before I began I had no idea of what treasures of nonsense I should find in the psychoanalytical literature."

The Phenomenon of Man. "A good deal of Teilhard is nonsense, but on further reflection I see it as a dotty, euphoristic kind of nonsense, very greatly preferable to solemn long-faced germanic nonsense."

The Act of Creation. "Like other amateurs, Koestler finds it difficult to understand why scientists seem so often to shirk the study of really fundamental or challenging problems." "The real reason is so much simpler; the problem is very, very difficult." "No scientist is admired for failing in the attempt to solve problems that lie beyond his competence. The most he can hope for is the kindly contempt earned by the Utopian politician. If politics is the art of the possible, research is surely the art of the soluble. Both are immensely practical-minded affairs."

A Biological Retrospect. "However, if complacency is to be deplored, so also is humility. Humility is not a state of mind conducive to the advancement of learning. No one formula will satisfy that purpose, for there is no one kind of scientist; but a certain mixture of confidence and restless dissatisfaction will be an ingredient of most formulae. Confident we may surely be, for the next twenty-five years will throw up many new ideas as profound and astonishing as any I have yet described, namely . . . but I have no time left to tell you what they are."

Two Conceptions of Science. "My theme is popular misconceptions of scientific thought. I shall argue that the ideas of the educated lay public on the nature of scientific inquiry and the intellectual character of those who carry it out are in a state of dignified, but yet utter, confusion. Most of these misconceptions are harmless enough, but some are mischievous, and all help to estrange the sciences from the humanities and the so-called 'pure' sciences from the applied."

Hypothesis and Imagination. "We may collect and classify facts, we may marvel at curiosities and idly wonder what accounts for them, but the activity that is characteristically scientific begins with an explanatory conjecture which at once becomes the subject of an energetic critical analysis."

The questions asked in this book are simple, but they are never superficial and not often entirely solved. I hope it will have an influence similar to that of *Growth and Form*: "It is to be seen in anyone who, having read it, tries to write a little more clearly and with at least an attempt at grace; or who realizes, perhaps for the first time as he turns its pages, that science cannot be divided into what is up to date and what is merely of antiquarian interest, but is to be regarded as the product of a growth of thought."

GEORGE PICKERING.

Nocturnal Enuresis

A New Approach to Nocturnal Enuresis. By C. R. A. Martin, M.B., B.S.(Lond.), D.P.H., L.R.C.P., M.R.C.S., F.R.S.H., D.P.A., Inter.LL.B. (Pp. 149+viii; illustrated. £1 2s. 6d.) London: H. K. Lewis. 1966.

The author presents a comprehensive review of nocturnal enuresis based on a painstaking survey of several thousand schoolchildren from the Birmingham area. Medical examinations were carried out as a routine at 5–6 years (on school entrance), at 10–11 years (on leaving primary school), and at 14–15 years (on school-leaving), and provided suitable opportunity for inquiry. Interesting figures are given for primary and acquired enuresis in the two sexes at different ages and the apparent influence of social and domestic circumstances. The effect of physical and psychological factors is briefly discussed, and particular reference is made to the role of hypersomnia and nocturnal polyuria.

After outlining the pattern of the disability the author turns to the subject of treatment. This is considered in two parts, the former embracing what may be termed conventional methods, including training, wet-bed "buzzers," a variety of drugs, and psychotherapy, and a subsequent chapter devoted to nocturnal antidiuretics. The latter clearly represent a major interest, which indeed affords the main justification for the title of the book. Based on the premise that some cases of enuresis are caused by a reduced secretion of antidiuretic hormone by the pituitary, treatment with vasopressin was given to a small series of otherwise intractable children, with encouraging results. As the author points out, the indications and scope for such treatment are difficult to assess, since, although an excess of A.D.H. can be reliably measured, subnormal secretion cannot easily be defined. Nevertheless, if further studies confirm that sustained improvement occurs when treatment is prescribed purely on empirical grounds, a considerable advance will have been made in the management of this distressing disability for which many will be grateful.

The book should appeal to all practitioners and those in charge of paediatric clinics to whom such cases are referred.

J. D. Fergusson.

Calcium and Bone

Calcium Metabolism and Bone Disease. A Textbook for Students and Practitioners. By W. P. U. Jackson, M.A., M.D., F.R.C.P., D.C.H. (Pp. 134; illustrated. 30s.) London: Edward Arnold. 1967.

The declared purposes of this book are to show that the study of calcium metabolism and metabolic bone disease is not as difficult as usually imagined, and to provide a text suitable for both medical students and those specialists who are concerned with these subjects—namely the urologist, orthopaedic surgeon, and paediatrician. In order to achieve these objects Dr. Jackson has used the concise but informal style of the seminar. This has enabled him to pack a tremendous amount of up-to-date information into a small number of pages without loss of clarity and without degenerating into a mass of indigestible facts.

The main figures and radiographs are clear and helpful. For such advantages, however, a price has had to be paid, and it is inevitable that many dogmatic statements are made on matters which are still the subject of much debate by the experts. Furthermore, no references are given and therefore the book cannot be taken as an authoritative work for use by the expert in the field. It must be said, however, that with one or two exceptions, noted below, the statements made fairly represent the opinions of the majority of the experts at the present time; also there are suggestions for further reading at the end of each chapter. The book will therefore hold considerable appeal to those for whom it was intended and it can be highly recommended for them.

All of the common, as well as some of the rare, metabolic diseases are well described. There are many helpful hints which reflect the author's considerable experience in this field. A surprising omission is the failure to describe the radiological differences between the spines of osteoporosis and osteomalacia. Two curious departures from orthodoxy require comment. First the impression is given that hypercalcaemia is a more important factor in causation of renal calculi than is hypercalciuria. Secondly, it is rather misleading to suggest that 3 parts per million of fluoride in drinking-water is harmful, since higher levels are required before any abnormalities are visible to the naked eye. These are small points of detail, however, and they do not detract from the overall value of the book.

G. A. Rose.

Operative Surgery

Textbook on Operative Surgery. 3rd edition. By Eric L. Farquharson, M.D., F.R.C.S.Ed., F.R.C.S. (Pp. 951+viii; illustrated. £6 6s.) Edinburgh and London: E. & S. Livingstone. 1966.

This book is now appearing in its third edition, and this alone is an indication that there is still a considerable demand for the one-author, one-volume textbook on operative surgery written by a general surgeon. The author states that he has endeavoured to describe in detail and with adequate illustrations those operations which a junior in general surgery might be required to perform or in which he might assist. This is a heavy task but one in which the author seems to have succeeded.

The book has been brought up to date, and several sections have been rewritten. In general the illustrations are good and there are some excellent accounts of surgical anatomy where it is especially felt to be required. In treatment the author follows the standard teaching, but occasionally he expresses his own views if they do not coincide, and this increases the interest for the reader. Occasionally an operation now less commonly used appears to be given undue prominence, or one favoured by the reader receives brief mention. This can hardly be otherwise and does not detract from the fact that this is an excellent book for those who are learning their surgery.

E. G. Muir.

Science in Medicine

The Scientific Basis of Medicine. Annual Reviews. 1967. British Postgraduate Medical Federation. (Pp. 382+ix; illustrated. 40s.) London: Athlone Press. 1967.

This volume contains twenty review articles based on the weekly open lectures arranged by the British Postgraduate Medical Federation. They were delivered between October 1965 and March 1966 and constitute the fifteenth annual series.

Osler said, "As is your pathology so is your medicine," and nowhere is that better illustrated than in these fascinating vignettes of a wide range of problems in the science of disease. That there is such a thing as the "art of medicine" is undeniable, but it is increasingly clear that the quality of the prevention, diagnosis, and cure of disease is absolutely dependent on fundamental and applied science. A doctor without science is as useless as a mariner without navigation. Every act of therapy should be an experiment. Such is the clear message of those penetrating articles.

It is very appropriate that the opening review by Sir George Godber should survey in a masterly way the impact of scientific discovery on the pattern of medical care and the implications this has on the organization of our National Health Service.

Nearly half the reviews come under the broad classification of cellular biology, and deal with such topical subjects as the immunological reaction of the cell surface by R. R. A. Coombs and the role of the mycoplasmas in human disease by D. G. ff. Edward. The reviewer found the account of immunological sympathectomy by Eleanor Zaimis particularly interesting. She traces the steps in the discovery of the nerve growth factor which is produced by mesenchymal cells, and the further discovery that the factor is immunologically competent and its antisera can prevent the development of the adrenergic nervous system in rats. This opens up a wide range of studies which are enlarging knowledge of the sympathetic nerves in homoeostasis.

In the field of clinical science the account by J. P. Shillingford of the haemodynamic effects of acute myocardial infarction is of the utmost importance in relation to the control of this dangerous disease. These life-saving procedures provide an answer to those who are inclined to regard the use of the "cardiac catheter" as unjustifiable experimentation.

The few reviews mentioned are selected at random to show the uniform excellence of the whole series. All doctors still interested in their work should make a point of reading this volume.

W. Melville Arnott.

Temporal Lobe Epilepsy

Biological Factors in Temporal Lobe Epilepsy. Clinics in Developmental Medicine No. 22. By Christopher Ounsted, Janet Lindsay, and Ronald Norman. (Pp. 135; illustrated. 21s.) London: William Heinemann. 1966.

This monograph discusses the problem of "temporal lobe epilepsy" from a viewpoint different from most of the publications on this controversial subject. The authors have made a detailed study of 100 children suffering from this condition attending the Park Hospital for Children at Oxford. Some of these children were under observation before they developed temporal lobe seizures.

There is a detailed analysis of many aspects of these children—for example, family history, birth weight, the occurrence of febrile convulsions, the age of onset of temporal lobe seizures, etc. The chapters on "the hyperkinetic syndrome" and on "catastrophic rage" are particularly valuable, although these phenomena are not confined to children with temporal lobe attacks or indeed to children suffering from any type of epilepsy. The authors, supported by pathological study of several cases, place considerable emphasis on status epilepticus and severe febrile convulsions as a cause of damage to the hippocampus and amygdaloid nucleus with the subsequent development of temporal lobe epilepsy. They stress the importance of this post-epileptic encephalopathy and the urgent need to control intracranial infections in infants and febrile convulsions as quickly as possible.

This monograph is of real value and should interest everyone concerned with the pathogenesis of epilepsy.

J. W. ALDREN TURNER.

Disputed Aetiology of Lung Cancer

Occupational and Environmental Cancers of the Respiratory System. By W. C. Hueper. (Pp. 214+xi; illustrated. DM. 34.) Berlin, Heidelberg, and New York. Springer. 1966.

Dr. W. C. Hueper is a distinguished American authority on cancer in its various aspects, and his new book *Occupational and Environmental Cancers of the Respiratory System* will be unpopular with those who hold that almost the only cause of lung cancer is the smoking of cigarettes. He has assembled an impressive body of evidence which shows that the occupational and environmental causes are of equal if not more importance. He says that the role of the cigarette has been studied comprehensively by numerous investigators, whereas very modest efforts have been made to obtain pertinent information about the occupational and environmental carcinogens. These he claims have considerably more potency than cigarette smoke, but also have more prolonged and intense contact with large portions of the general population. This disproportionate attention to cigarettes has produced a distorted assessment of the relative significance of the various carcinogens, and has interfered with an effective approach to preventive measures against respiratory cancer hazards of all types.

That there are many occupational and environmental respiratory carcinogens is undoubted. Dr. Hueper divides them into three categories: recognized, suspected, and potential. The recognized carcinogens include the inorganic arsenicals, asbestos, chromates and chrome pigments, nickel, isopropyl oil, mustard gas, mineral oil, coal tar, and radioactive substances. The suspected group contains beryllium, benzidine, iron oxide, soot—that is, incomplete combustion products of carbon, petroleum, wood, and gas; the chemicals contained in gasoline and diesel engine exhausts, as well as the thermic tobacco derivatives. The potential respiratory carcinogens are those agents for which the incriminating evidence is predominantly restricted to observations made in experimental animals. This group includes carbamates, nitrosamines, isoniazid, carbon polymers, and the oxidized aliphatic and aromatic hydrocarbons generated in heated vegetable oils and animal fats and by photo-oxidation of evaporated gasoline.

Dr. Hueper says that existing epidemiological information about occupational lung cancer is restricted to data obtained from surveys of relatively small industrial operations with excessive respiratory cancer risks. No country possesses any large-scale and systematized information on the position in large industries where carcinogens are produced or handled and in which many thousands of people are employed. The large American industries of this type include the iron and steel industries, the power industry, petroleum industry, metal ore smelting and refining industries, metallurgical industries, chemical, rubber, and plastic industries, asbestos industry, transportation, shipping, railroad, and aviation, and also the paper and textile industries. Even when fragmentary epidemiological data do exist, they seldom cover the workers who have left the hazardous occupations. Rarely any attempt has been made to ascertain the number of occupational respiratory cancers which occurred before the discovery of a cancer risk in an industry. It is, he says, intriguing to speculate about the number of cases of lung cancer which were elicited in chromate workers in a plant which at the time of the discovery of the hazard showed a lung cancer frequency of 40 times the standard rate amongst white workers and 80 times amongst coloured workers, considering the fact that this plant had been engaged on the production of chromates for over five decades. " It is also provocative to contemplate the medical diagnosis of the cause of death for workers dying from a pulmonary complaint after being employed in an asbestos brake-lining factory, before it was found on post-mortem examination of such workers that 50% of those who came to autopsy with the diagnosis of asbestosis, were also suffering from cancer of the lung."

The information which Dr. Hueper has collected shows that lung cancer rates in various parts of the world vary according to social class and income-bracket, the poorer members of most communities being most affected and that the rates vary greatly between one occupation and another. Further, they are higher in urbanized than in agricultural communities. He comments that such fluctuations in the liability to lung cancer among such diverse groups cannot justly be attributed to differences in constitutional susceptibility to cancer. They can be ascribed, he thinks, only to quantitative and qualitative variations in exposure to environmental and occupational respiratory carcinogens, some of which are not yet identified. There is no evidence, he says, that such variations in lung cancer frequencies for different worker groups are in any way causally associated with demographic differences in cigarette-smoking habits. Again this factor is not responsible for the high incidence of lung cancer in women working in smoke-filled kitchens or inhaling smoke from braziers, such as Mexican women in Southern California or the Bantu women in South Africa.

He points out that air pollution containing respiratory carcinogens causes a shift of the incidence of lung cancer to earlier ages, and he cites figures showing the high liability to lung cancer of British immigrants to New Zealand, South Africa, and the United States. He regards the age shift of lung cancer to younger English people as the result of a progressively intensified exposure of the children of England to carcinogenic air pollutants.

Whether one agrees or not with Dr. Hueper's interpretation of the detailed information which he has collected, it cannot be denied that his book is an important one, and that he is justified in quoting with some disdain a recent comment by a high medical official of the United States Public Health Service that as regards lung cancer risks from cigarettes no more research is necessary for the establishment of the facts. Dr. Hueper clearly believes that the occupational and environmental causes are more important.

A. I. G. McLAUGHLIN.

Books Received

Review is not precluded by notice here of books recently received.

Drugs Affecting the Peripheral Nervous System. Vol. 1. Edited by Alfred Burger. (Pp. 620+xxiii. £11.) London: Edward Arnold. 1967.

Androgens, Virilization and the Hirsute Female. By Eugene J. Segre, M.D. (Pp. 102+xiv. $6.75.) Springfield, Illinois: Charles C. Thomas. 1967.

Medical Electronic Laboratory Equipment. Edited by G. W. A. Dummer, M.B.E., D.Eng., M.I.E.E., M.I.E.E.E., M.I.E.R.E., and J. Mackenzie Robertson. (Pp. 1035+xiv; illustrated. £10.) Oxford: Pergamon. 1967.

Continuously Under Review. A Study of the Management of Out-Patient Departments. By Rosemary Stewart and Janet Sleeman. (Pp. 70. 15s.) London: G. Bell. 1967.

Local Analgesia: Brachial Plexus. 4th edition. By Sir Robert Mackintosh and William W. Mushin. Illustrated by Miss M. McLarty. (Pp. 62; illustrated. 15s.) Edinburgh and London: E. & S. Livingstone. 1967.

Mental Illness. Progress and Prospects. By Robert H. Felix. (Pp. 110. 35s. 6d.) London: Columbia University Press. 1967.

Hypophysentumoren. Hypophysektomie. Klinik. Therapie. Ergebnisse. By Professor F. Mundinger and Professor T. Riechert. (Pp. 467+xi; illustrated. DM. 178.) Stuttgart: Georg Thieme. 1967.

Prognose und Behandlung der Skoliose. By Dr. Heinrich Scheier. (Pp. 149; illustrated. DM. 49.) Stuttgart: Georg Thieme. 1967.

Ergebnisse der Gesamten Lungen- und Tuberkuloseforschung. Volume 17. Edited by St. Engel, L. Heilmeyer, J. Hein, and E. Uehlinger. (Pp. 155; illustrated. DM. 59.) Stuttgart: Georg Thieme. 1967.

Human Radiation Cytogenetics. Edited by H. J. Evans, W. M. Court Brown, and A. S. McLean. (Pp. 218. 70s.) Amsterdam: North-Holland. 1967.

The Healing Art. A History of the Medical Society of New Jersey. By Fred B. Rogers, M.D., and A. Reasoner Sayre. (Pp. 346+ix; illustrated. $10.00.) New Jersey: The Medical Society of New Jersey. 1966.

Clinicopathological Conference

A Case of Diarrhoea and Goitre

DEMONSTRATED AT THE ROYAL POSTGRADUATE MEDICAL SCHOOL

Clinical History

Dr. C. L. Cope: The patient (Case No. 242467; P.M. No. 11630) to be considered today was a retired Greek-Cypriot government servant, born in 1898. His mother was still alive at the age of 89 but had an enlarged thyroid and a tendency to diarrhoea. His wife and three brothers were alive and well, but his father had died at the age of 61 with congestive heart failure.

The patient was first seen at Hammersmith Hospital in August 1960 when he was admitted for bilateral herniorrhaphy. He was in hospital for 14 days. His cervical spine was reported to be scoliotic but no mention was made of a goitre.

In November 1960 he was seen at Hammersmith Hospital as an outpatient because of a 10-year history of diarrhoea. He was noted to have a large nodule in the thyroid gland, which displaced the trachea to the left. It was considered clinically to be non-toxic. Barium follow-through and barium enema were normal except for a few diverticula in the colon. There was a long-standing story of mild dysuria, but his return to Cyprus prevented further investigations.

In March 1962 amoebiasis was diagnosed in Cyprus and he was treated with emetine and stovarsol. His stools were reported to contain pus and red cells and the cysts of *Entamoeba histolytica*. In spite of this treatment he continued to have three to eight motions each day.

In March 1963 he returned to England and in June of that year he was readmitted to Hammersmith Hospital.

His complaint was that he had lost 7 kg. weight in the past two years, that he was easily tired, and that his stools were watery and pale, though without blood and not bulky. There was no dysphagia and no symptoms of thyrotoxicosis. The goitre, he thought, had been present for about four years, but had shown no evident growth in the last two years. There had been no episodes of symptoms of cardiovascular abnormalities and no paraesthesiae, headaches, or attacks of pallor. There was no history of flushing.

On examination his weight was 53 kg. He had a dorsal kyphoscoliosis. There was no skin abnormality, and no fibromata or café-au-lait spots. His pulse was 100 and blood pressure 130/80 mm Hg. The sleeping pulse was at first 100, but this fell to 80 in a few days. There was a large, very firm, and grossly nodular goitre which displaced the trachea and tilted the thyroid cartilage. It was slightly tender in places and moved on swallowing. There was no stridor and no bruit, and no clinical suggestion of retrosternal extension. He showed a trace of fine finger tremor, but no eye signs. There were a few small shotty glands in both posterior triangles but none elsewhere in the neck. His heart was of normal size, but there was a systolic ejection murmur at the apex. Nothing abnormal was found in the abdomen.

Investigations

On investigation for causes of the diarrhoea the stools showed only occasional traces of occult blood. Culture for salmonella and shigella was negative, and no cysts of *E. histolytica* were seen on eight tests. Sigmoidoscopy was normal to 15 cm. Barium enema showed extensive spasm in the sigmoid colon, with many diverticula in the sigmoid and transverse colon. These may have been the cause of the traces of occult blood. Barium meal and follow-through showed diverticula in the second and third parts of the duodenum. There was rapid transit and the rectum was reached in just over three hours. An *x*-ray film of the chest showed the heart and lungs to be normal. *X*-rays of spine showed ankylosing spondylitis with dorsal scoliosis. The intravenous pyelogram showed the kidneys and renal excretion to be normal. There were two diverticula in a trabeculated bladder. The urine contained no pus cells, but grew *Escherichia coli* on culture.

The chronic diarrhoea had caused relatively little metabolic change. The E.S.R. was 16 mm./hour. The haemoglobin was 13.6 g./100 ml., the M.C.H.C. 31.5, and the W.B.C. 7,000/cu. mm. with a normal differential count. The serum level of vitamin B_{12} was 520 mμg./ml. The urea was 23 mg./100 ml., and the sodium 137, potassium 3.6, chloride 96, and bicarbonate 29 mEq/l.

The total proteins were 7.1 g./100 ml., with albumin 3.8 and globulin 3.3. The α_2 and β fractions were elevated. The calcium was 4.9 and phosphate 1.8 mEq/l. The alkaline phosphatase was 12 King–Armstrong units. The xylose absorption was 4.1 g. after a 25 g. dose (normal 5–8).

Thyroid function tests showed the B.M.R. to be −5%. The 48-hour radioactive iodine output in urine was 63% (normal 35–70), with T index of 3.1 (normal 2.8–13); the 48-hour neck uptake was 19% (normal >20%); 48-hour plasma protein bound ^{131}I was 0.17% (normal up to 0.3). These tests suggested a mild degree of hypothyroidism.

Treatment

Treatment included a therapeutic trial of emetine for one week followed by diodoquine 650 mg. t.d.s., with emetine bismuth iodide 200 mg. daily. This produced no evident improvement. Symptomatic treatment with probanthine and codeine phosphate controlled the diarrhoea. He was discharged on 2 August 1963 with only mild improvement and an uncertain diagnosis.

He was seen again in outpatients in September 1963, when he continued to complain of general weakness and lassitude. There had been no further weight loss, and his bowels were fairly well controlled by codeine phosphate and chlorpromazine. For the first time he was beginning to find swallowing difficult. He returned to Cyprus in the following month.

He again visited Britain in 1965 and was seen in outpatients. His dysphagia was worse and he now tended to cough after swallowing fluids. On examination the goitre did not appear very different from the state two years before, but he now had a large firm supraclavicular gland on the right side. This was a new feature and was suspicious of malignancy. He was therefore readmitted for the third time on 10 August 1965 for biopsy.

Readmission

On examination his weight had dropped to 45 kg. The thyroid was now fixed on swallowing. There was no stridor and no bruit. There were distended veins over the goitre and the veins of his right arm were also distended. The vocal cords moved normally. The jugular venous pressure was not raised. The pulse was regular at 90–100, and the blood pressure was 120/70 mm. Hg. There were bilateral basal crepitations, and the liver edge could be felt 3 cm. below the costal margin.

The most important investigation was the lymph node biopsy. This showed medullary carcinoma of the thyroid gland with hyaline deposits.

X-ray of the chest showed an enlarging goitre mass extending through the thoracic inlet into the mediastinum. The spine showed severe ankylosing spondylitis, but *x*-ray of hands showed normal bone texture. The E.C.G. showed what were described as minimal non-specific abnormalities.

Culture of the urine produced a heavy growth of *E. coli* resistant to sulphonamide but sensitive to ampicillin.

Thyroid studies showed a neck uptake of 26% at 24 hours. The 48-hour urine excretion of ^{131}I was 59.8% with a T index of 4. A scan showed a particularly poor uptake on the right side of the gland.

The haemoglobin was 13.8 g./100 ml., the M.C.H.C. 31, and the W.B.C. 7,000 with normal differential. The blood urea was 12 mg./100 ml., the sodium 140, potassium 3.5, chloride 97, and bicarbonate 33 mEq/l. The serum bilirubin was 0.5 mg./100 ml., the thymol turbidity 3 units, zinc sulphate 7, and alkaline phosphatase 9 units. The acid phosphatase was 2.3 K.A. units with 0.3 tartrate labile. The lactic dehydrogenase was 135 units with 44% heat stable. The prothrombin time was 13 seconds. The serum calcium was 5.1 and phosphate 2.0 mEq/l.

The excretion of urinary 17-oxosteroids was 5.0 mg. daily and of 17-oxogenic steroids 5.5–9.5 mg. The urinary excretion of 5-hydroxy indole acetic acid was normal, and of vanillyl mandelic acid 4 µg./mg. of creatinine, a figure regarded as the upper limit of the normal range. Calcium excretion in the urine was 320 mg. daily and the output of indoles was 35 mg./24 hours (a normal figure). A glucose tolerance test showed a moderately diabetic curve with a high renal threshold. The stools still contained no pathogenic organisms and faecal fats were 4.4 g./24 hours.

Treatment

Treatment consisted in a course of deep *x*-ray therapy although the tumour was known to be rather insensitive. At first the dysphagia was aggravated, but later it improved. He was discharged on 15 October 1965.

By December 1965 the jugular vein was less obstructed. There was no further loss of weight, but the diarrhoea now needed larger doses of codeine for control. A trial course of neomycin gave no improvement in the diarrhoea. He again paid a visit to Cyprus.

His fourth and final admission to Hammersmith Hospital was on 29 March 1966. The malaise and weakness were more marked and the dysphagia was worse. He aspirated a lot of fluids. His speech was rather rambling, but he complained that something in his abdomen was making him short of breath. He was found to have pneumonia of the right lower and middle lobes. His liver was enlarged 7 cm. and had an irregular edge. The blood pressure was 95/60 mm. Hg. In spite of treatment with antibiotics he deteriorated rapidly and died two days after admission.

Clinical Diagnoses

(1) Medullary carcinoma of the thyroid.

(2) Secondaries in lymph glands and liver.

(3) Terminal right lobar pneumonia.

(4) Ankylosing spondylitis.

(5) Diverticulosis in duodenum, colon, bladder, and pharynx.

(6) Mild diabetes mellitus.

Post-mortem Findings

Dr. E. D. WILLIAMS: The necropsy on this thin elderly male was carried out 12 hours after death. No mucocutaneous tumours were present.

The most interesting findings were in the endocrine system. The right lobe of the *thyroid* (Fig. 1) was uniformly enlarged to form a smooth solid mass, 8×4.5×4.5 cm., with a variegated red-brown cut surface. Microscopy showed that this was a medullary carcinoma (Fig. 2), largely the spindle cell variant, with abundant amyloid deposition and focal calcification within amyloid (Fig. 3). In some areas the tumour was more anaplastic, forming ill-defined round masses of tumour cells, with many vacuoles but little or no amyloid; in these areas it resembled the tumour found in the cervical lymph node biopsy. Secondary deposits of medullary carcinoma were found in the cervical lymph nodes, a matted mass of nodes in the upper mediastinum, the pleura, throughout the grossly enlarged liver, and in the vertebral marrow. The left lobe of the thyroid was small, with a single small white nodule (0.4 cm. diameter) (Fig. 4) which proved to be a medullary carcinoma with abundant amyloid. In view of the scarcity of amyloid in the secondary deposits elsewhere, the solitary nature of this nodule, and the previously reported instances of bilateral medullary carcinoma, it was considered that this was a second primary tumour. Two normal parathyroids were found. The pancreas was rather autolysed, but the islets appeared normal. Both adrenals were enlarged (Fig. 5); the left (14 g.) contained a central soft rounded brown tumour (2.5 cm. diameter). The right adrenal (9 g.) showed a central collapsed partly cystic tumour (1.5×1 cm.). Both on microscopy were benign phaeochromocytomas (Fig 6), the right one being largely degenerate but also containing a small secondary deposit of medullary carcinoma.

In the *alimentary tract* the duodenal and colonic diverticula were confirmed; the villi had lost their epithelium but were not flattened. The intestinal nerve plexuses were normal.

The only significant abnormal finding in the urogenital tract was in the bladder. This showed two diverticula, and on section the muscle in places formed whorls and nodules in an abnormal growth pattern.

In the *respiratory tract* the trachea was deviated to the left, and both lungs were moderately overweight. Widespread large and small pulmonary emboli were present, with scattered infarcts, but no significant infection was found.

The *skeletal system* showed bony ankylosis of cervical dorsal and lumbar vertebrae.

There were no relevant findings in the *cardiovascular system,* nor, apart from secondary carcinoma, in the *reticuloendothelial system.* The *central nervous system* could not be examined, because necropsy permission was limited.

Pathologist's Diagnosis

(1) Bilateral primary medullary carcinoma of thyroid, with widespread secondary deposits.

(2) Bilateral phaeochromocytomas of adrenals.

(3) Diverticula of intestinal tract and bladder.

(4) Massive pulmonary emboli.

(5) Ankylosing spondylitis.

Discussion

Dr. COPE: This is a fascinating case. So far as I can gather the medullary carcinoma of the thyroid is a form which has been recognized only in the last 10 years. We did not diagnose it, except in so far as we called for a biopsy. Dr. Williams diagnosed it, and he is our expert on this disorder; we hope

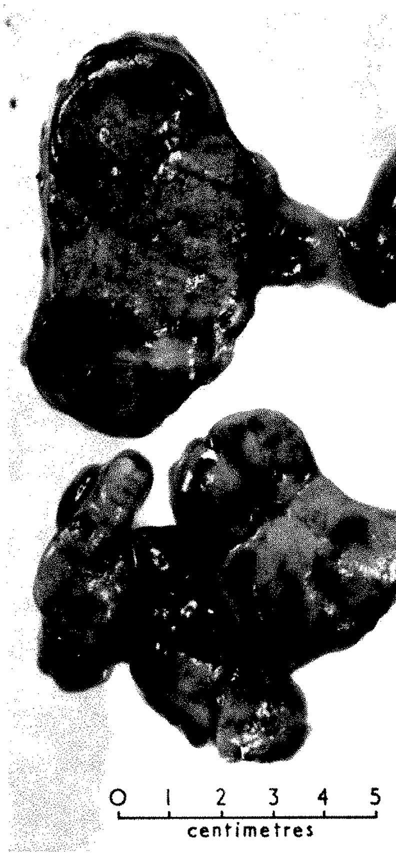


FIG. 1

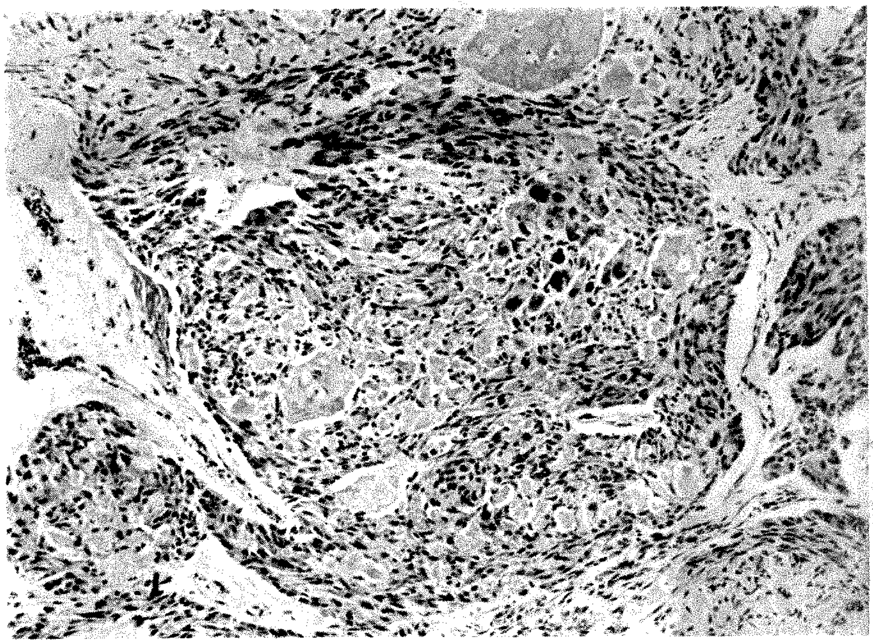


FIG. 2

FIG. 1.—Thyroid, with right lobe transected to show a massive well-circumscribed tumour, and mediastinal lymph nodes also replaced by tumour.

FIG. 2.—Medullary carcinoma of right lobe of thyroid. Note the abundant amyloid deposition. (H. and E. ×105.)

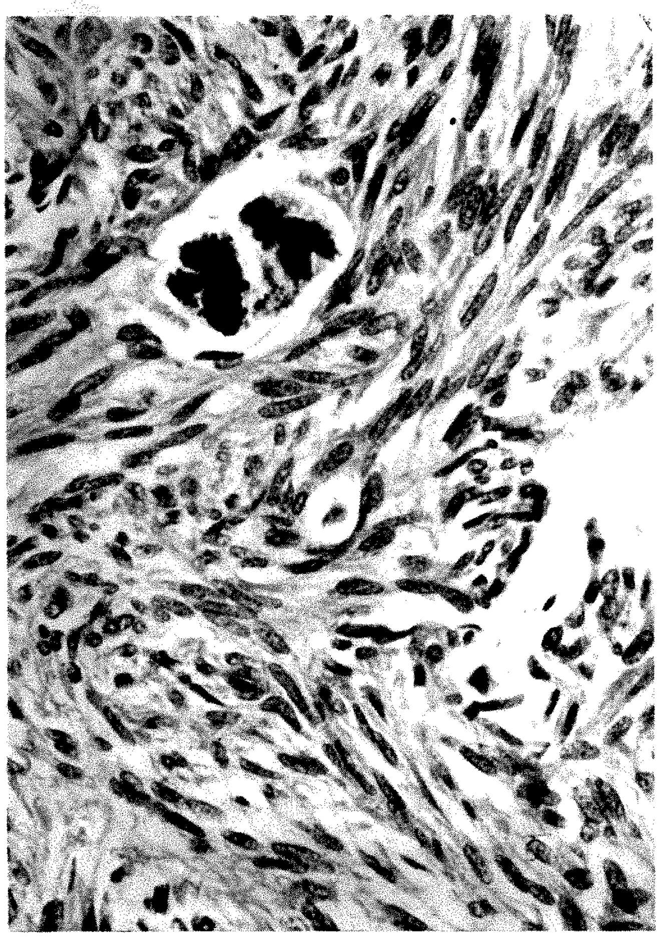


FIG. 3.—High-power view of the same tumour. The dark granular material is calcification within a deposit of amyloid. The carcinoma shows predominantly a spindle-cell pattern. (H. and E. ×440.)

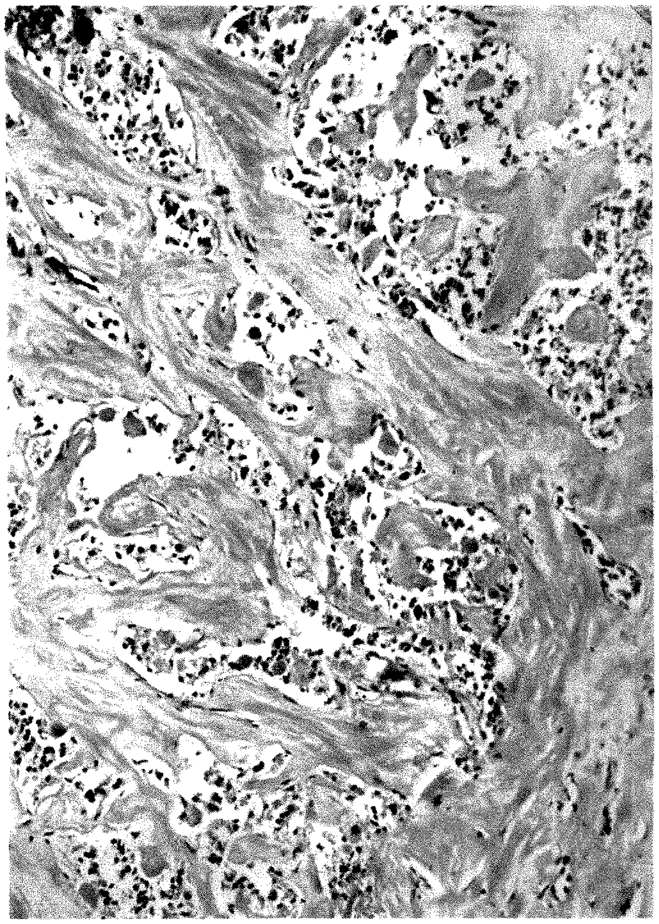


FIG. 4.—Tumour from left lobe of thyroid. This is also a medullary carcinoma with abundant stromal amyloid, and is probably a second primary tumour. (H. and E. ×110.)

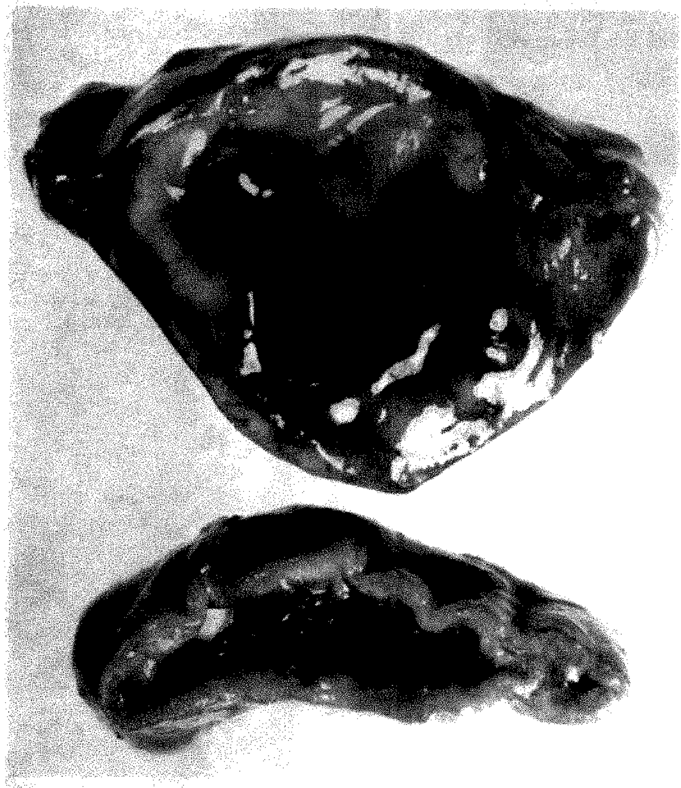


FIG. 5.—Both adrenals bisected to show bilateral phaeochromocytomas. (×3.3.)

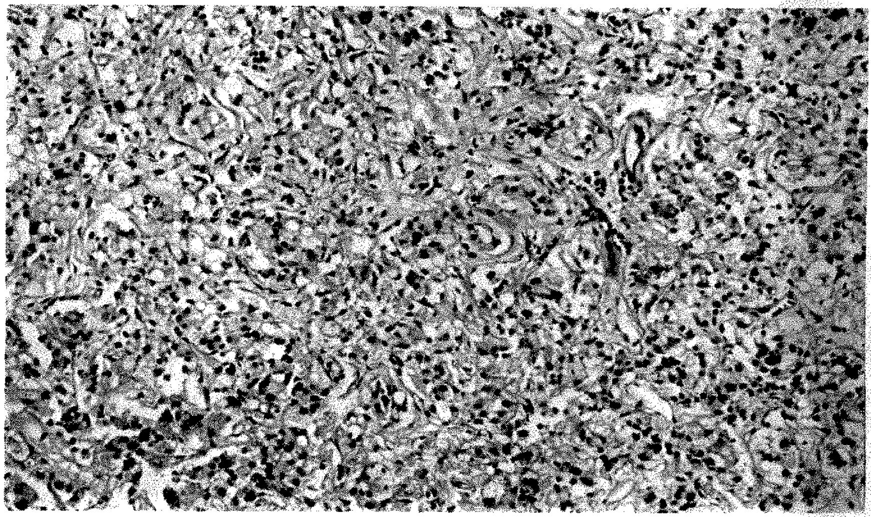


FIG. 6.—Phaeochromocytoma of left adrenal. The tumour shows the typical packeted arrangement of regular large cells with abundant granular cytoplasm. (H and E. ×105.)

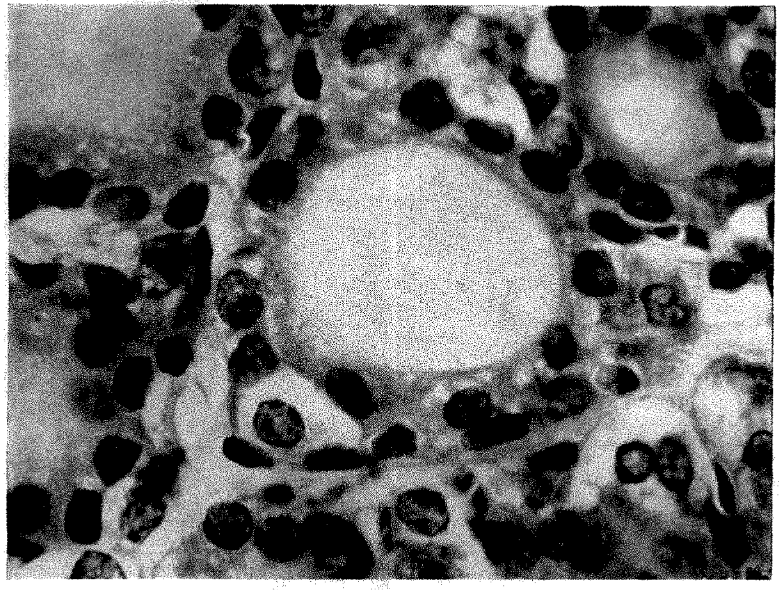


FIG. 7.—High-power view of a thyroid from an aged rat. The parafollicular cell is seen as a cell with pale cytoplasm separated from the colloid by the darker cytoplasm of the follicular cells. (H. and E. ×910.)

to hear a lot more about it from him in due course. We diagnosed the presence of malignancy clinically by two of the classical criteria, increasing dysphagia, and the appearance of a lymph node which was an obvious metastasis.

Cause of Diarrhoea

We did not, however, realize there was any link between this medullary carcinoma and the symptom of persistent diarrhoea. The association between medullary carcinoma and persistent diarrhoea is, I believe, a discovery made by Dr. Williams himself. Certainly we found no other cause for it; I do not think for a minute the diverticula were an adequate cause—there was no infection, and there was very rarely any occult blood. There was no other local cause, and I think Dr. Williams must be perfectly right in suggesting that there was a humoral cause for this intestinal hurry, which the patient undoubtedly had right through to the colon. At no time did we as clinicians consider a phaeochromocytoma, and even in retrospect there was no evidence of it. He never had any cardiovascular episodes, any episodes of paraesthesia, of pallor, of headaches, of paroxysms of hypertension, and never was any raised blood pressure recorded, so far as I am aware. The vanillyl mandelic acid test, which was done after we knew the diagnosis at the suggestion of Dr. Williams, was at the upper limit of normal, but not high enough to give us any real clue. Some of you may have seen the very opportune paper in the *British Medical Journal*[1] about this particular association of medullary carcinoma with phaeochromocytomas and its familial incidence. It is interesting that this particular patient had a mother who, when we last heard, was still alive at the age of 89 but had an enlarged thyroid and had complained of diarrhoea for many years of her life. Obviously it was not a death-dealing disorder in her case. The wife and three brothers were alive and they were all well. The patient's father had died at the age of 61 with what was described as congestive cardiac failure. One can only speculate whether that was in any way related to a phaeochromocytoma. We do not even know if he had a goitre. There are many points of interest here, the thyroid aspects, the reasons for the diarrhoea, and the question of diverticula as a possible alternative cause for the diarrhoea.

Diarrhoea and Thyroid Tumours

Dr. Williams: The relationship between the thyroid and the diarrhoea is based on a study of a large number of cases which I collected together with Professor Doniach and Dr. Brown from various London hospitals; we collected them mainly to look at the pathology of this type of tumour. In going through the records it became apparent that a surprisingly large number of them showed diarrhoea. The diarrhoea correlated with the extent of the tumour, in that very few patients with tumour localized to the neck had diarrhoea, and a very high proportion of patients with widespread tumour had diarrhoea. Also, in four patients there was evidence that when the tumour was resected the diarrhoea improved, in two of them to recur again when the widespread tumour recurred. Putting these observations together it seems likely that there was a humoral factor linking the tumour with the diarrhoea. The other points which made this a likely possibility are the resemblance that this tumour bears to certain other hormone-secreting tumours like carcinoids. This resemblance is both histological and histogenetic, as there is evidence to suggest that this tumour does not arise from the ordinary follicular cells of the thyroid but from a second type of thyroid cell, the parafollicular cell. This cell has a number of different possible functions, among them the production of calcitonin; in the sheep this cell has been shown to contain 5-hydroxytryptamine (5 H.T.).

We therefore have a tumour of a cell which is potentially capable of making 5 H.T., and which is likely to have a humoral function unrelated to thyroxin. The nature of the humoral factor leading to diarrhoea is another point. Despite the fact that this tumour may occasionally make 5 H.T., this does not seem to be the cause of the diarrhoea. Slightly increased 5-hydroxyindolacetic acid excretion was found in two out of the seven cases where we've had a chance of testing urine. In one case we found a raised level of kallikrein in the tumour. Kallikrein is the enzyme secreted by carcinoids which releases small chain polypeptides from their precursor kininogen, an alpha-2 globulin. We have since failed to find kallikrein in several other tumours, so I think there must be some other factor, and we are now investigating various other possibilities.

Professor C. Booth: What about calcitonin? If this tumour is derived from the cells which secrete calcitonin, why doesn't this tumour secrete calcitonin?

Function of Thyroid Cells

Dr. I. McIntyre: May I comment here? The thyroid is really two separate endocrine glands: the A cells, secreting the iodothyronins; and the C cells, which normally secrete calcitonin. This is reasonably well established now, both biochemically and immunochemically. Now, I would like to ask Dr. Williams whether he thinks this tumour arises from a third cell type within the thyroid, or whether he thinks it arises from the C cells. I think it's better to use the term "C cells" for the calcitonin-producing cells, because they cannot be described simply as parafollicular, as their position varies from species to species.

Dr. Williams: That question is best answered by reference to a photomicrograph of thyroid tissue (Fig. 7). This is a high-power view of a rat thyroid gland. It shows the follicles full of colloid and lined by follicular cells. In the centre is a second type of cell with a clear cytoplasm. The follicular cells link together to separate this clear cell from the colloid, and I think that should immediately make one suspect that its function is unrelated to the production of colloid or thyroxin. In the sheep these cells have been shown to contain 5 H.T., while in other animals the cells with a similar morphological position have been shown to contain calcitonin. Now, to answer Dr. McIntyre's comment. We can compare the thyroid to the pancreas. In some species of fish the islet cells line the ducts between the duct epithelium and the basement membrane, whereas in mammals they form the distinct cell groups known as the islets of Langerhans. Similarly in some species, for example the rat, the second type of thyroid epithelial cells lie between the follicular cell and the basement membrane, while in others, particularly the dog, they form "thyroid islets" of solid cells lying between the follicles. These cells may have a variety of different functions. Two of the functions that are known are that in some animals they can make 5 H.T., and that in others some at least of the cells can make calcitonin and therefore can be known as C cells. A C cell is defined in terms of production of calcitonin. Maybe there are several different types of epithelial cell in the thyroid apart from the follicular cell. I don't think at present we really have enough evidence to answer the question of whether there is a cell type for each hormone produced.

Dr. I. Gilliland: Are they necessarily homogenous cells, these "islets of Williams"? Even morphologically they differ from one place to another.

Dr. Williams: I prefer to let Professor Pearse answer that question.

Hypercalcitonaemia

Dr. Cope: May I ask Dr. McIntyre if it is yet known what the symptoms are of hypercalcitonaemia, and whether we may not perhaps be missing the world's first calcitonin-producing tumour?

Dr. McINTYRE: Unfortunately we can't measure calcitonin in serum. I think one would predict that the symptoms would be impaired resorption of bone and would be rather similar to the kind of picture which one might see in marble bone disease. Dr. Doyle and Dr. Foster showed that if calcitonin is given to animals for long periods the equivalent of "rugger jersey" spine is produced. So the long-continued over-secretion of calcitonin might produce impaired resorption of bone with "rugger jersey" spine and osteopetrosis. With a short history like this I don't think one would be able to detect bony changes. We need a means of measuring calcitonin in the blood.

Professor BOOTH: You don't think the calcification that Dr. Williams showed us in the amyloid tissue or in the ligaments in relation to the ankylosing spondylitis could have anything to do with this?

Dr. McINTYRE: I think it could, Professor Booth, but we just don't know.

Dr. WILLIAMS: If there was calcitonin production by the tumour would one not expect parathyroid hyperplasia secondary to this? I have seen one case of medullary carcinoma which at necropsy had unexplained parathyroid hyperplasia.

Thyroid C Cells

Professor BOOTH: Professor Pearse, have you anything further to add on the C cells?

Professor A. G. E. PEARSE: They have a number of characteristics, over a wide variety of species or genera, and in no single case are all the characteristics present. The electron-microscopic appearance is the one which is most uniform, and they can be seen very easily in electron micrographs of rat thyroid. The problem is to find C cells in the human thyroid. The classical method of showing them is by the Cajal silver stain which was used by Nonidez in 1931. The cells were first seen by E. C. Baber, who was an ear, nose, and throat surgeon in Brighton. He described them in 1877, and they should be called Baber cells if you use a name at all. A second method of showing them works in every animal in which I have tried it, but I have not tried it in man. This is because it is necessary to inject an amine-precursor, such as 5-hydroxytryptophan (5 H.T.P.). This is taken up and converted by the C cells to 5 H.T. Normally the cells don't manufacture 5 H.T., so I must take exception to Dr. Williams's statement on that point. There is no evidence that they manufacture it, only that they will if you give them a chance. C cells which have taken up 5 H.T.P. and converted it to 5 H.T. can be shown by the so-called fluorescent amine technique. One cannot ethically give a human being a large dose of 5 H.T.P. in order to show the C cells. However, one can do it with radioactive 5-H.T.P.; an easier way of doing it, perhaps. Only in the sheep and perhaps the horse are the C cells known to have 5 H.T. in them normally. There is one further method of showing them up. In many animals they contain high levels of α-glycerophosphate dehydrogenase. With a fluorescent antibody technique, using anti-pig calcitonin, the C cells of the pig and also of the dog show the fluorescent label. This indicates that calcitonin is stored in the C cells (C for calcitonin).

Professor BOOTH: Are they specific medullary cells, or do all medullary cells show this?

Professor PEARSE: We don't use this term except in the case of the human carcinoma. There are specifically interfollicular cells, but in most animals, as you've heard, they are part of the follicle wall. Not every cell that is interfollicular is a C cell; there are other cell types between the follicles, some of which might form a tumour.

Dr. COPE: Does a medullary carcinoma take up this particular antibody?

Professor PEARSE: We have never tried it—we haven't got enough to waste on human cases. In the normal human thyroid it is very difficult to find any C cells, even with the α-glycerophosphate dehydrogenase technique. I believe, although the article in the *B.M.J.*[1] said that these cells could not be detected in the human thyroid, that, in fact, they can be.

Professor BOOTH: What we've got, then, are some cells which may produce calcitonin, and Dr. Williams believes these cells are the origin of this tumour. We've now got to ask what the relation is between this tumour and the tumour of the adrenal.

Relationship to Adrenal Tumour

Dr. WILLIAMS: Perhaps I should comment on that. Firstly, there is no doubt there is a relationship. I now know of 40 cases, either seen by myself or published, of carcinoma of the thyroid and phaeochromocytoma. In 30 of these the tumour of the thyroid is a medullary carcinoma, and in three of the others the description leaves very little doubt that it was a medullary carcinoma—that leaves only seven, and none of those seven was described as clearly a papillary carcinoma of the thyroid, which is the commonest type. So I think there is no doubt that there is a specific relationship between the two. Secondly, the phaeochromocytomas are commonly bilateral, and commonly the whole syndrome is familial, as the article by Ljungberg and his colleagues[1] illustrates. Now, one of the explanations put forward is inheritance of a pleotropic gene of incomplete penetrance—which I think I am right in saying is an explanation that will explain almost anything. I am not saying it's not true, but I don't see how one could possibly prove it. The thyroid carcinoma also seems on occasions to be bilateral, so I suppose that the genetic explanation is the most likely one. Why tumours of thyroid and adrenal medulla should occur together is much more difficult to explain. The only analogy is the multiple endocrine adenoma syndrome, in which tumours of pituitary, parathyroid, pancreatic islet, and adrenal cortex occur. This certainly is familial, and maybe there is a growth factor that controls all these endocrines. If that is the case one has to postulate a second growth factor that controls the parafollicular cells in the thyroid, the adrenal medulla, and possibly also controls the growth of some of the autonomic nervous system. In a small proportion of cases with carcinoma of the thyroid and phaeochromocytoma a wide variety of autonomic abnormalities is also found: ganglioneuromatosis of the whole intestinal tract, also described in the bladder and the bronchus, and small mucosal neuromas of the eyelids, lips, and tongue. It is possible that there is a single factor controlling the growth of all these different tissues. We know now that there is a nerve growth factor, described by Levi Montalcini, that controls the growth of some nerves, and she has also found a skin growth factor. Thus it may be that there is an endocrine growth factor which is responsible either for the typical multiple endocrine adenoma syndrome or for this second type of syndrome with medullary carcinoma, phaeochromocytoma, and sometimes other neural abnormalities.

Professor BOOTH: Can we just get one thing clear—these are not overlapping syndromes—you're using the polyglandular one as a comparison.

Dr. WILLIAMS: I'm using the multiple endocrine adenoma syndrome as a comparison. To the best of my knowledge even in the more comprehensive studies of many families with the multiple endocrine adenoma syndrome phaeochromocytoma has never been recorded. To be absolutely honest even if confusing, there is an overlap in that parathyroid adenoma has been described in both. Four cases of medullary carcinoma of the thyroid and parathyroid adenoma have been recorded.

Clinical Course

Dr. COPE: I was just going to ask Dr. Williams whether in the light of his survey of these cases, and his peculiar knowledge of them, he could comment on the clinical course of these goitres. They are surprisingly slow growing for thyroid carcinomas generally, are they not?

Dr. WILLIAMS: There is a very great variability in prognosis. With some patients the survival is only a year or two, while the longest survivor that we've had in our series was 21 years. This patient was a man who died at the age of 42 who had had a thyroidectomy when he was 21. However, he had had a goitre before that, according to various reports either since birth or at least since the age of 8. With a tumour of the thyroid which is originating from a different cell type, it's not so surprising to find a spectrum of malignancy within that group of tumours—either relatively benign ones or relatively malignant ones.

Dr. GILLILAND: This must have been a most unusual man—there is a reference to his "having something in his abdomen makes him short of breath"—are these not hypertensive attacks he's having, or high blood pressure?

Dr. COPE: No, the blood pressure was never raised—I didn't see the point in giving innumerable figures. This "something in his abdomen making him short of breath" was in the last two or three days only. But he had a very large liver and he had two phaeochromocytomas. Maybe he knew he had one or the other.

Dr. GILLILAND: I am showing a case quite shortly—with Professor Welbourne—who had paroxysms only in the evening; this was missed for two years while she was in hospital because the attacks were never noticed during the day.

Dr. WILLIAMS: The phaeochromocytoma does not have to function, does it? A proportion of these patients can presumably go all through life and never have any symptoms at all.

Dr. GILLILAND: This patient, however, had a mild diabetes.

Professor J. GOODWIN: The diabetes and the diarrhoea might have been due to the phaeochromocytoma, might they not? I don't know quite why you attribute the diarrhoea necessarily to the carcinoma.

Dr. WILLIAMS: Because in a number of cases of diarrhoea and medullary carcinoma no phaeochromocytoma was found at necropsy. Also because the diarrhoea improved in some cases after resection of medullary carcinoma. I agree that phaeochromocytoma may occasionally present with extreme diarrhoea, but the link there is also humoral and unexplained so far as I'm concerned.

Professor GOODWIN: I think the "something in his abdomen making him short of breath" was pulmonary embolism.

We are grateful to Professor J. P. Shillingford and Dr. E. D. Williams for assistance in preparing this report, and to Mr. W. Brackenbury for the photomicrographs.

REFERENCE

[1] Ljungberg, O., Cederquist, E., and Von Studnitz, W., 1967, *Brit. med. J.*, 1, 279.

NEW APPLIANCES

New Urinary Diversion Appliance

Mr. H. B. ECKSTEIN, consultant surgeon, Queen Mary's Hospital for Children, Carshalton, Surrey, writes: With the rapidly increasing number of children surviving with myelomeningocele and hydrocephalus, the problem of urinary incontinence, and therefore urinary diversion, in childhood is becoming more important. Though a wide range of appliances are available for these patients, there is at present no completely satisfactory appliance.

The important features of an appliance for a urinary diversion either by an ileal conduit or by cutaneous ureterostomy are that it should be easy to apply and be easily cleanable and sterilizable; but since rubber bags cannot be cleaned properly and certainly cannot be sterilized adequately they should be either disposable or semi-disposable. It is impossible to clean and sterilize the outlet tap of the bag, and this should therefore not come in contact with the urine. The bag should contain a one-way valve to prevent reflux of urine on to and into the stoma when the patient is lying down.

With these basic conceptions in mind we have designed an appliance with plastic bags fitted with a slit valve and an external tap which will fulfil these criteria. We have tried these bags out on a number of children with considerable success. This appliance is manufactured by Eschmann Bros. & Walsh Ltd. and is now available through all appliance suppliers. While it may not be suitable for every single child, it is certainly an improvement on previously available models. The appliance is illustrated in Figs. 1-3 and is supplied initially in a basic set with replacement bags and flanges which are prescribable on E.C.10 forms.

It is marketed as the "Carshalton Appliance," and fitting instructions are enclosed with each set. Encrustation of the stoma, a common complication of uretero-ileostomies in children, has been virtually eliminated by the use of a disposable bag.

I should like to express my thanks to my colleagues for their helpful criticisms and advice and to Mr. Peter Steer, of Eschmann Bros., for his patience and help in making the many modifications to produce the final product.

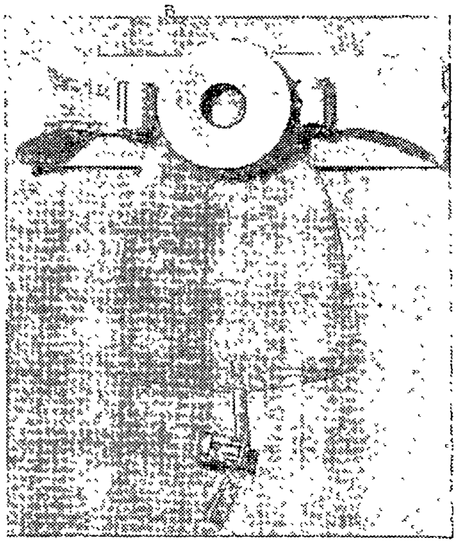


FIG. 2.—Assembled appliance.

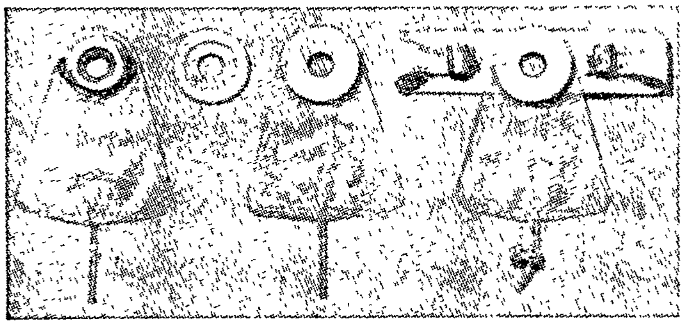


FIG. 1.—Different parts in assembly of appliance.

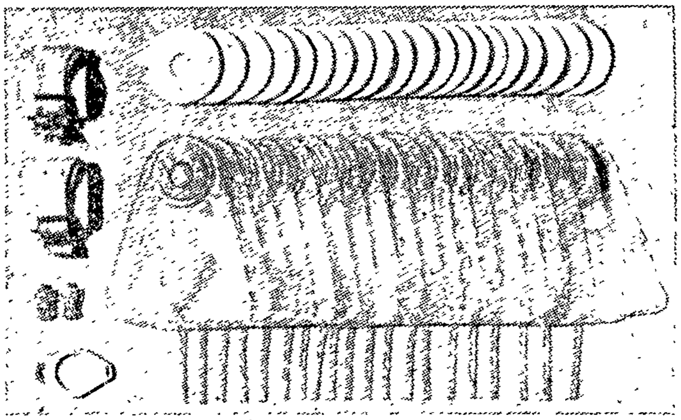


FIG. 3.—Contents of basic set. (Replacement set contains bags and adhesive flanges only.)

Middle Articles

HOSPITAL TOPICS

Organization of a Coronary Care Unit in a General Hospital

B. L. PENTECOST,* M.D., M.R.C.P.; N. MAYNE,† M.D., M.R.C.P.; PATRICIA LAMB,‡ S.R.N.

Brit. med. J., 1967, 3, 298–300

The current interest in intensive care units for patients with myocardial infarction centres on the fact that many die not of extensive myocardial damage but of potentially reversible arrhythmias. In recent years techniques of cardiac resuscitation have advanced considerably. Most nursing and medical staff are familiar with external cardiac massage and artificial ventilation, and many hospitals are in possession of some form of external defibrillator. The purpose of an intensive care area is simply to bring all patients at risk together in an adequately equipped ward unit and to provide the optimum facilities for early detection and treatment of complications after myocardial infarction. If the coronary care unit is to make any impact on the national mortality from myocardial infarction it must be adapted to the needs, and means, of the busy general hospital. The requirements of such a unit differ from those of an ordinary intensive care unit and do not appear to have been discussed in relation to the district hospital.

The General Hospital, Birmingham, admits approximately 250 patients a year with acute myocardial infarction. The coronary care unit must, however, be prepared to admit at least 300 patients a year, because many are admitted on suspicion of having sustained myocardial infarction and the diagnosis is subsequently not proved. A coronary care unit was opened in October 1966, and this paper discusses some of the problems of organizing and equipping such a unit in a general hospital.

Site and Structure

It is important for the coronary care unit to be as self-contained as possible; an independent unit in terms of both staff and any ancillary services which may be required urgently—for example, radiological screening and acid–base determinations. To nurse patients with myocardial infarction within an ordinary intensive care unit is unsatisfactory. They require a calm atmosphere and reassurance and would suffer considerable anxiety in such surroundings. However, it would seem that there may be a great advantage, in terms of sharing equipment and skilled staff, in the juxtaposition of these two forms of unit. We decided against partitioning off a section of a general ward as a coronary care unit. It is difficult to maintain constant vigilance on one group of patients in a busy ward, and, though complex electronic monitoring equipment may to some extent replace the nurse's powers of observation, warning signals are of no avail in the absence of staff immediately free to render assistance. In addition, we have found that when patients are singled out for close observation in a general ward, particularly when attached to an oscilloscope, they feel insecure and apprehensive. Conversely, in a small ward where such techniques of observation are seen to be applied universally the individual does not feel that he is particularly at risk.

A ward day-room was finally selected. It measures 560 sq. ft. (52 sq. m.) and accommodates five beds arranged radially. A larger area would confer greater freedom of access to the beds, particularly after an arrest when several staff and bulky equipment surround the patient, and would allow construction of cubicles with rigid partitions. There is, however, then some risk of losing the intimate contact with the patient which a small open ward confers, and monitoring equipment needs to be more elaborate. At present beds can be partitioned off with curtains, and one recessed area is set aside primarily as a resuscitative area, though resuscitation may be carried out on any of the five beds.

Sphygmomanometers are wall-mounted behind each bed beside a notice-board for the display of blood pressure charts and other clinical data. Oxygen is piped to the ward from the main hospital supply. Piped suction is not available and a portable sucker is stored in the unit. A liberal supply of power points is vital in view of the amount of electrically powered equipment. Some thought needs to be given to the placing of power points and cable lengths in order that the equipment is available to all parts of the unit.

The nursing station is simply a desk where notes may be written and nursing intructions given. There is no sister's office, so that the nurses are constantly in the ward. At night a nurse sitting at the desk may see all five patients and their attendant oscilloscopes.

The position of the coronary care unit within the hospital is of considerable practical importance. The unit requires to be as near as possible to its main source of patients—the casualty department—and to its main area of patient discharge, the male general medical wards. The General Hospital coronary care unit is well placed between the two principal male medical wards but at some distance from the casualty department. This is a disadvantage, for we play a smaller part than we would like in the initial resuscitation of the patient with a complicated myocardial infarction on his arrival in that department. In addition, the risk of cardiac arrest occurring in transit from casualty to the coronary care unit is not negligible. However, our current site facilitates good working relations with the wards to which we discharge patients and from which they occasionally return.

Apparatus and Equipment

Beds.—It is clearly desirable to avoid resuscitation on the floor of such a small ward unit. We have therefore adapted the ordinary hospital beds to allow external cardiac massage to be effectively performed without moving the patient to the floor.

---

* Consultant Physician, the General Hospital, Birmingham.
† Senior Medical Registrar, the General Hospital, Birmingham.
‡ Sister in charge of the Coronary Unit, the General Hospital, Birmingham

Beds are fitted with braked castors for stability during resuscitation and ½-in. (1.3-cm.) boards are permanently placed across the upper half of the bed frame. When propped upright with pillows the patient is unaware of the underlying boards. A 3-in. (7.5-cm.) polyethylene mattress is normally comfortable for the patients, but allows external cardiac massage to be performed effectively. The head of each bed has been sawn through at the uprights above the level of the spring frame and an obturator has been inserted into both upper sections. The head of the bed is then easily detached to allow tracheal intubation.

When transvenous cardiac pacemaking is indicated this procedure is carried out within the unit. One bed has been further adapted for this purpose. In order to permit the introduction of an *x*-ray source beneath the bed the legs have been lengthened by 3 in. (7.5 cm.). All metal springs have been removed and a 2-in. (5-cm.) radiotranslucent polyethylene mattress is supported by ½ in. (1.3 cm.) of plywood mounted on the bed frame. Satisfactory radiological screening may be obtained in this way and the bed is comfortable enough to lie on. The position of the pacemaker catheter tip may be checked if necessary. The walls, floor, and ceiling of the unit are sufficiently dense to eliminate the need for further protective screening around the unit for the amount of radiation involved. The swing doors leading to the coronary care unit have been lined with 1 mm. of lead.

Display and Monitoring Equipment

A wide range of electronic equipment is currently available to any type of intensive care unit. Some of this seems to be unnecessarily complex for our purpose—for example, monitoring body temperature and respiratory rate is of little value in the coronary care unit. We have come to use the oscilloscope simply as a display apparatus, seldom using the monitoring and alarm systems. This is possible in a fairly small unit when nurses have been taught some elementary electrocardiography. Initially the nursing staff were asked to perform routine tasks—for example, counting the frequency of ventricular extrasystoles for one minute in the hour. This in itself was of little value but served to draw attention to the oscilloscope. Interest was further stimulated by a collection of common electrocardiographic abnormalities, including infarction patterns and arrhythmias. As a result the nursing staff have become extremely skilled in the detection of arrhythmias. The provision of a simple single-channel recorder enables the nurse to make a permanent recording of any arrhythmia direct from the oscilloscope.

Most warning systems are activated by a change in heart rate outside a preset range. A nurse may detect additional abnormalities—for example, the early stages of atrioventricular block or an alteration in frequency or form of ventricular extrasystoles. In addition, as indicated by Thomas (1967), mechanical cardiac arrest may occur in the absence of change in the electrocardiogram so that direct observation of the patient remains of primary importance.

Patients do not resent the physical attachment to an oscilloscope provided that it does not entail conventional leads, which not only hamper the patient's movement but make any nursing procedure difficult. We have elected to place the limb leads on the left upper arm with a single exploring electrode on the anterior chest wall, thus leaving the right arm and both legs free. Other similar electrode arrangements have been described (Fluck *et al.*, 1967). Some form of small lightweight adhesive electrodes are best for this purpose.

The floor is kept as free as possible from unnecessary equipment, and for this reason we arrange oscilloscopes on a shelf behind the patient or on a small bedside stand. Probably wall rails for all equipment provide the ideal solution.

Apparatus is available for measurement and recording of intravascular pressures and cardiac output, but this is probably not necessary for practical purposes. The central venous pressure can always be measured by a simple water manometer via a polyethylene catheter advanced from the arm into the right atrium.

Radiological and Resuscitative Equipment

Although routine diagnostic radiology may be performed in the usual way it is advisable for the coronary care unit to be independent of the radiology department in the matter of screening. The rapid introduction of a cardiac pacemaker catheter into the heart by the transvenous route may be one of the most valuable contributions to the care of the patient. It is preferable to undertake this task in the unit and to avoid removal to another part of the hospital building which involves the patient in additional risk and delay. A portable image intensifier with closed-circuit television enables this to be performed within the coronary care unit and avoids the necessity of darkening the whole unit while screening.

The coronary care unit is equipped with a D.C. defibrillator and adequate apparatus for artificial ventilation—for example, oropharyngeal airways, self-inflating ventilating bag, laryngoscope with a wide range of cuffed endotracheal tubes, etc. The emergency drug cupboard is portable and contains all necessary resuscitative drugs, including 100-ml. infusion bottles of 8.6% sodium bicarbonate which are freshly dispensed by the pharmaceutical laboratory. Each piece of equipment has its own set position in the unit; this is important for speed of access in an emergency. An annexe of the unit contains blood-gas analysis apparatus for the rapid determination of arterial *p*H during resuscitation.

Electrical Hazards

The accumulation of electrical equipment poses certain hazards to the patient. Voltage build-up may easily occur on many forms of equipment, including cardiac monitoring apparatus. Normally it is unlikely that serious harm will result, since the high resistance of the patient's own tissues will prevent flow of current through the myocardium. However, the patient with a low resistance conduction line to the heart—for example, an indwelling cardiac pacemaker catheter or an intracardiac E.C.G. lead—is at considerable risk, as only a slight current (around 200 microamps) requires to flow through the myocardium to produce ventricular fibrillation. Though the pacemaker unit is screened from the A.C. mains, fatal voltage may still be applied to the myocardium unless all bare metal electrode attachments of the catheter are carefully insulated. All apparatus should be carefully and regularly checked for voltage build-up by a technique similar to that described by Whalen and Starmer (1967).

Staff

The coronary care unit provides a hospital service, and all patients suspected of having suffered a myocardial infarction are admitted to the unit under the overall care of their own consultant physician. One consultant physician and a senior registrar advise on the management of all patients within the coronary care unit, but the registrar and house-physician admitting the patient continue to look after him throughout his stay in hospital. These arrangements have the advantage of offering all junior staff experience in this work, and of providing a continuity of patient-care throughout the admission. The physician and senior registrar permanently attached to the coronary care unit provide uniformity of patient-care.

The nursing staff—one sister and seven staff nurses—are employed entirely in the coronary care unit. The observations required of the nurses and the speed with which they must reach decisions and act upon them make frequent change of nurses quite impracticable. Student nurses not infrequently spend short periods of time within the unit to gain some insight into its techniques and work, but an experienced member of the staff is always present. The nursing staff are often able to guide relatively inexperienced doctors in the identification and management of certain arrhythmias. In addition they explain to the patient and his relatives the nature and purpose of the equipment with which he comes into contact.

Duration of Patient's Admission

Most patients, male and female, spend three to four days in the unit, and, if they pursue an uncomplicated course, are then transferred to the general ward. Patients with serious arrhythmias, hypotension, or cardiac failure remain longer. Since it is our policy in the treatment of complete heart block to leave a catheter pacemaker in situ for three weeks in spite of a return to sinus rhythm, these patients remain with us for the whole of this period.

We encourage only short visits from close relatives for the first few days. The kitchen of the general ward to which the coronary care unit is attached supplies all meals. As the diet is predominantly fluid and extremely light for the first three days after admission the kitchen facilities required are not demanding.

Practical Experience

One is entitled to ask what sort of return is likely to be seen for this considerable outlay in money and staff. The following is not intended to be a detailed analysis of our work but a brief summary which gives some idea of what may be expected.

In the first six months of full operation, 144 patients were admitted to the unit and in all but three the diagnosis on admission was thought to be acute myocardial infarction. In 116 of them the diagnosis was eventually confirmed by electrocardiographic and biochemical evidence. There were 23 deaths, but without knowing more about individual patients, in particular the delay before admission to the coronary care unit, this figure has little significance. Of more interest is the fact that resuscitation has been required for ventricular fibrillation on 10 patients in the unit. One patient had two episodes of ventricular fibrillation and another had four. Five of these patients survived to be discharged from hospital. Two elderly patients had cardiac arrest during the journey from casualty and resuscitation was ineffective. This reflects on the importance of placing the coronary care unit within the vicinity of the casualty department. Of seven patients with complete heart block four required transvenous pacing for very slow heart rates with either syncope or cardiac failure. Of these seven patients six have left hospital. Two patients with ventricular tachycardia have required cardioversion under general anaesthesia; both survived.

There may be several other benefits to the patient in the form of early diagnosis and treatment of heart failure, hypotension, and some of the less immediately serious arrhythmias, and perhaps even from being nursed in a quiet area of the hospital with adequate analgesia. The patients almost without exception appear to be reassured by the constant presence of nursing staff and the calm atmosphere of the unit. The effect, however, of such factors on the morbidity and mortality of myocardial infarction is extremely difficult to assess.

REFERENCES

Fluck, D. C., *et al.* (1967). *Brit. Heart J.*, **29**, 170.
Thomas, M. (1967). *Proc. roy. Soc. Med.*, **60**, 368.
Whalen, R. E., and Starmer, C. F. (1967). *Mod. Conc. Cardiovasc. Dis.*, **36**, 7.

British Medical Association

Annual Scientific Meeting, Bristol, 10–14 July

The first part of the report of the Scientific Meeting appeared in last week's B.M.J. (22 July, p. 227). The report is concluded below.

Plenary Session on Recreation

Thursday, 13 July

The plenary session on recreation was chaired by the MARQUESS OF EXETER, the former Olympic hurdler. He was introduced by Mr. ROBERT V. COOKE (Bristol). In his opening address LORD EXETER said that there was increasing need in an industrialized world for men to have the opportunity of being fit and healthy, having interesting work to do, and enjoying constructive recreation. If these things were not available the world would soon be populated by neurotics.

Speaking on the need for recreation—in the true sense of the word—the BISHOP OF COVENTRY said that a number of factors were of value in *re*-creation: the first was doing the opposite of one's usual occupation, the second silence—which gave opportunities for reflection and appreciation of beauty—and the third reading. Equally important were faith and service. The present generation desperately needed the breadth of outlook which could be captured through re-creative recreation.

Sport

Sir ARTHUR PORRITT, turning to the role of sport, described recreation as the recharging of life's batteries. To be effective in refreshing the individual, games and other forms of physical exercise had to be fun, and not purposive like so much modern competitive sport. The Olympic Games had exaggerated competition, and the same thing was tending to happen in schools, where games were moving away from amateurism, which was the essence of true recreation.

Sir CHARLES WHEELER put forward the claims of the arts to have therapeutic powers. He quoted from *Painting as a Pastime*, in which Sir Winston Churchill had related the pleasure he found in painting. Sir Charles went on to expand on the joys of exploring what he described as the three kingdoms of colour, form, and light and shade. Within every individual there was the capacity for appreciation of these qualities, and those who wished to explore them could do so through the medium of the arts and be richer for the experience.

Gardening

Professor ALAN R. GEMMELL, discussing what he described as one of the most popular forms of recreation in England, outlined the virtues of gardening. The development of small modern gardens in Britain had followed the industrial revolution and had later spread all over the world. Gardening today owed its popularity to a number of factors. It provided a change of occupation, a means of physical exercise, and the intellectual satisfaction of a creative task.

Reading

Speaking on literature, Mr. **Kenneth Hudson** said that reading should not be regarded just as an anaesthetic or pain-killing drug, for it could give even the most sophisticated person an opportunity to broaden his outlook. He regretted that the experience of people like doctors and barmaids—who knew so much of life—was seldom recorded, and that those who wrote knew relatively little of life. Finally, Mr. Hudson condemned the "literature" which was inflicted on schoolchildren for the sake of examinations.

Music in the Twentieth Century

Professor **Willis Grant** outlined the development of music during the twentieth century. The scales and key systems which had been the basis of nineteenth century romantic music had been progressively abandoned, frequent changes of key giving way to polytonality, which like polygamy showed not rejection but a fondness for the subject. Later developments had included expressionism, atonality—in which keys were finally abandoned—microtones, and complete freedom from any rules governing rhythm or tonality. There were many present-day musicians who earned their living playing Mozart but believed that the future of music lay along these lines, said Professor Grant.

Dr. **William Evans** made the final contribution and spoke on the need for renewing, refreshing, and refurbishing what was weakened and needed strengthening—in this case, medicine. Good doctors were born rather than made through training, and much depended on better selection of medical students. Preclinical studies ought to coordinate the different disciplines, and clinical medicine required recreation of the relationship between doctor and patient. Examination at the bedside was being forsaken and there was excessive advertisement and prescribing of drugs. Dr. Evans suggested that final-year medical students and newly qualified doctors should gain practical experience by spending some months in general practice, and that family physicians ought to work with teaching hospitals in the training of students. Adequate time was the kernel of good doctoring, but the National Health Service did not allow for this and was in urgent need for re-creation.

Maternity Service

Friday, 14 July

A panel discussion on the maternity service was held, with Mr. J. R. **Nicholson-Lailey** (Taunton, Somerset) in the chair. Dr. D. F. **Henley** (Leicester) spoke for the local authority, whose present contact with the maternity service was the provision of midwives. The role of the district midwife had come under review latterly because more confinements occurred in hospital (68% now in Leicester) and more than 20% of patients were discharged early. Each midwife still managed about 50 deliveries a year on the district.

The shortage of midwives had led to the introduction in 1964 of individual radio links between the midwife and the ambulance station at a cost of £10,000. Dr. Henley showed the apparatus to the audience. It could transmit and receive from inside the home over a range of about 10 miles. It had proved of tremendous value. Co-operation between the general practitioner and the local authority was rapidly expanding, but it had not proved possible to attach midwives to specific practices. Attachments to group practices and joint antenatal clinics were working well. Dr. Henley knew that neither the district midwives nor the patients would like a unified and more impersonal hospital-based service.

Looking into the future, Dr. R. P. C. **Handfield-Jones** (Haddenham, Bucks) assumed that domiciliary midwifery would decline but there would always be some. More deliveries would be done in both hospital and general-practitioner units. The perinatal mortality survey had revealed the shortcomings of general-practitioner obstetrics. Selection for domiciliary delivery and equipment for emergencies had not always been satisfactory. However, since this survey had been undertaken 80% of new entrants to general practice had done house appointments in obstetrics, and Dr. Handfield-Jones believed that more rather than less general practitioners would be practising obstetrics in the future. They would regard the supervision of most of the pregnant women in their practice as part of the job.

Role of General Practitioners

Mr. J. A. **Stallworthy** (Oxford) had campaigned to include the general practitioner as a vital member of the maternity service. General-practitioner units now dealt with 10,000 deliveries a year with very low maternal and perinatal mortalities. For planning purposes it was essential to recognize and define the group of high-risk patients. About 25% of those booked for home confinements were eventually transferred to hospital, and this group had the highest rate of maternal and perinatal complications. More education of both the public and the medical staff, more organization to get the right patient in the right place with the right facilities, and more teamwork were Mr. Stallworthy's recommendations for a better maternity service.

Representing the Royal College of Obstetricians and Gynaecologists, Sir **John Peel** was concerned about the relationship between consultants and general practitioners. He felt that the college had sometimes been misrepresented on this matter. It regarded the general practitioner as a vital part of the maternity service. The decrease in domiciliary midwifery meant that some midwives might have as few as five deliveries a year. This raised training problems. There was no future in competition between consultant, general practitioner, and midwife. A B.M.A. survey some time ago had shown that only a third of general practitioners did obstetrics enthusiastically. Sir John thought this figure would be much the same today, although the number of general-practitioner units had increased by 65% in recent years.

Discussion

Questions covered all aspects of the service from the isolation of patients in the hospital to methods of resuscitating babies. Dr. **Handfield-Jones** demonstrated the Blease–Samson resuscitator, which he regarded as essential for all general-practitioner obstetricians. But there was disagreement about whether midwives should be trained to intubate babies. All agreed that flying squads should be available everywhere. Alterations in the existing obstetric list were not regarded as feasible, but Sir **John Peel** said that adequate resident hospital experience was the only true criterion of admission.

Dr. **Henley** summarized the arguments for and against maternity nurses. It was agreed that the creation of two classes of midwives was most undesirable. However, instead of training all midwives in the same way, Mr. Stallworthy thought that those who wanted a career in district midwifery might select areas where more of it was done and have their training directed towards such a career. The legal problems of district midwives delivering patients in hospital and general-practitioner units would have to be overcome. Finally, the question of whether there were enough obstetric patients to provide training for midwives, medical students, general-practitioner obstetricians, and specialist obstetricians was considered. Sir **John Peel** and Mr. **Stallworthy** thought that bringing peripheral hospitals into the orbit of the teaching groups would provide plenty of obstetric patients and tap the experience and ideas of those not at present in teaching hospitals.

Urinary Incontinence in the Aged

Opening a meeting on recent trends in the management of urinary incontinence in the aged, with Mr. J. **Cosbie Ross** (Liverpool) as chairman, Mr. N. O. K. **Gibbon** (Liverpool) described the mechanism of the various types of incontinence and related these to the pathological conditions found in the aged.

Incontinence could be due to defective bladder storage (stress incontinence), failure to empty the bladder (overflow incontinence), and failure of voluntary bladder control (" true " incontinence and nocturnal enuresis). Ideally incontinence should be treated by removing the cause, and when urethral obstruction was present this was often possible. When the bladder had become atonic during recumbency temporary catheter drainage was often effective. In stress incontinence operation was more likely to be successful in the female than in the male, for whom various appliances were available. When cerebral disorders were present much could be achieved by physical and mental rehabilitation, including bladder drill and vesical distension under cystometric control. Anticholinergic drugs, the use of posterior pituitary extract at bedtime, and special urinals made life more tolerable for those with incontinence.

Contributing Factors

Mr. J. P. Mitchell (Bristol) said that some contributing and treatable factors in incontinence of the aged were chronic constipation, chronic cystitis, urinary infection, obstruction, and prostatectomy. The effects of the latter were usually temporary. Three types of patient who were difficult to manage were those who were unsuitable for operation, those who were immobile, and those whose incontinence was due to cortical deficiency resulting from cerebral arteriosclerosis. Mr. Mitchell then described the various types of appliances that could be worn by the incontinent patient. Appliances were of two types, for occasional dribbling between micturition and for total incontinence, appliances for the latter requiring a greater capacity. The apparatus should have some type of valvular control, be made of non-irritant material, and be either easy to clean or disposable. Indwelling catheters should be avoided at all costs.

The last speaker, Dr. T. N. Rudd (Southampton), emphasized that senile incontinence was primarily based not on lesions of the bladder and pelvic floor but on cerebral vascular disturbance. It should therefore be regarded as a functional disturbance analogous to hemiplegia and aphasia. Whenever possible active retraining of the bladder should be undertaken, using sound psychological management and avoiding all discouraging influences. Recently attention had been directed to the role of the pelvic floor in the control of bladder function. Muscular tone in the bladder could now be maintained by physiotherapy and by electronic stimulation of the pelvic floor.

In reply to a question, Mr. Mitchell agreed that patients with indwelling catheters tolerated them longer with prophylactic antibiotic treatment. But eventually they succumbed to infection. Mr. Gibbon considered the catheter a dangerous instrument, although it could be used for quite a long time with frequent changing and bladder washouts. Dr. Rudd thought it desirable to elevate the mood of incontinent patients by the use of suitable drugs.

Rheumatoid Arthritis—Conservative and Surgical Management

A discussion of modern trends in the medical and surgical management of rheumatoid arthritis were introduced by Professor J. H. Kellgren. He defined the disease and outlined its natural history, which followed three main paths: remitting, progressive, and malignant. Any assessment of the effectiveness of therapy had to be made against the background of this variability in the progress of the disease.

Variability was again stressed by Dr. Michael Mason, who said that half the sufferers from rheumatoid arthritis did not suffer from joint deformity, and only about 10% became crippled. Severe cases had an associated vasculitis and this, together with infection, amyloidosis, or atlanto-occipital subluxation might be a cause of death. The treatment of rheumatoid arthritis should include healing the local lesions in the joints, together with management of the general illness and the patient's psyche. It might be possible to help the patient by modifying his environment.

Dr. Mason said that specific therapy with injections of gold or corticosteroids should be considered in those patients with an established diagnosis in whom the disease was active and progressive and in whom symptomatic relief was proving impossible. He recommended corticosteroid therapy in addition in patients with fulminating disease, those with crippling morning stiffness who were finding difficulty in continuing at their work, and those patients who were showing a rapidly progressive destruction of their joints. There was little experience yet with immunosuppressive therapy in rheumatoid arthritis. In a small series of nine patients treated with azathioprine at the London Hospital only one patient had failed to respond when the drug had been given in a dose of 2.5 mg./kg./day, but five patients had eventually to stop treatment because of side-effects.

Surgical Reconstruction

Mr. Douglas Savill stressed the need for co-operation between physicians and surgeons in the management of rheumatoid arthritis. Surgical reconstruction of the damage done by disease which had become inactive had been done for many years. Advances in technique had now made it possible to operate on joints and tendons when the disease was still active. "Prophylactic" surgery could relieve pain, and thus preserve function during early involvement when procedures such as synovectomy might assist progress of the disease.

When the disease was in its intermediate stage surgery might be able to help the patient by allowing him to continue at work. Examples of this were the repair of the painless rupture of tendons that could occur in the rheumatoid hand. Removal of nodules on tendons or prophylactic decompression might enable a patient to maintain good movement of the affected part.

Though the results of a controlled trial of the use of synovectomy in affected knee and metacarpophalangeal joints were not yet available, he thought that many patients obtained considerable symptomatic relief, and that if the operation was done early progress of the disease might be averted. However, he had seen continued deterioration of the joints as judged by their radiographic appearances after synovectomy. The most difficult problem was knowing the right time to operate; in some cases involvement of the cartilage with pannus occurred so rapidly that there was only a fleeting opportunity to intervene with any chance of benefiting the patient.

Medical Films

Films were shown daily during the Scientific Meeting. Several were given a repeat showing, and an opportunity was given for any of the films to be repeated by request. There was a very wide range of interest in the programme, some films dealing with highly technical subjects, while others were more suitable for general practitioners and one or two were intended for showing to lay audiences.

Examples of technical films of specialized interest were "Concomitant Aortic and Mitral Valve Replacement" (Dr. Arthur C. Beall, jun., Baylor University College of Medicine, Houston, Texas), "Myocardial Revascularization" (Dr. Vineberg, Upjohn Ltd.), "Total Replacement of Larynx and Pharynx—an Operation for Carcinoma" (Mr. R. K. Roddie and Mr. H. T. John, Southmead Hospital) and "Intensive Care Regime in a Case of Tetanus" (Dr. G. Quayle). Films of this type can present complex new procedures with a clarity and brevity that cannot be bettered.

More general subjects included "The Treatment of Burns" (Mr. John Watson, Queen Victoria Hospital, East Grinstead), "Topical Steroids in Practice" (Glaxo Laboratories), and "Ankylosing Spondylitis" (Professor S. de Seze, Paris). "Doctor on a Tightrope" (Medical Defence Union) was an excellent example of the way in which a lighthearted presentation can make a strong impression; this film is likely to be of particular value to newly qualified doctors.

"Dead Easy" (Borough of Slough Health Department) was another good film—it won a Silver Award in the B.M.A. Film Competition of 1965—which was of interest and value not only to doctors but also to lay audiences.

Few of the films were new. Most were two or three years old and some considerably older, and in one or two cases it was apparent that, though films, like textbooks, become out of date, they cannot so readily be revised. Of the 21 films shown 11 were award winners in B.M.A. film competitions, and the overall standard was very high. Any doctor prepared to spend an hour or so during the course of the meeting in attending the film theatre could form an excellent impression of the value of this form of teaching in health education and undergraduate and postgraduate training.

Scientific Exhibition

The Scientific Exhibition was the fourteenth to be held in conjunction with the B.M.A. Annual Meeting. It was opened by Mr. Robert V. Cooke, then President-Elect, who made a tour of the 45 stands, of which 16 were from hospitals in the Bristol region.

Prize-winning Exhibits

The Lawrence Abel Cup for the outstanding exhibit was awarded to "The Fractured Malar," from the department of plastic and jaw surgery, Frenchay Hospital, Bristol (Mr. J. W. Ross and Mr. R. T. Routledge). This exhibit was notable for the excellent use of photography to illustrate the method and importance of early recognition and treatment. The cardinal signs and symptoms were clearly demonstrated, and one section was devoted to some of the sequelae which may follow untreated or badly treated fractures.

Certificates of Merit with High Commendation were awarded equally to three exhibits. The first, "Towards Useful Hands," department of plastic surgery, Frenchay Hospital, Bristol (Mr. R. W. Hiles and Mr. M. Deane), was a pictorial demonstration of reconstructive surgery, showing the procedures used from operative technique to rehabilitative physiotherapy. The second in this category was a display, "The Main Characteristics of the Six Common Ringworm Fungi" (Dr. Robert P. Warin, Dr. Clifford D. Evans, Dr. Roger R. M. Harman, and Miss Mary E. English, United Bristol Hospitals), and here again particularly good use was made of coloured pictures clearly set out to show the clinical conditions caused and their characteristic features. The Royal Army Medical College's exhibit from the department of military surgery (Major F. P. Thoresby and Major N. A. Boyd) was the other stand receiving an award in this category. It showed the results of animal experiments comparing methods of treatment of gunshot wounds which had been contaminated with gas-gangrene organisms. High velocity bullet wounds contaminated with spores of a virulent strain of *Clostridium oedematiens* were inflicted on the quadriceps muscle of anaesthetized sheep. Pencillin therapy alone after wounding gave much better survival rates than with surgical procedures with or without penicillin. However, the maximum period of grace afforded by antibiotics before surgery was essential in human gunshot wounds had yet to be established.

Certificates of Merit

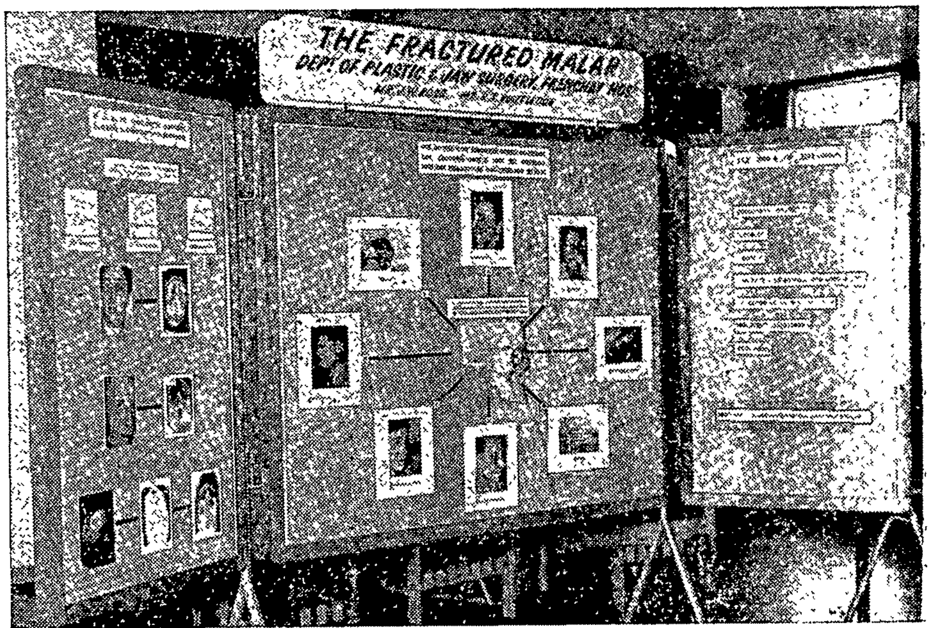
Certificates of Merit were awarded jointly to an exhibit showing the use of "Fluorescein Angiography in Ophthalmology and Neurology" from the neuro-ophthalmic department, National Hospital for Nervous Disease, London (Mr. M. Sanders, Mr. D. Archer, and Mr. T. ffytche); "The Pyloric Regurgitation Test" from the department of gastroenterology, Southmead Hospital (Mr. W. M. Capper, Mr. J. O. Kilby, Dr. Graham R. Airth, and Mr. M. J. Gibson); and "Control of Incontinence by Electrical Stimulation" from the Royal Devon and Exeter Hospital, sphincter research unit (Mr. K. P. S. Caldwell, Mr. P. Cook, Dr. F. C. Flack, and Mr. D. James). Striking photographs demonstrated the use of fluorescein angiography in papilloedema, retinal vascular disease, and neoplastic and degenerative lesions of the retina and choroid. In the exhibit showing control of incontinence the methods of stimulation of muscles involved in both urinary and foetal incontinence were displayed, together with the equipment used.

Malignant Disease

Mr. D. C. Bodenham and Dr. O. C. Lloyd (Frenchay Hospital, Bristol) had used excellent colour photography to illustrate the principal features of malignant melanomas of particular interest to the general practitioner. The importance of sex and age on the incidence at different sites was emphasized. Also from Frenchay Hospital (Dr. R. Sandry and Mr. G. M. Fitzgibbon) was a demonstration entitled "Variations in the Clinical Appearances of Basal Cell Carcinoma." This comprised an excellent series of photographs illustrating the variable manner in which the basal cell carcinoma may present, mimicking conditions such as chronic eczema or malignant melanoma. "Lumps in the Breast" (Professor Francis E. Stock and Mr. J. F. Kane, department of surgery, University of Liverpool) provided another good opportunity for the use of explanatory photographs to assist in the differential diagnosis of this condition. The use of temperature as a method of diagnosis in various breast conditions was demonstrated by the department of measurement and clinical research, St. Martin's Hospital, Bath (Dr. K. Lloyd Williams and Mr. K. D. Patil). The temperature differences created by a tumour were a measurement of its biological activity, and could be influenced by the administration of hormones.

Other Exhibits

A great diversity of subjects were featured on other stands. These ranged from a demonstration of electrical anaesthesia in a goldfish produced by passing a direct current through the tank (Professor John Clutton-Brock, department of anaesthetics, the University of Bristol) to the Royal Naval Physiological Laboratory's presentation of a telemetry system for medical and physiological monitoring (Mr. C. C. Wilton-Davies and Mr. J. D. Andrews). This system is designed for the monitoring of active subjects in the open, in pressure chambers, and in the sea. The department of pathology, the Welsh National School of Medicine (Dr. E. E. Payne and Mr. P. J. Stinchcombe), showed a demonstration of the necropsy findings in the brains of six professional boxers. The punch-drunk state was popularly recognized as one of the hazards of boxing, and many boxers had been examined in an endeavour to confirm or refute its existence. There were, however, very little pathological data to support any hypothesis about the causative lesion. Dr. Peter Samman and Dr. Peter Hansell, of the departments of dermatology and medical illustration, Westminster Hospital, London, contributed an exhibit designed to assist in the recognition of nail disorders, and the conditions they showed accounted for over 80% of all nail disorders seen in practice.



The Lawrence Abel Cup winning exhibit, from Frenchay Hospital, Bristol.

WITHOUT PREJUDICE

I ended last week's piece with the hint that the medical profession had a right to consider ways and means of working in the N.H.S. in terms of enlightened self-interest. My correspondent who said that as a G.P. he would prefer to work on a salaried basis and was well content with his lot qualified in 1952. By the same post I had another letter from a general practitioner (qualified in 1953) telling me he wanted to get into touch with the Belfast doctor whose group had regular sessions with a consultant. He himself worked in a group now periodically visited by a paediatrician.

The efficient organization of work in groups, preferably in close contact with hospitals and consultant opinion, is essential if time is to be available for the proper conduct of clinical medicine. Not only that, but intelligent organization of work is profitable. A striking example of this is shown in the July issue of the *Practitioner*. A general practitioner of what one might call the N.H.S. generation, Dr. T. Russell, transformed the work of his practice by converting a partnership into a group practice. He carried out a time-and-motion investigation of the practice, which he describes as a "study in cost effectiveness."

"It has been said of general practice," he writes, "that it is incapable of being streamlined without detriment to that quality of personal care that a patient expects to get from his family doctor. This dictum is flatly untrue . . . ." The work was concentrated in a highly efficient "group surgery." "Also we have that most blest of all things—an effective examination-room system and technique that effectively trebles or even quadruples our consultation rate." They make selective appointments for their patients, because they have organized time instead of letting time disorganize them. "Thus the sum total of all these measures is a truly astonishing increase in our cost effectiveness. Our profits are high, our patients are happy, *and we have time to spare*" (my italics).

General practitioners ought to found a 1948 club, membership being limited to those who have qualified since that date. Exchange of information in such a group might speed up the changes needed to bring the practice of medicine up to date. The demonstrations by Dr. Russell and many others show how group or health-centre practices properly organized can provide the time for the thorough examination of the patient which must be the basis of the practice of clinical medicine. This must be the primary concern of the doctor. This is what he is trained for. This is what the patient wants. It is this which gives the doctor the continued experience without which his clinical acumen becomes blunted.

* * *

I have been chivvied for giving so much space lately to the problems of general practice. I am unrepentant. If we can get a bit closer to the solutions of the many problems of general practice, then, I believe, the other pieces of the N.H.S. will in due course fall into place. There are now so many excellent models of group practices and health centres that there is surely every reason to take advantage of these ways of doing good work that at the same time is more profitable. Enlightened self-interest demands this. Within the frame provided by the group there are many possible variations that will be determined as much as anything else by geography and the social and industrial environment.

The question of private or public practice in this modern setting of the group practice or health centre is, I believe, irrelevant. In the strict sense of a doctor's ethic every patient is a private patient whatever the source of his pay. Every sick person is entitled to exactly the same consideration—and privacy—as every other sick person. I would make them all private patients in one sense of the old contractual relationship by seeing that all make at least some payment at the time of consultation, with exemption for the young, the old, and the chronically ill. This is done in other countries with national health schemes, and in Russia patients are made to pay for their drugs.

From the group or the centre—especially when the health centre is attached to a district hospital—the general physician with extra ability and training can move into the hospital. And in time he will be able to move into the public health service when its centre is in the medical group and not in the town hall. The public health doctor will then be paid as a doctor.

* * *

Enlightened self-interest must come in at this point. A universal salaried service has for the administrator all the virtues of simplicity. It would bring the doctor effectively under the control of the administrator, of the State. There is a strong political tide seeking to bring everyone down to a level of equality that makes nonsense of human variability. So I would urge my fellow professionals to preserve as wide a field as possible for variety of service and enterprise and energy.

By and large this will have to be within the ambit of the N.H.S. There is only one alternative to the N.H.S. and that is private practice outside it. I think it is a mistake to try to discourage private practice. The amount of private practice will depend very much on the public. It is the right of the patient rather than the right of the doctor. To foster a conflict between private and public practice is a disservice to both. There is every reason for looking at the one as supplementing the other. It would be better, I think, to wed the two in a public N.H.S. financed partly on a basis of charges and with devolution from the centre to the re-formed regions. This would give the Ministry of Health time and opportunity to act as a power-house of ideas. It shouldn't concern itself with details any more than the G.P. should bother with the trivia of practice which can be better handled by others less qualified.

* * *

With the problems of general practice on the way to solution the hospitals wait for their Beeching. In the meanwhile Lord Cohen's proposals in the House of Lords earlier this year should help to stem the flow of emigration. Scrap all existing titles of posts. Establish hospital medical posts of increasing annual seniority and pay. Anyone who has satisfactorily pursued a course of specialist training should be assured of a specialist position at the end of his training, with promotion to senior rank in due course.

I believe that the devising of new ways of making the N.H.S. run efficiently is the first priority. The structure is faulty. It creaks and groans. There's an awful lot of waste to begin with. As Professor Dunlop of Harvard said not long ago of the position in the U.S.A.: "Nothing could be worse in our society today than to say we need another three or five billion dollars for medical care, and then simply duplicate or multiply the arrangements we now have."

* * *

The Director of Simulation and Forecasting Studies at the Rand Corporation in California, known as the "Think Tank," told a group of businessmen in New York recently, "Fatalism is a fatality. The future is no longer viewed as unique, unforeseeable, and inevitable. There are instead, it is realized, a multitude of possible futures, with associated probabilities that can be estimated and, to some extent, manipulated." Among the multitude of possible futures for the practice of medicine the N.H.S. will be there for a long time, until it is replaced in, say, 30 years' time by a European Medical Service. We ought to be making plans for this now. *Vale!*

PERTINAX

Correspondence

Letters to the Editor should not exceed 500 words.

Post-concussional Sequelae

SIR,—I find it difficult to correlate Mr. A. R. Taylor's opinions on the post-concussional sequelae (8 July, p. 67) and some points in your leading article on the same subject (same issue, p. 61) with my general neurosurgical experience, which includes a great number of patients with both civilian and military head injuries. I believe that the so-called "post-concussional syndrome" is unlikely to be caused by neuronal damage; it was rarely seen in penetrating head wounds and it is not a feature following operations which stretch the brain stem—for example, the removal of an acoustic neurinoma. In surgical posterior fossa lesions "head dizziness" is not common; the dizziness these patients refer to is most frequently due to cerebellar unsteadiness of the legs. White fibre damage in other areas of the brain does not cause either constant or postural headache.

In head injuries with clinical evidence of neural damage (psychometric deterioration, limb weakness) it is usually the family rather than the patient who seek medical advice. These patients tend to become facile and less concerned with their future. The reasons why patients after even mild head injury are more frightened than patients with injuries to other parts of the body was long ago discussed and explained by Paul Schilder.[1]

I believe that in the "post-concussional sequelae" spasm of the nuchal muscles plays a dominant role, whether the headache be constant and dull, as in the majority of compensation cases, or be brought on by bending of the neck. This assumption can readily be proved by the invariable tenderness of muscles at the back of the neck and the prompt, if temporary, relief of headache in non-compensation cases by the injection of local anaesthetic, the wearing of a collar, and physiotherapy. The tension is also responsible for the dizziness and headache; dizziness which may culminate in frequent blackouts. These are the somatic expressions of psychogenic tension, mainly a fear that another head injury might occur, and the gain motive plays a large part in compensation cases. The headache and dizziness coupled with unemployment lead to irritability and forgetfulness which I should not call "neurotic," for the patient's personality remains essentially intact and can quickly return to normality when his claim has been settled. I agree with Professor Miller's[2] appreciation of the syndrome in compensation cases. It would be unfortunate if the present annual increase of compensation cases were to receive encouragement from your articles.

In conclusion, I plead that Trotter's[3] definition of concussion be adhered to.—I am, etc.,

J. SCHORSTEIN.

Department of Psychological
Medicine,
Southern General Hospital,
Glasgow S.W.1.

REFERENCES

[1] Schilder, P., *Brain and Personality*, 1931. New York.
[2] Miller, H., *Brit. med. J.*, 1961, 1, 919.
[3] Trotter in *Choyce's System of Surgery*, 1912. London.

Hetacillin and Ampicillin

SIR,—The vigour of the pharmaceutical industry has produced a flood of antibiotics, but often the problem for the prescriber is to distinguish the significant from the insignificant new drug before confusion arises. The report by Mr. R. Sutherland and Dr. O. P. W. Robinson (24 June, p. 804) on hetacillin (Versapen) is therefore timely. Hetacillin has been launched as a new broad-spectrum, semi-synthetic penicillin with properties similar to those of ampicillin (Penbritin). This similarity is neither disputed nor surprising, for hetacillin is in large measure converted to ampicillin in the body and in neutral aqueous solutions generally. It follows, therefore, that any therapeutic significance for hetacillin, as an alternative to ampicillin, must depend on whether or not absorption and blood concentrations are greater with hetacillin. Reports from America, where hetacillin was developed, make this claim[1]; the results of Sutherland and Robinson show the opposite.

I have recently compared blood levels of ampicillin and hetacillin in a crossover study in which 12 healthy human volunteers were given 250 mg. of each drug on separate days. Blood levels were measured by a standard cup plate assay method, using large plates seeded with *Sarcina lutea* and control solutions of each antibiotic made up in normal human serum. The results shown below confirm the findings of Sutherland and Robinson that absorption of ampicillin is more rapid and leads to higher blood levels compared with hetacillin.

Mean Serum Concentrations in 12 Human Subjects

Antibiotic	Mean Serum Concentration (µg./ml.)				
	½ hr.	1 hr.	2 hr.	3 hr.	4 hr.
Ampicillin, 250 mg.	1·14	1·89	1·95	1·24	0·64
Hetacillin, 250 mg.	0·07	0·39	0·95	0·96	0·47

Consideration of the differences between the serum concentrations following the administration of ampicillin and hetacillin at each interval of time, in each individual, goes some way towards explaining the discrepancy between the results reported from America and quoted by the manufacturers of hetacillin, and those of Sutherland and Robinson. These differences, calculated by subtracting the lowest serum concentration from the highest for each individual at each interval after the administration of each antibiotic, are shown below.

Differences (in µg./ml.) Between Serum Concentrations After 250 mg. Ampicillin and Serum Concentration After 250 mg. of Hetacillin in 12 Subjects

Subject	Interval after 250 mg. Doses				
	½ hr.	1 hr.	2 hr.	3 hr.	4 hr.
1	1·16	0·71	*(0·17)*	*(0·03)*	0·43
2	0·22	0·7	1·55	0·51	0·53
3	1·11	1·42	1·57	*(0·02)*	0·25
4	0·27	0·6	0·62	0·45	*(0·11)*
5	0·31	2·70	2·54	0·9	0·4
6	3·43	4·2	*(0·7)*	*(0·78)*	*(0·11)*
7	0·02	0·85	1·37	0·62	0·14
8	1·5	2·38	0·77	0·07	0·26
9	0	0·33	1·65	0·69	0·37
10	2·06	2·65	0·75	0·15	0·02
11	1·16	0·73	1·20	1·0	*(0·04)*
12	1·83	0·80	0·81	0·06	*(0·03)*

Note: The nine sets of figures in brackets indicate the occasions on which the serum concentrations were higher following the administration of hetacillin than following ampicillin. In all other instances the serum concentrations were higher after the administration of ampicillin.

It will be seen that in only nine instances out of 60 did the serum concentration after hetacillin exceed that following the administration of ampicillin. Furthermore, in these nine instances the difference was very small and probably within the range of error of the method. Subject 6 appears to be an exception, because in this subject the serum concentration following hetacillin exceeded that following ampicillin by 0.7 µg./ml. at two hours and by 0.78 µg./ml. at three hours. This subject was, however, an exceptionally good absorber of both drugs and a peak level of ampicillin of 5 µg./ml. was achieved after one hour, while the peak level of hetacillin was 3.1 µg./ml. at three hours. In all 12 subjects the peak concentration achieved after ampicillin exceeded the peak concentration after hetacillin, usually by a very significant amount; also the peak concentrations of hetacillin tended to occur later than those of ampicillin.

I conclude, therefore, that hetacillin generally gives lower blood concentrations than ampicillin, and that it does not have significant new properties. It does seem that there is a continuing need for an organization which is prepared to carry out or arrange objective assessment of conflicting reports on the properties of antibacterial agents.—I am, etc.,

MARK RIDLEY.

Department of Clinical
Microbiology,
St. Thomas's Hospital,
London S.E.1.

REFERENCE

[1] Bunn, P. A., Milicich, S., and Lunn, J. S., *Antimicrobial Agents and Chemotherapy, 1965*, p. 947, 1966.

Investigating Hypertension

SIR,—Your recent leading article (1 July, p. 4) entitled "Investigating Hypertension" appears to give a somewhat incomplete and misleading impression of the current position in this field. Indeed, it is a little difficult to see what point your writer is trying to make.

When is investigation of hypertension "fruitless"? Apparently when continued after "the small number of potentially curable patients" have been detected—the others are to be spared. You go on to suggest that the I.V.P., "supplemented by radiographs taken during the first five minutes of the examination" (surely standard practice for years ?), together with a radioisotope renogram, may be the best way of selecting those who may benefit from further inpatient investigation.

If such a practice were to be universally adopted there would be little progress in the field of hypertension. You make no reference to the complex biochemical problems which offer a considerable challenge to physicians currently engaged in this work: into the problems of recognizing aldosteronism in its various forms; or in detecting pressor-secreting tumours of the adrenals or kidneys—conditions which could not possibly be identified using the screening procedures you suggest. Nor do your comments contain more than scant reference to the merits of aortography, though you quote the series described by Chamberlain and Gleeson.[1] Those authors chose the rather curious parameter of surgical benefit ultimately acquired by the hypertensive patients they investigated with which to judge the value of aortography in hypertension. Quite apart from the smallness of their series and its highly selected nature, it was surely a novel approach for the radiologist to demur on the grounds of doubtful ultimate surgical benefit. There are analogies in other fields where surgical benefit may ultimately be small, such as gastric carcinoma or bronchial carcinoma, but few would suggest that full assessment was unjustified. In any event, medical benefit, in the form of accurate diagnosis and consequent more definitive medical management, might result.

Surely we must get our priorities right. In good clinical practice accurate diagnosis must come before treatment whenever possible, and we should avoid the temptation to attempt to short-cut what is usually a rather painstaking and detailed inquiry. Thus without angiography it may be impossible to identify such conditions as fibromuscular dysplasia, renal-artery aneurysm, thrombosis or embolism in a branch of the renal artery, or renal-artery anomalies. These latter are exceedingly common, and, we believe, important. We have published two papers in which these aspects have been discussed, though you refer to neither.[2 3]

It is agreed that many difficulties surround the practical aspects of investigating hypertension, but surely the decision is still a clinical one. If the patient has hypertension sufficiently significant in the physician's judgement to warrant treatment then investigation should usually be undertaken first. If this is to be done at all then it should be complete, and requires full biochemical and radiological assessment in most instances. We are not impressed by the arguments that this is impracticable, for it is not too difficult to organize facilities to this end, and the procedure need be done only once in the lifetime of most of the patients. About 1,000 patients have been assessed in some detail (including the procedure of aortography) in recent years as part of the general medical work at this hospital.—I am, etc.,

PHILIP W. ROBERTSON.

Royal Air Force Hospital,
Wolverhampton,
Staffordshire.

*** The leading article was concerned with the initial detection of renal lesions that may be responsible for hypertension, and the problem of selecting patients for further inpatient investigation into a renal cause for their disease. It did not discuss topics such as the investigation of aldosteronism; there is of course no suggestion that other than renal causes should be overlooked in the assessment of the hypertensive patient. We regret not referring to the papers[2 3] by Wing Commander Robertson and his colleagues, though both papers have been criticized by workers unable to confirm his group's findings.[4] He has commented on this.[5] Many doctors would disagree with Wing Commander Robertson's suggestion that the hypertensive patient who is to be treated should "in most instances" undergo complete radiological investigation, including aortography, as he implies. This is one of the points the leading article was at pains to make. Even in young hypertensive patients, the group in whom vigorous investigation is most promising, the preliminary report of a recent survey[6] shows the small returns to be gained from renal arteriography in the presence of a normal pyelogram.—ED., *B.M.J.*

REFERENCES

[1] Chamberlain, M. J., and Gleeson, J. A., *Lancet*, 1965, **1**, 619.
[2] Robertson, P. W., Klidjian, A., Hull, D. H., Hilton, D. D., and Dyson, M. L., ibid., 1962, **2**, 567.
[3] Robertson, P. W., Hull, D. H., Klidjian, A., Dyson, M. L., *Amer. Heart J.*, 1967, **73**, 296.
[4] Davies, E. R., and Sutton, D., *Lancet*, 1965, **1**, 341.
[5] Robertson, P. W., Klidjian, A., Hull, D. H., and Dyson, M. L., *Lancet*, 1965, **1**, 556.
[6] Breckenridge, A., Dollery, C. T., Preger, L., and Laws, J. W., *Quart. J. Med.*, 1966, **35**, 603.

Accident Service

SIR,—No doubt much wisdom was spoken at the symposium on accident service at the Annual Meeting (see 22 July, p. 230), but the points of emphasis which reached the national press and television suggested a derangement of the priorities.

Surely we must accept as a first priority the proper care of the millions of injured who attend the hospitals each year. This means emphasizing as the number one need sufficient suitably staffed and equipped departments in designated hospitals to apply modern standards of treatment to the injured. Shortage of money or other priorities, or both, seem likely to stand in the way of this being achieved for many years.

Accident ambulances with special equipment have been tried by this and other units, and given up. Standard equipment for ambulances and general intercommunication between hospital and ambulance would be a valuable development. This will be achieved only with a National Ambulance Service. Helicopters will not make any significant contribution to the management of the injured. Of those who died before getting to hospital in this area, an investigation carried out about five years ago led to the conclusion that in nearly 80% death occurred within ten minutes of the injury. Nothing but prevention could have saved these people.—I am, etc.,

J. C. SCOTT.

Accident Service,
The Radcliffe Infirmary,
Oxford.

Coroner's Verdict and Industrial Compensation

SIR,—I followed with interest the correspondence in the *B.M.J.* relating to Dr. Gavin Thurston's article in the Current Practice section "Reference to the Coroner" (6 May, p. 361). Dr. N. F. Coghill (3 June, p. 637) and Mr. R. S. Murley (17 June, p. 764) make valid criticisms of the reference system and also valuable suggestions about how it could be improved.

As industrial medical officer to a large asbestos textile manufacturer, I am involved in the follow-up of employees receiving benefit for asbestosis reported to the coroner after death.

Mesothelioma of the pleura is now a prescribed disease. As this is a rare condition and as there is world-wide interest in its occurrence, the Working Group on Asbestos and Cancer under the auspices of the Geographical Pathology Committee of the International Union Against Cancer (U.I.C.C.) made certain recommendations regarding its diagnosis, and a consultative panel of pathologists was set up in Great Britain to whom all cases should be referred.[1]

Recently I learned of a coroner recording a verdict of death from mesothelioma of the pleura due to exposure to asbestos on the basis of the coroner's pathologist's report, when evidence was produced at the inquest that the Pneumoconiosis Medical Panel (P.M.P.) did not consider this to be the case. Neither the P.M.P. nor the coroner's pathologist found evidence of asbestosis. The histological sections were examined by a member of the consultative panel of the U.I.C.C., who diagnosed adenocarcinoma of the lung in the absence of asbestosis, confirming the findings of the P.M.P. The coroner preferred the opinion of his own pathologist.

The questions raised by this verdict are of wide-ranging consequence. The dependants of the deceased, if any, will be denied death benefit by the Ministry of Social Security irrespective of the coroner's verdict, as the P.M.P. do not consider death due to mesothelioma. The dependants might feel justified to appeal against this decision on the basis of the coroner's pathologist's opinion. No matter which way the local appeal tribunal decides, should they appeal, the case will probably eventually have to be decided by the Industrial Injuries Commissioner. The above sequence of events need not occur if the coroner accepts that the opinion of the P.M.P. and his pathologist differ, and asks for the opinion of the consultative panel of the U.I.C.C. before recording his verdict. The coroner's verdict, if it differs from the P.M.P. decision, is likely to lead to unnecessary confusion and distress on the part of the relatives and dependants. Both the P.M.P. and the coroner's pathologist very kindly discussed this case with me, and both presented solid reasons for their opinions.

The coroner does not always wait for a report from the P.M.P. before deciding his verdict. Many pathologists do not prepare the lungs adequately before examining them and do not make use of the consultative panel of the U.I.C.C. in doubtful cases of mesothelioma. Why does the coroner have to insist on a quick answer for the cause of death, thus not allowing adequate investigation in cases of this nature ? Why does the coroner have to pronounce his verdict at all in these cases, when there exists a panel of experts more qualified to decide—that is, the P.M.P. or the U.I.C.C. Consultative Committee ?

Dr. Thurston points out that " recording of causes of death is important for the national statistics on which so many calculations and decisions depend." The asbestos industry is fully aware of the health hazards associated with it, but inaccurate death certification can only serve to give the wrong impression and harm an enlightened industry producing a product for which in many instances there is no known substitute.—I am, etc.,

H. C. LEWINSOHN.

Turner Brothers Asbestos Co. Ltd.,
Rochdale, Lancs.

REFERENCE

[1] Report of Working Group on Asbestos and Cancer, *Brit. J. industr. Med.*, 1965, 22, 165.

Avoidable Hazards

SIR,—Your leading article " Asbestosis " (8 July, p. 62) was most timely. It is probably not realized that asbestos is used by some dental surgeons in postoperative packing materials following the operation of gingivectomy. It is very likely that a considerable number of dental nurses are exposed to quite heavy concentrations of powdered asbestos in the preparation of these dressings. I have noticed that some nurses shake the bottle before opening. A white cloud of fine asbestos powder appears immediately the lid is removed.

As there are other dressing materials available which do not contain asbestos and which are just as good there is no justification in continuing to use these preparations.—I am, etc.,

Leeds 16. JOHN E. DEB. NORMAN.

Chloasma and the " Pill "

SIR,—Dr. D. B. E. Quamina observed (3 June, p. 638) that chloasma is becoming more common as a side-effect of oral contraceptives, especially in Caucasians living in sunny countries. He says that very little reference has been made to this contraceptive chloasma and believes that analysis of a large series may help to determine whether it is the oestrogen or the progestogen in the pill which causes this complication. This presupposes that only one of these hormones is culpable. Oestrogen alone can cause chloasma, even in the male,[1] but I have not come across chloasma caused by progestogen in the absence of oestrogen. It is my opinion that the progestogen acts on the oestrogen-primed melanocytes,[2] and that chloasma is most likely to be precipitated by sunlight in chloasma-prone patients who have been taking anovulants for a long time, or in high dosage. Thus marked chloasma has been reported from Europe after as little as three months' medication with the large doses of anovulants sometimes used to control gynaecological troubles[3]; and several surveys have shown that the incidence of chloasma increases with the length of time for which the anovulant has been taken.

From various series already published it can be concluded that, for a given oestrogen dosage in a " combined pill," the greater the dosage of progestogen the greater the incidence of chloasma. Changing from one brand of anovulant to another would thus be of no help unless there was a reduction of hormone dosage. Chloasma can also be caused by " sequential therapy." [4]

Dr. Quamina, in Trinidad, is in an excellent position to help to unravel the chloasma mystery. The incidence of chloasma among the anovulant-taking women of another Caribbean island (Puerto Rico) is reported to be as high as 34%.[4] Is there a similar percentage among the natives of Trinidad ? I had imagined that the most deeply pigmented races would be chloasma-free, but it has been stated[5] that chloasma can be seen frequently in the African negro woman if a careful examination is made.—I am, etc.,

RONALD CARRUTHERS.

Department of Dermatology,
General Hospital,
Launceston, Tasmania.

REFERENCES

[1] Jadassohn, W., *Arch. Derm.*, 1958, 78, 427.
[2] Carruthers, R., *Med. J. Aust.*, 1966, 2, 17.
[3] Thiers, H., Villedieu, P., and Moulin, G., *Giorn. Ital. Derm.*, 1966, 107, 1335.
[4] Resnik, S., *J. Amer. Med. Ass.*, 1967, 199, 601.
[5] Rice-Wray, E., and de Ferrer, S. A., *Sem. Méd. Méx.*, 1966, 50, No. 647.

Antinuclear Factors

SIR,—The comment in your leading article on " Antinuclear Factors " (10 June, p. 654) that " despite the absence of any certain evidence it may be safely concluded that they have some role in the pathogenesis of [connective tissue] disease " is in our view incorrect.

Only 84% of patients suffering from systemic lupus erythematosus, 81% of patients with systemic sclerosis, and 35% of patients with discoid lupus erythematosus have antinuclear antibodies, even in the active phase of the disease.[1] The titres of antinuclear antibodies are not necessarily proportional to the activity, progress, or treatment of disease.[2] These antibodies are found in several diseases and no antibody is characteristic of any particular disease. They are found in symptomless relatives of patients suffering from connective tissue diseases[3, 4] as well as 4% of control subjects not suffering from connective tissue diseases.[1] Antinuclear antibodies cross the placenta without harming the foetus or newborn child,[5-7] and have been transfused into human volunteers without causing disease.[8-10] Transfusion of serum containing L.E. cell factor does not cause any damage to rats made tolerant to human serum proteins[11] nor does it inhibit the growth of cells in tissue culture.[12-13] Thus there is no evidence that antinuclear antibodies can initiate tissue damage.

Nevertheless, tests for antinuclear antibodies are valuable in clinical practice. In a recent assessment of the value of one test (the rat liver immunofluorescence test) we[14] have found that the connective tissue diseases can be divided into two groups. The first group includes disorders like systemic and discoid lupus erythematosus and systemic sclerosis in which high titres of antinuclear factor are frequently found, and the second those diseases like polyarteritis nodosa, various types of vasculitis, and dermatomyositis in which antinuclear factor is usually absent. We concluded that (*a*) the presence of antinuclear factor in high titre (more than 1 in 64) usually indicates a connective tissue disease such as systemic or discoid lupus erythematosus, systemic sclerosis, Sjögren's syndrome or rheumatoid arthritis, and almost certainly excludes polyarteritis nodosa or dermatomyositis ; (*b*) patients with a titre of 1 in 64 or higher and showing no or few abnormal symptoms or signs should be followed for a long time because they are at risk to develop a connective tissue disease of the first group ; and (*c*) in the absence of any other evidence of connective tissue disorder low titre antinuclear antibodies (1 in 16 or less) can be ignored.

The role of antinuclear antibodies in human disease has still to be determined—We are, etc.,

N. R. ROWELL.

Skin Department,
The General Infirmary,
Leeds.

J. SWANSON BECK.

University of Aberdeen,
Aberdeen.

REFERENCES

[1] Beck, J. S., *Scot. med. J.*, 1963, 8, 373.
[2] —— and Rowell, N. R., *Quart. J. Med.*, 1966, 35, 119.
[3] Holborow, J., and Johnson, G. D., *Arthr. and Rheum.*, 1964, 7, 119.
[4] Fennell, R. H., Maclachlan, M. J., and Rodnan, G. P., ibid., 1962, 5, 296.
[5] Beck, J. S., and Rowell, N. R., *Lancet*, 1963, 1, 134.
[6] —— Oakley, C. L., and Rowell, N. R., *Arch. Derm.*, 1966, 93, 656.
[7] Moghtader, R., Kahn, F., Moussy, P., Rousselet, F., and de Sèze, S., *Presse méd.*, 1967, 75, 381.
[8] Bencze, G., Cserhati, S. Kovacs, J., and Tiboldi, T., *Ann. rheum. Dis.*, 1958, 17, 426.
[9] —— Kovacs, J., and Cserhati, J., *Brit. med. J.*, 1959, 2, 864.
[10] Marmont, A., Negrini, A., and Damasio, E., *C. R. Soc. Biol. (Paris)*, 1962, 156, 1012.
[11] Clark, R. F., Burkhart, C. R., and Bates, H. R., *Arthr. and Rheum.*, 1963, 6, 573.
[12] Scheffer, E., *Proc. Kon. ned. Akad. Wet.*, 1961, 64, 501.
[13] Williams, A. M., and Schilling, R. F., *Proc. Soc. exp. Biol. (N.Y.)*, 1961, 107, 302.
[14] Rowell, N. R., and Beck, J. S., *Arch. Derm.*, 1967. In press.

Combined Antifungal and Antibiotic Therapy

SIR,—Professor P. C. Elmes's assertion in *Prescriber's Journal*[1] that " one in five strains of *Monilia* are resistant to nystatin " has been refuted effectively in the pages of the *B.M.J.* by such distinguished and authoritative writers as Professor E. Drouhet (18 March, p. 699), R. Holt and R. L. Newman, G. T. Stewart, and H. I. Winner (1 April, p. 51). We are in full agreement with these previous correspondents, having in 11 years of extensive use of nystatin encountered many therapy-resistant patients, but no resistant strains of *Candida albicans*. Permit us, however, to comment on another aspect of P. C. Elmes's article which has received rather less attention.

Professor Elmes considers that " antifungal agents are only necessary in serious infections or if local lesions persist after the tetracycline is stopped. . . . Combination tablets such as Mysteclin or Lederstatin are therefore unnecessary. . . . " Fleeting reference is made to systemic candidiasis, but the practitioner is left without guidance about the prevention of such dissemination in patients receiving prolonged antibiotic therapy. Combined anticandidal and antibacterial therapy is strongly indicated in patients in whom oral and gastrointestinal candidal reservoirs may become a focus for systemic invasion or widespread mucosal and cutaneous involvement. This applies particularly to infants with a history of oral, cutaneous, or gastrointestinal candidiasis, as well as to patients with debilitating diseases predisposing to candidal infection (diabetes mellitus, leukaemia, etc.). Such patients frequently receive prolonged antibiotic therapy, and the combination of nystatin with tetracycline is prudent here in order to prevent systemic candidal dissemination from gastrointestinal foci. Systemic candidiasis is markedly underdiagnosed ; in P. C. Elmes's own words, it is "seldom suspected . . . and . . . the diagnosis is usually made at autopsy."[1] Yet systemic candidal infections are increasing in frequency, particularly among patients with leukaemia and lymphomas. A 15-fold increase of such infections in the past decade was revealed by necropsy studies at an institution devoted to the treatment of malignant diseases.[2] We ourselves have recognized more than a score of such cases during the past few years at a 400-bed general hospital in New York City. As many as four patients at a time have been under treatment in the wards, some of them successfully.[3]

The cost tables given by Professor Elmes show that combinations of nystatin and tetracycline (Mysteclin, Lederstatin) cost only slightly more (29s. 3d.) than tetracycline capsules alone (22s. 6d.). Although the price of nystatin is not listed, the cost of administering the two antibiotics separately would probably be considerably higher.

Possible improper or promiscuous use by some practitioners of a useful combination does not warrant its removal from the pharmacopoeia. This would be as illogical as the removal of parenteral penicillin because too many injections are given. Good therapy demands the thoughtful prescription of drugs that fit the needs of a carefully investigated patient suffering from a specific type of infection. There are instances when the combination of an antibacterial and an antifungal agent is the treatment of choice, or when possible error on the side of prudence is preferable to a perfect diagnosis made post mortem.—We are, etc.,

PHILIP J. KOZINN.
CLAIRE L. TASCHDJIAN.

The University of the
State of New York,
Downstate Medical Center,
Brooklyn, New York. U.S.A.

REFERENCES

[1] Elmes, P. C., *Prescriber's Journal*, 1966, 6, 75.
[2] Hutter, R. V. P., and Collins, H. S., *Lab. Invest.*, 1962, **11**, 1035.
[3] Taschdjian, C. L., Okas, A., Kozinn, P. J., Caroline, L., and Halle, M. A., *J. infect. Dis.*, 1967, **117**, 180.

Protective Helmets and Traumatic Epilepsy

SIR,—Two points call for comment in the interesting article by Dr. R. H. P. Fernandez (24 June, p. 830). The case for "skidlids" for motor-cyclists has been argued on statistics which showed how seldom severe head injuries occur in victims who have been wearing a protective helmet. If Dr. Fernandez, with the large amount of data which he evidently has for industrial head injuries, could quote the incidence and mortality of injuries in men wearing helmets it might strengthen the case for compulsory protection in certain occupations. It would also be interesting to know the number of unprotected victims for whom helmets had been recommended, and perhaps even provided, by the management, and who had ignored this advice. Certainly it is an impression that helmets are much more widely worn in Continental Europe and in the U.S.A., at least in the building industry, which is seen at work by the passing tourist.

Dr. Fernandez rightly devotes space to the problem of traumatic epilepsy, which is one of the commonest causes of permanent disability—that is, non-employability—after head injury. Because this often develops in patients who have otherwise fully recovered, it is particularly important to understand its natural history in order to advise both the patient and his employer. Dr. Fernandez quotes Caviness as having shown that in many patients the epilepsy is a temporary affair with a good prospect of remission. However, this conclusion was based on a study of gunshot wounds from the first world war, and there are many differences between this population and civilians suffering blunt head injury. I have previously discussed in these columns the prediction of epilepsy after blunt injuries.[1] Elsewhere I have emphasized the less favourable outlook for remission after blunt head injury compared with missile injuries.[2] Briefly, early epilepsy (within a week of injury) has a 75% chance of permanent remission, but epilepsy developing later (whether or not there has been early epilepsy) persisted in more than 80% of 200 patients followed up for more than two years after their first fit. For the industrial medical officer the practical implications of this are that if a man does develop epilepsy he should be permanently redeployed in a job which is compatible with the occurrence of an occasional seizure, rather than offered temporary arrangements in the belief that the epilepsy will soon cease to be a problem.—I am, etc.,

W. BRYAN JENNETT.

The Institute of Neurological
Sciences,
Killearn Hospital,
Glasgow.

REFERENCES

[1] Jennett, W. B., *Epilepsy after Blunt Head Injuries*, 1962. London.
[2] —— *Brit. med. J.*, 1965, **1**, 1215.

Enuresis and Psychiatry

SIR,—May I add to the points made by Dr. Ian G. Wickes (15 July, p. 176) ?

Enuresis is one of those bastard problems which are tossed from one physician to another, each hoping that he will not be left with the baby. First we make a vain search for physical cause ; then a quick pass to the paediatrician ; child-guidance follows with electric gadgets ; and finally the psychiatrist. The problem drops back into our laps, so we bless the statistician and say: "He will probably grow out of it by the time he is 10."

The common factor in all the methods of approach mentioned above—and they all have their successes—is suggestion. Opinions on the dangers of symptom removal, although academically valid, make nonsense in light of our daily practice.

The surgeon treats belly-aching by removal of a normal appendix ; our gynaecological colleagues cure a multitude of troubles by diagnostic measures alone. In psychiatry is it not possible that we are merely relieving the symptom of depression when we use our modern drugs ? We are certainly not curing a disease.

Enuresis is not a hopeless problem. Those who are interested will find that a high rate of success can be achieved in family practice. Patience is essential, along with an established personal relationship with the patient ; but record-keeping, conditioning, bribery in the case of the child, suggestion, drugs, and even electric pads will bring success in a majority of cases.—I am, etc.,

Dundee,
Angus.

R. A. B. RORIE.

Unusual Examples of Adnexal Torsion

SIR,—Torsion of the lateral part of a Fallopian tube after sterilization was first reported by Kohl.[1] Since then other cases have been described.[2-4] It is difficult to say if the part of the tube which twists is healthy before the torsion, or whether it is the seat of a hydrosalpinx. However, the division of the tube deprives the lateral part of any stability which it might obtain from continuity with the medial part, thus facilitating torsion. In this context the following case is of interest.

A 31-year-old prediabetic housewife was Rhesus-negative. Her third baby was affected by maternal antibodies, and survived after an exchange transfusion. The mother was subsequently sterilized in 1963. For nine months before admission she suffered from recurrent abdominal pain, and had been treated for biliary colic, although the biliary tract had not been investigated.

She presented as an emergency with pain and vomiting. Her temperature was 101° F. (38.5° C.). There was tenderness in the right iliac fossa, but no peritonism. A tender cystic mass 3 in. (7.6 cm.) in diameter was found in the right anterolateral fornix. At laparotomy it was noted that a Pomeroy operation had been performed. The lateral part of the right Fallopian tube was cystic and gangrenous, and twisted five times on its mesosalpinx. The biliary tract was healthy. Right salpingo-oophorectomy was performed and the specimen mounted for museum display.

Sterilization by the Pomeroy technique is already under criticism. The pregnancy rate may be 1.7%,[5] while Drake has drawn attention to the occurrence of ectopic pregnancies.[6] Salpingectomy would not guarantee prevention of subsequent pregnancy in or outside the uterus, but would remove the risk of tubal torsion.

A 23-year-old housewife complained of deep dyspareunia after the birth of her first child. The uterus was found to be retroverted, and the ovaries had prolapsed into the pouch of Douglas. The uterus was anteverted without difficulty in the clinic, and a No. 8 Hodge pessary inserted into the vagina. Two hours later the patient developed lower abdominal pain and vomiting. She returned to hospital next day. Her temperature was 98.8°F. (37° C.). There was slight tenderness in the left iliac fossa, but no peritonism. The uterus was still anteverted, but behind it was a tender cystic mass 3 in. (7.6 cm.) in diameter. At laparotomy the left tube and ovary were found to have undergone torsion through one turn and to be gangrenous. The right ovary contained a few small cysts, and lay in the pouch of Douglas. Left salpingo-oophorectomy was performed and the round ligaments shortened. The right ovary was then stitched to the pelvic brim. Microscopy revealed that the left ovary was largely replaced by a cyst 6 in. in diameter.

This case demonstrates a simple mechanical aetiology only too well. No comparable report has been found in the literature.

These patients were admitted to Queen Mary's Hospital, Roehampton, London S.W.15, under the care of Mr. R. D. de Vere. I am grateful to him for his advice and help.

—I am, etc.,

B. S. Cox.

Queen Mary's Hospital,
London S.W.15.

REFERENCES

[1] Kohl, G. C., *Obstet. and Gynec.*, 1956, 7, 396.
[2] Sandler, M. J., *Amer. J. Obstet. Gynec.*, 1958, 76, 41.
[3] Kendrick, J. G., *Obstet. and Gynec.*, 1965, 25, 124.
[4] Zobin, E. F., *Akush. i Ginek*, 1965, 41, 148.
[5] Prystowsky, H., and Eastman, N. J., *J. Amer. med. Ass.*, 1955, 158, 463.
[6] Drake, P. H., *Brit. J. clin. Pract.*, 1966, 20, 269.

Down's Syndrome in India

SIR,—I was interested in your leading article "Worldwide Study of Malformations" (1 April, p. 3). I was surprised that no case of Down's syndrome (mongolism) was found among 70,000 births reported from Alexandria, Bombay, and Calcutta. I have been working with neonates for several years, and have found the incidence of Down's syndrome to be almost the same as reported from the West. In a study of 4,353 newborn infants[1] there were six infants with Down's syndrome—i.e., 1.4 per 1,000 births. The incidence is the same in more recent data collected last year. We have one case of Down's syndrome for 750 births. The incidence of other malformations in the report mentioned above was: musculoskeletal system 1.47% (talipes 19; polydactyly 18); central nervous system 0.9% (anencephaly 13, meningomyelocele 9); digestive system 0.6% (harelip 5, cleft palate 3, both combined 4); skin 0.5%; and urogenital system 0.2%. The overall incidence was 3.4%.—I am, etc.,

SHANTI GHOSH.

Department of Paediatrics,
Safdarjang Hospital,
New Delhi, India.

REFERENCE

[1] Ghosh, S., and Bali, L., *Ind. J. Child Hlth*, 1963, 12, 448.

Tolerance to Mandrax

SIR,—Dr. R. D. L. Ewart and Dr. R. G. Priest (8 July, p. 92) have shown that the withdrawal of Melsedin (methaqualone) in a dependent patient can lead to delirium tremens similar to that seen in barbiturate dependence. We wish to present evidence indicating that tolerance can be acquired to methaqualone, just as to the barbiturates.

We have previously reported[1 2] the features of methaqualone overdosage in 29 patients admitted to this hospital during a seven-month period immediately following the introduction of Mandrax (methaqualone and diphenhydramine) to this region. There was good correlation between the severity of poisoning and the plasma levels of methaqualone, which at admission ranged from 0.2 to 3.1 mg./100 ml. (mean, 1.5 mg./100 ml.). Levels exceeding 3.0 mg./100 ml. were regarded as dangerous. At the same time it was pointed out that this relationship would probably not hold if tolerance to the drug developed.

That this has indeed happened is indicated by a survey of a further 78 cases of Mandrax poisoning treated after the 29 already reported. From June to December 1966 28 patients were admitted with levels ranging from 0.2 to 3.5 mg./100 ml. (mean, 1.7 mg./100 ml.), and from January to June 1967 50 patients with levels 0.2 to 8.3 mg./100 ml. (mean, 2.3 mg./100 ml.). In spite of this significant rise in mean plasma level very few of these patients showed the features of severe poisoning which characterized a high proportion of the previous series of cases. Since there have been no changes in the policy governing the admission of poisoned patients, in the criteria of clinical assessment, or in laboratory technique, we conclude that the data reflect the development of tolerance—and this, in a population for which methaqualone has been actively prescribed over a period of barely two years.

It is relevant that methaqualone levels of about 10 mg./100 ml. have been found in at least two non-fatal cases of poisoning. Ibe[3] specifically described one such patient as an addict; it seems feasible that habituation, even if not addiction, was a factor in the case described by Caridis[4] and Young.[5]

We have drawn attention[6] to the difficulties and dangers of attempting to correlate the severity of barbiturate poisoning with blood levels; tolerance is no less a problem with methaqualone than with the barbiturates. We have, however, not yet encountered withdrawal features indicating physical or psychic dependence on methaqualone.—We are, etc.,

STANLEY S. BROWN.
JEAN C. CAMERON.

Royal Infirmary,
Edinburgh.

HENRY MATTHEW.

Poisoning Treatment Centre,
Royal Infirmary,
Edinburgh.

REFERENCES

[1] Lawson, A. A. H., and Brown, S. S., *Brit. med. J.*, 1966, 2, 1455.
[2] —— —— *Scot. med. J.*, 1967, 12, 63.
[3] Ibe, K., *Arch. Toxicol.*, 1965, 21, 179.
[4] Caridis, D. T., *Brit. med. J.*, 1966, 2, 1655.
[5] Young, J. P. W., ibid., 1967, 1, 301.
[6] Matthew, H., and Lawson, A. A. H., *Quart. J. Med.*, 1966, 35, 539.

Common Market—a Challenge, not a Danger

SIR,—I would like to endorse warmly the letter by Dr. S. R. Scagliola (8 July, p. 108). For some time now I have been both amused and mildly irritated by the fears of many colleagues that entry into the Common Market would mean the invasion into Britain of very large numbers of Continental doctors.

The facts are, very simply, that on the whole professional earnings are higher on the Continent than in Britain, and this would seem an adequate disincentive. This does not hold true for the bright graduates in university appointments; their financial plight is in many countries, including Italy, quite serious and undoubtedly a number of them would like to hold paid appointments in research institutes and the better hospitals in Britain. This could not be taken as a threat to our standards and professional financial prospects should some of them wish to remain here and pursue a hospital or university career, as they would have to run the gauntlet of our appointment committees in healthy competition with British qualified doctors.

I would take it that if they wish to enter general practice the General Medical Council would require a year's pre-registration appointments in approved hospitals, and this would be an adequate safeguard.
—I am, etc.,

E. MONTUSCHI.

The Italian Hospital,
London W.C.1.

Treatment of Choriocarcinoma

SIR,—The reply of Professor W. S. Tow and Mr. W. C. Cheng (10 June, p. 699) to my letter (15 April, p. 178) requires no modification of my comments on their paper (4 March, p. 521), and I would like to try to clarify the situation.

Following surgical evacuation of a mole some trophoblast usually persists within the uterine wall. It exhibits a wide spectrum of activity, ranging from a local infiltration of cells detectable in some cases only by their endocrine activity, to the large villous masses, hypervascularity, and metastases of invasive mole in others. Choriocarcinoma is thought to occur in about 2% of cases in Britain, and it arises mainly in those with disease which remains subclinical. If choriocarcinoma does not develop the trophoblast tends to die out within three or four months, but it may still die out after persisting for even longer. Non-choriocarcinomatous proliferations may require radical treatment (hysterectomy or chemotherapy) to relieve symptoms or to prevent destruction of the uterus, or because they cannot be distinguished clinically from choriocarcinoma. The greater the interval after a mole has been evacuated the greater the risk that continued trophoblastic proliferation is, or will become, choriocarcinoma. Choriocarcinoma sometimes kills only two to three months after evacuation of a mole, but if treatment is started before irreversible damage has occurred, and within six months of evacuation, current methods of treatment are virtually always successful. If delayed till more than about six months after evacuation therapeutic failures still occur, and instead of chemotherapy lasting only three to four months it may then go on for one to two years before the patient's ordeal ends in either full health or death.

If all the sequelae of mole could be prevented by completely safe chemotherapy this would have advantages, particularly in countries where follow-up is impossible, but the safety and effectiveness of routine prophylactic chemotherapy has not yet been established. The generally practised alternative requires treatment of selected cases. Case selection introduces arbitrary decisions, because the risk of continued observation has to be balanced against the wish not to treat unnecessarily.

It is clear from what Professor Tow and Mr. Cheng tell us that their basis of selection for radical treatment is considerably wider than ours, and it therefore includes cases who would be treated conservatively here. Their reasons for their wider selection may be perfectly sound in Singapore. Further, there has never been any doubt that hysterectomy is usually effective for invasive mole; but whether it is appropriate depends on the patient's age and whether she has children. It is appropriate more often in Singapore than in the United Kingdom for these social reasons. Tow and Cheng argue that because invasive mole is sometimes followed by choriocarcinoma it therefore *is* early choriocarcinoma and carries the same prognosis and requirements for treatment as choriocarcinoma. Having defined choriocarcinoma so as to include a group which is acknowledged to respond to hysterectomy, it is hardly surprising they find it more useful than those who do not include such a group within their treatment series and who prefer to use the term choriocarcinoma in its recognized sense. The criteria of Tow and Cheng for hysterectomy, applied to our series, would result in fewer hysterectomies being performed. Hysterectomy should be reserved, as they themselves assert, for selected cases and not used in childless women who do not need it or in patients with advanced disease who die as a consequence of it.

Far more important than a contrived argument about hysterectomy is the problem of ensuring the effective follow-up of all mole cases, so that patients who need treatment receive it before the chance of recovery is lost. Patients still die because the follow-up methods available are inadequate or not even used. A reliable centralized follow-up system could now be devised with the technology available in the United Kingdom. There is a case for making hydatidiform mole a notifiable disease.—I am, etc.,

K. D. Bagshawe.

Fulham Hospital,
London W.6.

Trephine Biopsy of the Lung

Sir,—Dr. S. J. Steel and Dr. D. P. Winstanley report (1 July, p. 30) that they have not encountered any instance of air embolism in one hundred trephine biopsies of the lung.

I hope they will not allow one hundred consecutive pieces of good fortune to convince them that their technique is safe. The insertion of a cannula into the lung and the removal of its trocar can cause rapidly fatal air embolism. I have known one such case. If the technique can be modified so that the cannula is kept occluded throughout this risk may be reduced.—I am, etc.,

A. L. Jacobs.

Whittington Hospital,
London N.19.

Scopolamine with Morphine

Sir,—Dr. J. S. Crawford questioned recently (21 January, p. 172) the accuracy of a statement made in an earlier leading article (26 November 1966, p. 1282) to the effect that combinations of scopolamine with morphine in the management of labour caused more depression of respiration in the newborn than did morphine alone. Some results obtained here using the pregnant rat at term as a laboratory model are of interest in this context.

Drugs were given to the mothers by the subcutaneous route after determination of the normal rate of respiration. The frequency of maternal respiratory movement was assessed again after 30 minutes and any change expressed as a percentage of the control values. The mothers were then killed by dislocation of the neck, the young delivered by caesarean section, and five from each mother placed in the separate chambers of a respirometer, the details of which were described recently.[1] Respiratory activity of the young was expressed as oxygen consumption/100 g./minute, corrected to s.t.p. Six mothers, and therefore 30 newborn, were used to study each drug and dose combination. Some of the results obtained are summarized in the accompanying table.

Scopolamine alone at a dose level of 4 mg./kg. had negligible effect on maternal and neonatal respiration. Morphine alone at 1.25 mg./kg. did not significantly affect the maternal respiratory rate, but resulted in the young being born with a substantially reduced oxygen consumption (17.9% depression from control values). When the mothers were treated with both drugs in combination the young were no more depressed than with morphine alone, but the maternal respiratory frequency was very significantly reduced. The same pattern emerged using different dose combinations, and the effects of 0.5 mg./kg. scopolamine with 6.25 mg./kg. morphine is also shown in the table.

Effects of Morphine and Scopolamine Administered to Pregnant Rats at Term on the Respiratory Rate of the Mothers and the Rate of Oxygen Consumption of the Newborn

Drug	Mean Depression of Maternal Respiratory Rate (% Control)	Mean Depression of Neonatal O_2 Consumption (% Control)
A Scopolamine, 4·0 mg./kg. ..	0*	2·75† ± 1·91
B Morphine, 1·25 mg./kg. ..	0·48† ± 2·58	17·9 ± 2·67
A+B	16·2 ± 3·9	15·28 ± 2·64
C Scopolamine, 0·5 mg./kg. ..	0*	4·43† ± 1·00
D Morphine, 6·25 mg./kg. ..	9·4 ± 1·8	25·4 ± 1·61
C+D	42·3 ± 3·2	25·9 ± 1·16

* The means for scopolamine alone actually represent insignificant degrees of stimulation.

† Not significantly different from the relevant means for placebo-treated animals.

These results suggest that, so far as the rat is concerned, scopolamine does not potentiate the neonatal respiratory depression caused by maternally administered morphine. The projection of results from the animal pharmacology laboratory to man should be treated with caution. However, although there appears to be no recent reliable report of a clinical investigation of scopolamine–morphine combinations in the management of labour, the data presented by Flowers[2] using pethidine support the pattern observed in the rat study. The Apgar scores of infants delivered from mothers receiving scopolamine and pethidine were very clearly not different from those of infants born of mothers treated with pethidine alone.—I am, etc.,

Gareth F. Blane.

Pharmacology Laboratories,
Reckitt and Sons Ltd.,
Hull, Yorks.

References

[1] Blane, G. F., *Brit. J. Pharmacol.*, 1967. In press.
[2] Flowers, C. E., *Obstetric Analgesia and Anesthesia*, 1967, p. 207. London.

Infant-scalp-vein Needles

Sir,—Dr. C. F. P. Wharton (10 June, p. 702) and Mr. H. F. Nagamia (1 July, p. 48) have recently reported that an infant-scalp-vein drip is superior to conventional intravenous cannulae for treatment of adults in certain clinical situations. I should like to add a further indication for the preferential use of this type of drip.

In myelosclerosis and aplastic anaemia the veins become sclerosed and thrombosed, owing to the oft-repeated venepuncture needed for regular transfusion. A stage is reached when it is almost impossible to insert a conventional cannula, so that after many unsuccessful attempts—each of which causes further venous sclerosis—the patient may be greatly distressed.

For several months I have been using an infant-scalp-vein drip for the weekly infusion of packed cells into a patient suffering from myelosclerosis. Insertion of the needle is far easier than with ordinary intravenous cannulae, so that the patient has much less discomfort and apprehension. It takes on average between three and four hours to infuse 270 ml. (½ pint) of packed cells when the hydrostatic pressure forcing the blood into the vein is increased by elevating the bottle of blood as high as possible. If a leg vein becomes obscured by oedema, secondary to congestive failure, the oedema should be removed by a diuretic the day prior to the infusion. The use of the diuretic would also prevent circulatory overload.—I am, etc.,

A. D. Holliday-Rhodes.

St. Catherine's Hospital,
Birkenhead, Cheshire.

Is Anaesthetist Dentist's Agent?

Sir,—The annual report of the Manchester Local Dental Committee for the year ended 31 March 1967 states that a dentist was found to have broken his contract under the N.H.S. "by virtue of having charged patients an additional fee for the administration of endotracheal anaesthetics."

I must point out, as the distinction is important, that the Minister's final decision in this case conspicuously failed to state that the dentist had *charged* a fee, and therefore failed to support the executive council's contention that the anaesthetist was the agent of the dentist who had therefore in law charged these fees. Indeed, the Minister did not even mention this point, although the executive council had asked for a specific ruling on whether or not the anaesthetist is in law the agent of the dentist.

Throughout this case the Ministry was informed that I had charged these fees, and counsel for the dentist, at his appeal to a N.H.S. tribunal, pointed out that I had a legal right to charge these fees, and that I was not in law the agent of the dentist. This tribunal's findings were never published, nor were they quoted by the Minister in his final decision.

The Minister, unable to find that the dentist had charged a fee via the anaesthetist as his agent, gave it as his final decision (from which there is no appeal under the N.H.S. regulations)[1] that the dentist had broken paragraph 6(2) of his N.H.S. contract by *suggesting* a fee, for the dentist had very properly warned his patients that I might charge a fee for tracheal intubation and in each case advised the Dental Estimates Board when I had charged such a fee.

Paragraph 6(2) states: "Except as otherwise provided in the regulations, a practitioner shall not suggest, demand or accept from any patient or from any other person the payment of any fee or remuneration in respect of any treatment which he is required to give under these terms of service."

Having failed to state that the dentist had charged additional fees for endotracheal anaesthetics, and knowing from the evidence that I had, the Minister penalized the dentist for his so-called breach of contract by ordering that the fees, which he knew I had charged, should be withheld from the dentist's remuneration and returned to the patient.

I am writing this letter (as a supporter since my student days of a National Health

Service, with over 17 years' experience of the N.H.S.) because legally I have no standing in this dispute and therefore no opportunity to challenge the Minister's decision in open court—a test which it would not pass. Inside the N.H.S. the Minister has enormous powers, and that these powers should be used within the law is even more important than the details of this case. It is, however, particularly regrettable that the N.H.S. should now be the biggest single obstacle to the greater availability in the dental surgery of the most important safety factor in modern anaesthesia—tracheal intubation.

"Undoubtedly the safest method of operating in the oral cavity is under endotracheal anaesthesia. . . . But the numbers of patients are too great for such a methodical approach" according to your recent leading article on dental anaesthesia (25 February, p. 447). The numbers will not be too great when the Ministry removes the disabilities improperly imposed on the consultant anaesthetist working in the dental surgery.—I am, etc.,

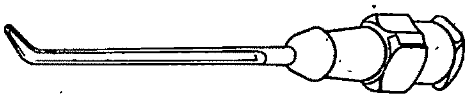
Manchester. **Arnold M. Danziger.**

Reference

[1] The N.H.S. (General Dentist Services) Regulations, 1964, No. 755, p. 15.

Cardiac Catheter Introducer

Sir,—I was interested in Dr. J. Mackinnon's letter (6 May, p. 377) referring to a shoehorn-type of catheter introducer for small veins or arteries. A very suitable and cheaper version can be readily made by a hospital instrument-maker from an ordinary Luer lok needle. The needle (15 to 18 gauge) is bisected along most of its length, and the short tip is bent at a right angle.



The catheter is passed along the hollowed-out tip, which occupies less of the vessel lumen than the two blades of an angled non-toothed iris forceps which I had previously used. It follows that this simple instrument is suitable for all types of vascular catheterization and need not be restricted to heart catheterization.

I claim no originality for this description, as I recently saw it used in several centres in the U.S.A.—I am, etc.,

W. G. Smith.

Sir Charles Gairdner Hospital,
Shenton Park,
West Australia.

Amitriptyline and Heart Block

Sir,—That amitriptyline and nortriptyline in therapeutic doses can precipitate complete heart block is suggested by the following clinical history. Complete heart block after overdose of amitriptyline has been reported in children,[1] and has been recorded in experimental animals.[2] We have been unable to find any other reports of complete heart block following the administration of amitriptyline or nortriptyline in therapeutic doses.

A 73-year-old woman was readmitted to Wellington Hospital in April 1967 because of transient blackouts of recent onset. It was found that she was having episodes of complete heart block, alternating with sinus rhythm, and that Stokes–Adams attacks accompanied the onset of the bradycardia. Her past history included osteoporosis of the spine, mild iron-deficiency anaemia, and mental depression. In December 1966 she had commenced therapy with ferrous gluconate, calcium gluconogalactogluconate, calciferol 50,000 b.d., and nortriptyline ; the dose of the last had been increased gradually to 50 mg. t.d.s., but was reduced to 25 mg. t.d.s. because of postural hypotension. There was no past history of cardiovascular disease, and apart from an apical systolic murmur there were no abnormal cardiovascular signs during periods of sinus rhythm. Serum calcium remained normal on this regimen.

Her arrhythmia and Stokes–Adams attacks were treated with sublingual isoprenaline and oral isoprenaline hydrochloride, and her usual therapy was continued. Because of continuing Stokes–Adams attacks, all therapy was stopped and intravenous isoprenaline given. After two days there were no further Stokes–Adams attacks, nor evidence on E.C.G. monitoring of heart block, and for the next 11 days, while maintained on isoprenaline hydrochloride 15 mg. four-hourly, she remained in normal sinus rhythm. Nortriptyline 25 mg. t.d.s. was recommenced, and she continued on isoprenaline. Four days later mefenamic acid (Ponstan) was commenced for back pain. After seven days on nortriptyline further episodes of heart block with Stokes–Adams attacks were observed. Isoprenaline was increased to 45 mg. three-hourly, but attacks continued. After three days of occasional episodes of heart block it was considered possible that nortriptyline might be responsible, and it was discontinued. Stokes–Adams attacks continued for another day, but there were no episodes over the following three days. Since amitriptyline therapy was helping her depression, and its continued use was therefore desirable, it was decided to observe the response of the patient to an intravenous injection of amitriptyline (nortriptyline injections were not available). Isoprenaline 45 mg. three-hourly was continued during this time.

While resting in bed the patient was given 25 mg. amitriptyline, diluted to 20 ml., at the rate of 2.5 mg. every 2 minutes for 20 minutes. Continuous E.C.G. monitoring revealed no abnormality for the first hour after injection, but at 69 minutes post-injection complete heart block occurred without any subjective awareness. Sublingual isoprenaline rapidly reverted her to sinus rhythm, but for the next few hours there were further episodes of complete heart block; but no true Stokes–Adams attacks. By the following day, and during the next 12 days, she remained free of symptoms, nor did an hourly pulse chart reveal any evidence of bradycardia, despite a reduction in, and final withdrawal of, isoprenaline during that time.

It thus appears likely that the occurrence of complete heart block, with or without Stokes–Adams attacks, during or shortly after the cessation of two oral courses of nortriptyline, and following the intravenous administration of amitriptyline, was precipitated by those drugs.—We are, etc.,

R. B. Smith.
Barbara J. Rusbatch.

Medical Unit,
Wellington Hospital,
Wellington, New Zealand.

References

[1] Sunshine, P., and Yaffe, S. J., *Amer. J. Dis. Child*, 1963, 106, 501.

[2] Lamarche, M., *et al.*, *Nutley Cont. Circ.*, 1966, 53, 143.

Cervical Smears

Sir,—Like Dr. M. B. Carson (15 July, p. 177), I have been carrying out cervical smears on all my female patients between the ages of 25 and 60 years for the past 18 months.

In a relatively small series of 350 smears (out of 2,900 in a single-handed practice) I have had four patients with positive smears, all of whom have had cone-biopsies and the diagnosis of carcinoma-in-situ thus confirmed. (Incidentally, one of these patients is aged 24.)

In one of the other patients, aged 44, the cone-biopsy confirmed the diagnosis, and, there not being signs of any invasion, it was advised that she be followed up by three-monthly routine smears. When I submitted Form E.C.74 duly signed by the patient—who is fully aware of her diagnosis and the importance of having her three-monthly smears—and having indicated on the form that the patient required regular repeat smears, my claim for payment was rejected because "the patient had a smear taken in the previous five years."

This, Sir, strikes me as the most incredible of all incredible anomalies in which the Ministry of Health is so excelling. Having uncovered and treated what the test is designed to do, as soon as the test becomes an important and valuable prognostic tool it no longer attracts a fee. It is insulting enough to have to claim a ridiculous fee and to get the patient to sign—as if we were all crooks—but when the test becomes a follow-up measure then one is obviously no longer providing a service, at least not in the Minister's thinking.

What then, if I may ask, is the purpose of the test ?—I am, etc.,

London E.1. **K. E. Schopflin.**

Sir,—In relation to Dr. M. B. Carson's letter (15 July, p. 177), I can report how this regulation is carried to the bureaucratic extreme. I have just had payment refused for a smear because I carried this out precisely 17 days before the patient's 35th birthday. The age limit for smears seems particularly inappropriate in this practice, since the only two deaths from carcinoma of the cervix in the past years have been in patients in whom it was first diagnosed at the age of 33 years.—I am, etc.,

Street,
Somerset. **R. D. Last.**

Experiments on Man

Sir,—Further to my letter (8 July, p. 109) offering qualified support to Dr. M. H. Pappworth's views, as expressed in his book *Human Guinea-pigs*, it has occurred to me that the printing of the name of my hospital might be construed in some quarters as implying that "human experimentation" was, or has been, taking place there.

I would be most grateful if you would allow me to make it absolutely clear that the opinions I expressed (which I maintain) were entirely my own, and that to the very best of my knowledge and belief absolutely nothing that could be thus interpreted takes or has taken place at this hospital. I am proud and pleased to be able to say this in all honesty.—I am, etc.,

Queen Elizabeth Hospital,
Birmingham 15. **B. W. Roper.**

Appointment Systems in General Practice

SIR,—Dr. A. Smith's letter (15 July, p. 180) stressing the value of the doctor-patient relationship is surely an argument against rather than for the appointment system in general practice. I like to regard my patients as personal friends coming in for a chat (incidentally involving diagnosis and supervision of treatment) rather than as clients for whom an appointment has to be arranged. If Dr. Smith's patients are prepared to wait three days to see him, what is so harmful about the occasional half-hour in the waiting-room?

Even the hardest-worked general practitioner can eliminate a crowded surgery by dint of a little extra effort—for example, by starting half-an-hour before the scheduled time. Then there is the therapeutic value of the waiting-room milieu itself. Many a person has found the most beneficial part of a visit to the doctor to be the opportunity of "comparing notes" with other sufferers in the surgery. There are all too few places to-day where people can congregate and talk, with the immense benefit this simple exercise brings them. Do not let us too readily squeeze sensitive and often lonely human beings into units which fit into our preconceived notions of efficiency. By doing so much of a general practitioner's effectiveness is lost.—I am, etc.,

S. L. HENDERSON SMITH.

Huddersfield,
Yorks.

Repeat Prescription Cards

SIR,—Following the publication of my paper "Appointment Systems in General Practice. How Patients Use Them" (24 June, p. 827) I have received so many requests from doctors asking for details of the repeat prescription card which we use in our practice that I find it impossible to send each of them a specimen.

It is a stiff, folded card measuring 11.5 cm. × 7.5 cm. and has printed on the outside:

KEEP CAREFULLY

To get a repeat Prescription without seeing the Doctor leave this card at the surgery in an unsealed, self-addressed envelope and collect your Prescription the following day.

If you stamp your envelope it will be posted to you.

The doctor's name and address are on the back, and inside on the left is space for the patient's name and address, the prescription or prescriptions, and a short description of each drug. The right side is headed "Dates of Renewal."

I hope this description will help interested practitioners.—I am, etc.,

J. S. K. STEVENSON.

Stevenston,
Ayrshire.

Merit Awards to Hospital Staff

SIR,—There is no doubt that Mr. C. Remington-Hobbs (1 July, p. 52) is coming to the heart of the objections to present assessments in the N.H.S. when he refers to the need for complete openness and objective assessment. In certain fields a reasonable statistical analysis would probably be helpful to throw light on better modes of treatment in any case. A concrete suggestion from me regarding this for psychiatry was printed in the *B.M.J.* (3 April, 1965, p. 923). Unfortunately there seemed to be very little interest in an attempt at more objectivity at that time.

There seem to be strong feelings throughout the country that genuinely objective assessments often do not occur. Thus it is felt that, notwithstanding Mr. Remington-Hobbs's categories of research work and so on, these factors may be ignored under personal pressures. The feeling appears to be that what counts is whether one is in or out of favour with members of the "in group" (often with London or teaching hospital connexions). Thus it may be felt that support from people of the greatest experience and integrity, indeed from large numbers of doctors, is cast aside if these people are not powerful members or connected with this "in group." Startling contradictions seem to be solved not by candid examination of documents and background but by a rubber-stamping of the powerful "in group's" wishes.

These feelings would be dispelled as unjust suspicions by awkward, unworthy characters, etc., if there was genuine openness. One can see no reason for the present Star Chamber approach. If there are startling conflicts based not on fact but on opinion or alleged facts never brought to the light of day then reasonable unease will continue. Truth does not need to be hidden or to work in the dark, and one must agree with G.P.s, who on the whole seem to be both fair and sensible about what often goes on regarding merit awards and the like.—I am, etc.,

Colchester, Essex. HARRY JACOBS.

Form E.C. 73

SIR,—I would like to draw your attention to the "accident" aspect of this form. I find that though the Council were glad to receive the record of my injection they are not willing to pay for a tetanus toxoid injection—given along with A.T.S. as emergency treatment to a patient on another physician's list.

This strikes me as an omission that should be rectified.—I am, etc.,

A. B. LEYS.

Bo'ness,
West Lothian.

Opportunities in British Medicine

SIR,—The Ministry of Health is to send an interview board to persuade British graduates in U.S.A. and Canada to return to this country (15 July, p. 128). Why wait until these doctors have left Britain? Why not interview applicants for immigrant visas and surprise them with information on the career opportunities mentioned in the Ministry's advertisement? This step may save a few return fares to the United Kingdom. Or, at second best, the interview board might inquire why the prospective immigrants are leaving the country, and, making use of this information, make recommendations on career structures and conditions of service in this country.

When I worked in the U.S.A. I met some British doctors who were there because they had found it almost impossible to make use of their skills in Britain. Their prospects had seemed poor when they left Britain, and time and distance had not improved the view. However, the interview board may well have a vision which is not apparent to most of us here.—I am, etc.,

Edinburgh 12. P. D. ROBERTSON.

Points from Letters

Indomethacin and Duodenal Ulcer

Dr. D. G. EMERY (Selly Oak, Birmingham) writes: I thought it would be interesting to report that in one patient with a known duodenal ulcer the use of indomethacin suppositories resulted in an increase in his gastric symptoms. The condition was so marked that he had dyspeptic symptoms only on the day after using a suppository the previous evening. His symptoms were controlled by increasing his antacids.

Neurotoxic Effects of Piperazine

Dr. W. E. BEER (Caernarvonshire and Anglesey General Hospital, Bangor) writes: I was most interested to read Dr. D. C. L. Savage's letter (24 June, p. 840). I recall a similar case. A young woman was being treated with piperazine citrate for threadworms. Dosage was within the recommended range. She was considerably alarmed to find that while combing her hair, picking up an object, or opening a door her hand would at times jerk off course. She happened to be on tetracycline at the same time for another condition, and I wondered if it was the combination of therapy that was somehow responsible or if it was the piperazine. In view of the experience of Dr. Savage's case, piperazine would appear to be responsible. The condition cleared on discontinuation of both drugs.

Too Easy to Forge?

Dr. M. D. RIPKA (London N.W.1) writes: Under the heading "Too Easy to Forge?" (24 June, p. 852) your legal correspondent refers to prescription forms supplied to doctors by the London Executive Council as having been criticized at London Sessions for being in a form likely to facilitate forgery. The Chairman of the Inner London Sessions Appeal Committee is reported to have said: "I hope in future that the London Executive Council will take it into their heads not to issue prescription forms with the name of the doctor stamped on them." The Chairman should be enlightened that the stamping of a doctor's name on prescription forms is most helpful to the pharmacist actually catching a forger, as he is thereby able to contact the doctor concerned if he has any suspicions about a prescription. . . . In the past, before the doctor's name was stamped on his prescription form, it was often impossible for the pharmacist to decipher the doctor's signature and effect any checking he desired to do. . . . Apart from investigating possible forgeries it is a great help when queries arise—for instance, those caused by unavailability of drugs, or inability to decipher items prescribed.

Intestinal Obstruction by Food

Miss D. E. O'DOHERTY (Sutton, Surrey) writes: Your leading article (24 June, p. 782) about unusual foods causing intestinal obstruction recalled to me a case I had several years ago of an elderly woman sent into the local hospital as an emergency.

She was extremely emaciated and suggested a late stage of carcinoma. She was acutely obstructed and at laparotomy I found a smooth ovoid mass about the size of a pigeon's egg impacted in the lower ileum. This was removed without great difficulty, and on closer examination proved to be a closely packed mass of fibrous material. On teasing this out the material filled a fair-sized kidney dish, and looked to me like grated coconut fibre.

On inquiry later the patient confessed to a great liking for coconuts and admitted to eating a whole one a few days previously. She made a good recovery.

Obituary Notices

Sir EARDLEY HOLLAND, LL.D., M.D., F.R.C.P., F.R.C.S., F.R.C.O.G.

Sir Eardley Holland, a former president of the Royal College of Obstetricians and Gynaecologists, and consulting obstetrician and gynaecologist to the London Hospital, died at his home in West Dean, Chichester, on 21 July. He was 87.

Hay Wrightson

Eardley Lancelot Holland was born on 29 October 1879, the son of W. Lancelot Holland, of Puttenham, Surrey. His mother was the daughter of Canon Eardley-Wilmot. He was educated at Merchiston Castle School, Edinburgh, and then came south to King's College, London. He took his medical training at King's College Hospital, then near the Strand, qualifying with the Conjoint diploma in 1903, and graduating M.B., B.S. with first-class honours in medicine in 1905. He took his Fellowship of the Royal College of Surgeons in the same year, and in 1907 proceeded M.D., and was awarded the gold medal for midwifery and diseases of women. The Fellowship of the Royal College of Physicians came later, in 1920, and that of the Royal College of Obstetricians and Gynaecologists on its foundation in 1929. After holding early hospital appointments he undertook further study at the University of Berlin, and on his return to England was for a time resident medical officer at Queen Charlotte's Maternity Hospital, and at the Hospital for Women, Soho Square. From 1907 to 1916 he was assistant obstetric surgeon at King's College Hospital, and also, during the whole of that period except for the last two years, tutor in obstetrics. From 1907 to 1916 he was also gynaecological surgeon to the Metropolitan Hospital. In 1916 he obtained his appointment as obstetric and gynaecological surgeon to the London Hospital, of which another bearer of the family name of Holland, the late Lord Knutsford, was the vigorous chairman. He retained that appointment until 1946, when he retired to an honorary consulting position. The first world war broke in upon his early career at the London, and he served as temporary captain in the R.A.M.C., being employed as surgeon specialist in France, in charge of No. 20 General Hospital. During the second world war his task was a very different one; he was in charge of the maternity services of the Ministry of Health on behalf of London women evacuated into Hertfordshire from 1939 to 1943. Other hospital appointments which he held were those of consulting obstetric surgeon to the City of London Maternity Hospital, and gynaecologist to the Florence Nightingale Hospital.

A man of many activities, in addition to a large private practice, he seemed to have a hand in all the developments affecting his own branch of medicine, and much beyond it. One of his actions on becoming president of the Royal College of Obstetricians and Gynaecologists in 1943 was to set up a strong committee to review the many deficiencies in the maternity services of that time, and to impress the views of obstetricians on those concerned. The aim of the committee was to modify the National Health Service Bill, then under discussion. The report of the committee, published in 1944, was a comprehensive review of the whole subject, including the social and economic factors concerned. The British Medical Association took exception to some remarks in the report about general practitioners which seemed to suggest a desire to exclude the general practitioner from midwifery practice. Eardley Holland was violently opposed to the term "general-practitioner obstetrician" which, he said, was an absolute sham and a misuse of the word "obstetrician." He remarked how few individual obstetricians could gain a real insight into the causation of maternal mortality because they saw relatively so few deaths. He himself, he said, did not gain such an insight until the beginning of the second world war, when it became one of his duties to investigate every maternal death in the Home Counties. The commonest cause he found to be shock or haemorrhage, or both.

Holland was a member of the Central Midwives Board; editor of the *Journal of Obstetrics and Gynaecology of the British Empire*; a member of the Board of Advanced Medical Studies of London University; and examiner in midwifery and diseases of women to the universities of Cambridge, London, and Durham, the Royal College of Surgeons of England, and the Central Midwives Board. He was the obvious president for the 12th British Congress of Obstetrics and Gynaecology held in London in 1949. Two years later he delivered the William Meredith Fletcher Shaw Memorial Lecture before the Royal College of Obstetricians and Gynaecologists, taking for his subject "The Princess Charlotte of Wales: A Triple Obstetric Tragedy." He was also a member of the General Council of King Edward's Hospital Fund for London, where he interested himself particularly in the provision of radium for the treatment of cancer. He was on a number of committees of the British Medical Association, among them the Medical Planning Committee and the Consultants and Specialists Committee, and was a representative at the Annual Meeting of the B.M.A. in 1943–4.

A writer of clarity and precision, the outstanding literary work with which his name is associated is the *Manual of Midwifery*, in which he collaborated with Dr. T. Watts Eden, and which ran through many editions. Later he became its sole author, and several further editions were brought out under the title of Eden and Holland's *Manual of Obstetrics*. He acted as chairman of a subcommittee of the Ministry of Health, which produced a report in 1922 on the causation of foetal death. In 1933, together with R. C. Jewesbury and Wilfrid Sheldon, he wrote *A Doctor to a Mother: the Management of Maternal and Infant Welfare*; and later, with Dr. Janet Lane-Claypon (later Lady Forber—see obituary below), he published a child-life investigation, involving a study of 1,673 stillbirths and neonatal deaths. To Eden's *System of Gynaecology* he contributed an article on hernia in women, and he wrote much else, mostly in the form of papers in the professional and scientific journals. He was editor of *British Obstetric Practice*, which appeared in 1955 and ran through further editions.

His name was widely known throughout the world in the field of obstetrics and gynaecology. He was an honorary Fellow of the Royal Society of Medicine, and of the American, French, German, and Brazilian gynaecological societies, and of the Royal Medical Society of Budapest. He was honorary M.D. of Dublin, honorary LL.D. of Birmingham and of Leeds, honorary Fellow of the Royal College of Surgeons of Edinburgh, and honorary Master of Midwifery of the Society of Apothecaries of London. He was knighted in 1946.

He married, firstly, in 1913, Dorothy Marion, daughter of Mr. Henry Colgate, F.R.C.S., of Eastbourne. She died in 1951, and in 1952 he married Olivia, daughter of Mr. Leslie Constable, J.P., of Fittleworth, Sussex. By his first marriage he had three daughters.

J. H. P. writes: The death of Eardley Holland marks the end of an era in the history of obstetrics and gynaecology in this country. He was almost the last survivor of that small band of gynaecologists who, under the leadership of Blair-Bell, had founded the Gynaecological Visiting Society of Great Britain and Ireland. Eardley Holland took an active part in the deliberations within the society which ultimately led to the foundation of the College of Obstetricians and Gynaecologists. He was not only a founder Fellow but he was co-opted to the first council which was formed in 1929, and became honorary treasurer of the College the following year. He played, therefore, a vital part in stabilizing the finances of the College in its first years. When he relinquished the honorary treasurership he was elected vice-president, and became president in 1943. It was during his presidency that the first of a series of reports on a national maternity service was published. This report was of particular importance in view of the impending National Health Service. Although a staunch believer in the College of Obstetricians and Gynaecologists, he favoured the closest co-operation with the other colleges, and it was during his presidency that agreement was reached between the Royal College of Surgeons and the Royal College of Obstetricians and Gynaecologists, whereby each had a representative on the council of the other.

Eardley Holland's undergraduate medical education was, like that of Blair-Bell, at King's College Hospital. After graduating he worked for a time in Germany. Throughout the whole of his life he remained a firm admirer of the German school of gynaecologists, and from among them he had many close personal friends. He was always deeply distressed that he should have had to live through two wars involving a country with which he had so many close personal ties. After an outstandingly brilliant undergraduate and postgraduate career it was not surprising that he should have been appointed to the staff of King's when a vacancy occurred in 1914. This was just after that hospital had moved to its present site on Denmark Hill. This fact, together with the outbreak of the first world war, interfered with the development of the hospital at that stage, and Eardley Holland accepted an invitation to join the staff of the London Hospital, where there were far better facilities at that time for both clinical research and practice. It was from that department that he soon produced his classic paper on stillbirths, and went on to develop a deep and lasting interest in regard to the country's maternity services. The social aspects of midwifery occupied a prominent place in his work, in his thinking, and in his writings. The latter were very numerous. Eden and Holland's textbook was as much a necessity for one generation of undergraduates as *British Obstetric Practice*—which he edited after his retirement—became to a later generation of postgraduates.

Eardley Holland was possessed of a very imposing physical appearance, upright and grand, almost haughty, yet he was always courteous and considerate. Quite often he was irascible, but more often kindly and gentle. He was a man with very firm likes and dislikes, who never hesitated to speak his mind whether it was to bestow praise or to administer a reprimand. Like all outstanding leaders he displayed great interest in the younger generation. My memory of meeting for the first time this rather awe-inspiring person, when a young man on the threshold of my career, is of being greeted with encouragement and praise for what, in retrospect, was an endeavour of little merit.

Personalities seem to be disappearing from the contemporary medical scene, but personality was something Eardley never lacked. Anyone with such forthright and freely expressed opinions inevitably had a few detractors, but they were vastly outnumbered by his admirers. Obstetrics and gynaecology owe a very great debt to this man, who worked throughout his lifetime to improve the maternity services of this country, whether it was in his own hospital department or through the activities of the Royal College. He derived great satisfaction from the improvements which took place during his lifetime.

Lady FORBER, D.SC., M.D.

Lady Forber (née Lane-Claypon), a former dean of King's College for Women (now Queen Elizabeth College), London, died on 17 July at Seaford, Sussex. She was 90.

Janet Elizabeth Lane-Claypon was born in Boston, Lincolnshire, on 3 February 1877, and entered University College, London, graduating B.Sc. with first-class honours in physiology in 1902, and taking the D.Sc. in 1905. She had a distinguished student career, and in addition to being a university scholar and gold medallist she held a B.M.A. research scholarship in 1902–3. For her clinical studies she entered the London School of Medicine (now the Royal Free Hospital), graduating M.B., B.S. in 1907. After holding several hospital appointments she proceeded M.D. in 1910. In that year she was appointed lecturer in physiology and hygiene at Battersea Polytechnic and in 1912 at King's College for Women. From then till 1916 she was an assistant medical inspector to the Local Government Board. In 1916 she became dean and lecturer in hygiene at King's College for Women, a post she held until 1923. In 1920 she was appointed a magistrate. She married in 1929, as his second wife, Sir Edward Rodolph Forber, who died in 1960.

A friend writes: One of the earliest acts of the Medical Research Committee—the Medical Research Council's immediate predecessor—was to commission Dr. Janet Lane-Claypon to write a book on *Milk and its Hygienic Relations*, which appeared in 1916. She later assisted in the preparation, jointly with Dr. (later Sir) Eardley Holland, of a report of the Medical Research Council's Committee on antenatal and postnatal problems of child life, which was published in the Council's Special Report Series in 1926. During the time Dr. Lane-Claypon was dean at King's College for Women she actively encouraged research in the departments under her control, and from time to time would approach the M.R.C. in support of applications from research workers there.

E. NEUMARK, M.D., M.C.PATH.

Dr. E. Neumark, lecturer in pathology at St. Mary's Hospital Medical School, London, died suddenly on 12 July. He was 55.

Ernst Neumark was born in Germany on 20 September 1911, and came to Britain as a refugee at the age of 22. He received his medical education at University College Hospital, London, qualifying with the Conjoint diploma in 1939. After hospital appointments he joined the pathology department of St. Mary's Hospital Medical School in 1943, and there he remained until his death. In 1947 he graduated M.B., B.S. and became a naturalized British subject in the same year. He proceeded M.D. in 1949, and in 1963 became a member of the College of Pathologists.

D. M. P. writes: The sudden death of Ernst Neumark removes from haematology one of its best-known personalities. He attended regularly at conferences and was a prolific writer (in four languages). Among other things, he translated, and with C. J. C. Britton was the co-editor of, Leitner's *Bone Marrow Biopsy*. He also contributed to Savill's *System of Clinical Medicine*. His most recent work concerned the influence of external temperature on the distribution of fatty marrow. But perhaps his most important contribution was in introducing to English pathology Di Guglielmo's disease. For many years he was medical adviser to the Haemophilia Society, and he took an active part in the formation of the World Federation of Haemophilia. In 1960 he visited many European laboratories, especially in Italy, where he was made an honorary member of the Società Internazionale di Ematologia. It was, however, as organizing secretary of the seventh European Congress of Haematology in London in 1959 that he became so well known personally. Nothing was too much trouble in attending to the needs of delegates, and his assiduity went far to making this particular congress such a success. The many friendships he formed were fostered by the hospitality provided in his home.

Ernst Neumark loved lecturing and demonstrating and organizing clinicopathological conferences. He will be remembered with affection by many generations of students, and by all his pathology colleagues, many of whom have gone to senior appointments elsewhere. It cannot be said that his clinical colleagues always found him easy—his interests were too numerous and his character too volatile for steady clinical rapport—but they also will remember him with affection. There can be no denying the enthusiasm he had for his work, and especially for the great occasions. He was a splendid showman, and the excellent state of the museum at St. Mary's could stand as his memorial.

A man of obvious culture, he was a good companion, and his skill on the accordion could make a party hilarious. He could be obstinate in his opinions, right or wrong, but was steadfast in his loyalties—a good Jew, devoted husband, and loving father.

Sir CLAUDE FRANKAU, C.B.E.
D.S.O., M.S., F.R.C.S.

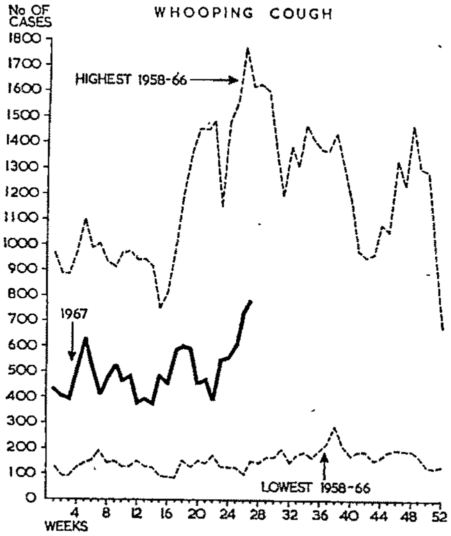
C. F. M. writes: When I first met Claude Frankau (obituary, 8 July, p. 116) he was surgical registrar at St. George's and gave a lot of his time to teaching and encouraging his juniors and students. In due course he was appointed assistant surgeon, and I believe he held the record for the length of time he bore this status before rising to that of full surgeon, owing to the relative youth of his seniors. This fact, however, did not prevent him from establishing an extensive private practice, for he was held in great esteem because of his diagnostic acumen and technical skill. He had a decisive manner which inspired confidence in both colleagues and patients. Through the years he served his country and St. George's with unflagging energy, and those who had the benefit of his teaching will never forget the patience, humour, and enthusiasm with which he passed on his knowledge. He could be witheringly caustic on occasion, but no one resented a blistering from him, as it was always deserved and taught a lasting lesson. As a surgeon he had all the skills: dexterity, gentleness, judgement, and the knowledge to put them to the best use. As a man and a friend he was everything which is implied by these terms at their best. His example has inspired many who hold illustrious positions in the surgical world of today.

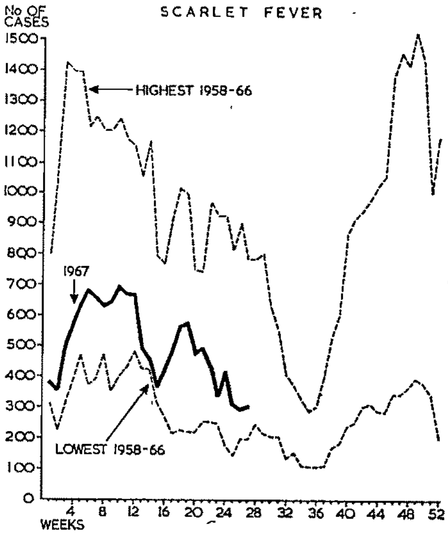
News and Notes

EPIDEMIOLOGY

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of whooping-cough and scarlet fever in England and Wales. Figures for 1967 are compared with the highest and lowest figures for each week in the previous years shown.





Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available.

	Week Ending 7 July	Week Ending 14 July
Dysentery		
Gloucestershire	18	**24**
Greater London	80	**78**
Islington	11	**23**
Lancashire	97	**66**
Warwickshire	38	**30**
Yorkshire East Riding ...	10	**12**
Yorkshire West Riding ...	51	**75**
Edinburgh	22	**19**
Glasgow	21	**15**
Food-poisoning		
Essex	19	**15**
Greater London	163	**60**
Hillingdon	136	**30**
Lancashire	29	**28**
Blackpool C.B. ...	1	**11**
Yorkshire North Riding ...	1	**18**
Richmond R.D. ...	0	**17**
Yorkshire West Riding ...	9	**53**
Bradford C.B.	0	**45**

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending 8 July (No. 27) and corresponding week 1966.

Figures of *cases* are for the countries shown and for Greater London. Figures of *deaths* and *births* are for the whole of England and Wales (London included), Greater London, the 17 principal towns in Scotland, the 10 principal towns in Notrhern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	1	0	0	0		1	0	4	0	
Dysentery ..	500	80	75	24	10	541	93	34	10	7
Encephalitis, acute ..	3	1		0		1	0		0	
Enteric fever: Typhoid ..	3	0	0	0		1	2	1	0	
Paratyphoid	0	0	0	0		6	2	18	0	
Food-poisoning	364	163	17	2		134	25	28	1	
Infective enteritis or diarrhoea under 2 years				30	46				14	35
Measles* ..	5,448	388	26	157	115	7,191	839	118	74	170
Meningococcal infection ..	10	0	0	0		14	1	2	0	
Ophthalmia neonatorum .	5	1	1	0		18	3	1	0	
Pneumonia† ..	82	7	65	2	2	61	7	55	2	1
Poliomyelitis, acute: Paralytic ..	0	0	0	0		3	0	0	0	
Non-paralytic	0	0	0			0	0	0		
Puerperal fever§	97	25	0	1		104	49	2	0	
Scarlet fever ..	302	50	14	22	6	321	37	24	7	11
Tuberculosis: Respiratory ..	235	34	32	11		316	79	39	8	
Non-respiratory ..	56	1	5	0		54	12	9	4	
Whooping-cough	782	151	52	11	25	371	55	22	12	8

DEATHS	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0		0	0	0	0		0		0
Dysentery ..	0	0		0		0	0			
Encephalitis, acute ..					0					0
Enteric fever ..	0	0	0	0		0	0	0		
Infective enteritis or diarrhoea under 2 years	7	0		1	1	7	1			0
Influenza ..	6	0	0	0	0	4	1	1		0
Measles ..	0		0	0	0	0		0		0
Meningococcal infection ..			0					0		
Pneumonia ..	533	79	16	19	5	495	84			7
Poliomyelitis, acute ..	0	0		0	0	0	0			0
Scarlet fever ..	0		0	0	0	0		0		0
Tuberculosis: Respiratory .. Non-respiratory ..	32	11	1	0 0	2 0	35	4	3		0 1
Whooping-cough	0	0	0	0	0	0	0	0		0
Deaths 0–1 year	282	54	13	9	7	279	40	20		11
Deaths (excluding stillbirths)	9,233	1427	519	130	115	9,113	1421	484		141
LIVE BIRTHS	16,172	2719	906	275	425	16,817	2855	976		548
STILLBIRTHS	217	36	12			270	45	6		

* Measles not notifiable in Scotland, whence returns are approximate. † Includes primary and influenzal pneumonia. § Includes puerperal pyrexia.

PARLIAMENT

Abortion Bill Under Fire in the Lords

[FROM OUR PARLIAMENTARY CORRESPONDENT]

Even the title of the abortion law reform Bill has come into question since the measure left the Commons and went to the Lords for second reading on 19 July. The Bill, Medical Termination of Pregnancy, got through this stage by 127 votes to 61, but it was subjected to some rough handling, presaging a contentious committee stage on 26 July. The third reading will not take place until the end of October, when Parliament resumes after the summer recess for a few days' "spill over" session to dispose of outstanding business before the 1967–8 session begins.

LORD SILKIN, sponsoring a measure of this kind for the third time since November 1965, said the Bill had been considerably emasculated in the Commons. It embodied a number of compromises, and he thought it could have been accepted in its present form by even its strongest opponents as reasonable and fair. It appeared that "the more one throws to the wolves the hungrier they become."

The **ARCHBISHOP OF CANTERBURY** said he very much wanted to see reform of the law on abortion, but the Bill contained some very bad features, and unless it was amended he could not support it. It would be possible to omit the reference to the existing children of the family—"the social clause coming in again through the back door"—and to move the provision about the substantial risk of the birth of a handicapped child and make it part of the provision about the mother's total environment. With these amendments the Bill would make the mother's life and health the sole matter for diagnosis by the doctor and the sole ground for abortion.

Non-medical Reasons

LORD BROCK, speaking as a surgeon, said the amendments made to the Bill had satisfied many doctors, and some medical bodies, that the main basis for abortion was medical. It was against the ethics of most surgeons, he said, to take part in abortion for non-medical reasons. While many had been prepared to go a long way in stretching the medical criteria as far as they could, there was a limit to what could be expected. Many surgeons were uneasy and felt that even now the boundaries of medical indication for termination of pregnancy had been overstepped, and that the implementation of the Bill would disregard them. "I must make it quite clear," he said, "that, although some surgeons will agree to do operations for non-medical reasons, most will refuse to do so, and their resolution has hardened as a result of the pressures put upon them." Many fears would be allayed, he added, if the phrase "any existing children of her family" were removed.

He objected to the title of the Bill. It was loose, vague, and open to misrepresentation. As he saw it, the meaning intended was the termination of pregnancy for medical reasons. Such a title would be simple, direct, and clear. He suspected the real reason behind the present title was just "legal abortion." The word "medical" was used in an attempt to make abortion more acceptable.

Criticizing Clause 4, the conscience clause, he said he felt that no doctor, and certainly no surgeon, should have to explain or justify a statement that it was against his will to do an operation for non-ethical reasons, and least of all should he be compelled to prove it in a court of law.

The Bill should contain definite indications that it recognized it would be unethical for a doctor to do operations against the tenets, morals, or conscience of his profession.

Approved Experience

LADY SUMMERSKILL, after some reflections on the failure of the Government to accept responsibility for so important a social change, pointed to a serious omission in the Bill. Clause I provided for a pregnancy to be terminated on the opinion of two registered medical practitioners, but it did not specify that one of them should be a doctor approved for the purpose. Why go to the length of providing an adequate and proper place for an operation, she asked, if you are not going to provide an adequate and proper person to do it? An approved register or list of doctors permitted to provide special services was not new. If it was found that a doctor on the approved list abused his position he could be removed. That did not mean he would be struck off the *Register*.

LORD AMULREE, on the other hand, was pleased that the Bill did not restrict the type of doctor who could perform an abortion. It did in a sense do so by the provision that the operation must be in a National Health Service hospital. That must mean there was some choice about the type of doctor who was to do it.

If the real purpose of the Bill when it started was to convert case law into statute law he was uncertain about the phrases "any existing children of her family" and "the patient's total environment actual or reasonably foreseeable" and the conscience clause.

Illegal Abortions

LORD PLATT wanted to know what were social and medical reasons. Even if the apparently offending phrases were interpreted as being a social rather than a medical provision, surely doctors for centuries had taken into account the social conditions of their patients. He had always taught his students that they did not understand the full implications of a case unless they had taken into account the social state in which the patient lived, and every other relevant consideration.

He hoped that those who were inclined to talk about the sanctity of human life would remember the 50,000 to 100,000 human foetuses which were being destroyed annually in conditions of squalor or dreadful extravagance. He would not be in favour of a grossly emasculated Bill that would leave them with the status quo and do nothing to lessen the number of illegal abortions.

LORD SEGAL could extend only a tepid welcome to the Bill, which in his view was badly in need of amending. He welcomed the conscience clause, by which a doctor was enabled to opt out of performing an operation to which he had a conscientious objection.

Treatment Centres for Drug Addicts

It was stated on behalf of the Government in the House of Lords on 19 July that so far there are 10 hospitals in London providing inpatient treatment for heroin addiction and 13 outpatient treatment. At six of the latter a service is available in the casualty department 24 hours a day, at three others there is a service five days a week, and at the remaining four facilities are available less frequently. At most of these hospitals staff are not exclusively concerned with the treatment of addicts. At Birmingham inpatient and outpatient treatment is provided at All Saints' Hospital, where the outpatient department is open from Monday to Friday, 8.30 a.m. to 6 p.m. In the rest of the country inpatient and outpatient treatment is available if required in most psychiatric hospitals.

Services in the London area, where the main concentration of addicts is believed to be, are still being developed, and it would be premature, and against the interests of addicts generally, to publicize the names of hospitals at present. General practitioners in the areas concerned are made aware of the services as they become available.

Bills Passed

The Sexual Offences (No. 2) Bill, permitting homosexual acts between consenting adults in private, was given the third reading in the House of Lords on 21 July.

The Dangerous Drugs Bill, with a new clause increasing from 2 to 10 years the maximum period of imprisonment for smuggling drugs, was read the third time in the House of Lords on 21 July.

Emigration of Doctors

Dr. **DAVID KERR** (Wandsworth Central, Lab.) asked the Minister of Health on 24 July for a statement on his study of emigration and immigration of doctors.

Mr. **ROBINSON**: "An analysis of information available from the Central Index of doctors maintained by the Health Departments and the British Medical Association about doctors entering and leaving Great Britain during the two years from 30 September 1962 to 30 September 1964 has now been completed. The results indicate a net loss of about 300 British- and Irish-born doctors a year, a figure well below some earlier estimates, balanced by a gain of roughly the same number of doctors born elsewhere. Details will be published shortly, and work on similar analyses for later years is proceeding."

MEDICAL NEWS

Royal Society of Medicine

At the annual meeting of the Royal Society of Medicine held on 18 July the following fellows were elected officers for 1967–8: *president,* Sir **HECTOR MACLENNAN** ; *honorary secretaries,* Dr. **G. E. W. WOLSTENHOLME** and Mr. **R. S. HANDLEY** ; *honorary treasurers,* Mr. **MYLES L. FORMBY** and Dr. **W. D. WYLIE**.

Honorary Professorship

The title of honorary professor has been conferred on Dr. **W. M. COURT BROWN** by the University of Edinburgh. Dr. Court Brown is director of the Medical Research Council's Clinical Effects of Radiation Research Unit at the Western General Hospital, Edinburgh, a post held since 1956. He joined the scientific staff of the Council in 1950 and from 1950 to 1956 he worked in the department of medicine at the then Postgraduate Medical School of London. During this early period he was specially concerned with studying the late harmful effects of radiation exposure to man, and with Dr. **RICHARD DOLL**, F.R.S., of the Council's Statistical Research Unit, he investigated the nature of the dose-effect relationship for the radiation induction of leukaemia in man. Since 1956 Dr. Court Brown has become increasingly interested in various aspects of human cytogenetics, in particular with the development of population cytogenetics, in the clinical significance of chromosome aberrations, and in radiation cytogenetics.

R.C.S.I. Appointment

Dr. **ALAN D. H. BROWNE** has been appointed professor of obstetrics and gynaecology at the Royal College of Surgeons in Ireland. He graduated from Trinity College, Dublin, in 1947, and after a period of training in Dublin and Manchester he returned as assistant master of the Rotunda in 1951. He was consultant gynaecologist to Dr. Steevens's Hospital and Drumcondra Hospital, Dublin, from 1955 until his appointment as master of the Rotunda Hospital in 1960. Dr. Browne is a Fellow of the Royal College of Physicians in Ireland and of the Royal College of Obstetricians and Gynaecologists. He holds the M.D. of Dublin University.

Cancer Registration

A supplement to the Registrar General's statistical review for 1961 contains data derived from the National Cancer Registration Scheme (see *B.M.J.*, 1964, 1 August, p. 265). Of 111,613 patients registered in 1961 56,829 (51%) were male and 54,784 (49%) were female. Among males the commonest forms of cancer were lung cancer (29%), cancer of the stomach (10%), and rodent ulcer (8%) ; among females cancer of the breast (24%), cancer of the large bowel (13%), and cancer of the womb (12%). The registration rate for all forms of cancer was higher in urban areas (2.5 per thousand population) than in rural areas (2.2). Of 46,385 cases of cancer in males registered in urban areas 30% were of lung cancer ; in rural areas 23% of the 10,444 cases registered related to this condition. The report gives survival analyses for a number of specific sites. (*Registrar General's Statistical Review for the year 1961, Supplement on Cancer,* H.M.S.O., 7s. 6d. net.)

Hospital Building in 1960s

Opening a new ward block at St. Albans City Hospital on 18 July, the Minister of Health, Mr. **KENNETH ROBINSON**, gave figures to show the accelerating pace of hospital building. In the five years ending September 1966, he said, building schemes to the value of £223m. were completed, representing well over half the total for the entire period of the National Health Service. The value of schemes in progress at the end of September last was £234m. New work to the value of £122m. was expected to be started during the current financial year.

Danger of Lead Poisoning

A warning was sent last week by Sir **GEORGE GODBER**, Chief Medical Officer, Ministry of Health, to medical officers of health in England and Wales stressing the need to guard against lead poisoning from battery casings used as fuel. In his letter Sir George refers to the incident in Bradford recently reported in the *B.M.J.* (1 July, p. 56) and to another in Rotherham in 1954, when two children died and many others were affected. He points out that plants may be found to contain lead where they have been grown on soil with a high lead content and that this could occur where battery casings have been buried at an insufficient depth or when ash from the burning of battery casings has been deposited in a garden.

Age of Consent

The Committee on the Age of Majority, appointed by the Lord Chancellor under the chairmanship of Mr. **JUSTICE LATEY**, reported last week. Its terms of reference were "to consider whether any changes are desirable in the law relating to contracts made by persons under 21 and to their power to hold and dispose of property, and in the law relating to marriage by such persons and to the power to make them wards of court."

Though consent to medical treatment was not specifically named, the committee felt qualified to recommend that consent at 16 should be established. In reaching this conclusion it found support in the B.M.A.'s memorandum of evidence, which stated that consent by a person of 16 or upwards who appeared to the doctor to be capable of understanding what was involved and of expressing his own wishes should be considered valid without confirmation by his parent or guardian (see *Supplement,* 30 April 1966, p. 119). It also noted that the practice of accepting consent at 16 had proved satisfactory. Nevertheless, the committee is strongly of the opinion that the doctor, "for reasons of ethics and prudence," should make contact with the parents of a minor (or the husband in the case of a woman) unless the minor refuses permission. In its view, if the age of consent is to be lowered, it becomes more than ever essential that the nature and extent of the proposed treatment should be explained to the patient by a *medical practitioner* (committee's italics), and that it should be stated on the consent form, and signed by the practitioner, that this has been done.

The committee recommends that young people should be free to give their blood at 18. It also recommtnds that they should be free to marry at this age without the consent of their parents or of the courts. (This accords with Council's choice of age in its memorandum.) Two dissenting members of the committee considered that society was justified in "leaning against" young marriage and recommended that parental or court consent to marry should continue to be necessary until the age of 21. (*Report of the Committee on the Age of Majority,* Cmnd. 3342, H.M.S.O., 15s. net.)

Society of Apothecaries of London

At a soirée held on 18 July the Master of the Society of Apothecaries of London, Mr. **HAROLD EDWARDS**, on behalf of the court, bestowed the Society's Gold Medal in Therapeutics for 1967 on Sir **PETER MEDAWAR**, F.R.S., in recognition of his eminence in the field of experimental medicine.

Sir Arthur Porritt

Sir **ARTHUR PORRITT**, Governor-General and Commander-in-Chief (designate) of New Zealand, has had the G.C.M.G. conferred on him.

People in the News

▶ Dr. **D. G. WALKER** has been appointed by the British Postgraduate Medical Federation to the post of part-time regional adviser in dental surgery for the four metropolitan and Wessex hospital regions from 1 October.

▶ Dr. **I. G. W. PICKERING**, Director of Prison Medical Services, has been appointed a member of the Prisons Board.

▶ Dr. **R. FRASER MACKENZIE** has been appointed medical officer, Eastern Region, British Railways.

▶ Dr. **KENNETH W. NEWELL** has been appointed director of a new W.H.O. division of epidemiology and communications science.

▶ **D. B. CLAYSON**, Ph.D., of Leeds University, has been awarded the title of professor in the department of experimental pathology and cancer research.

News in Brief

St. Christopher's Hospice, Sydenham, was opened by **PRINCESS ALEXANDRA** on 24 July. An account of the aims of the hospice was published in the issue of 15 July (p. 169).

PRINCESS ALICE, COUNTESS OF ATHLONE, formally opened this week a rehabilitation unit at Finchley Convalescent Home, London N., which admits patients from the National Hospital, Queen Square, and Maida Vale Hospital.

Grants and Awards

Research grants to Glasgow University include £32,500 (£6,500 a year for five years) from the Medical Research Council for research in the department of medicine, Western Infirmary, on iron and porphyrin metabolism and lead poisoning; £12,176 from the Nuffield Provincial Hospitals Trust to develop computer techniques in medical cardiology; and £35,000 from the Wellcome Trust towards the cost of a unit for cell culture in the department of biochemistry.

Grants totalling £9,433 have been made in the first series of Kodak awards (see *B.M.J.*, 4 March, p. 579). The largest (£3,000) will support research into stress in children separated from their mothers.

Coming Events

British Industrial Biological Research Association and Society of Chemical Industry (Food Group).—Symposium, "Current Developments in Food Manufacture and Food Safety Evaluations," 20 September, 2.30 p.m., School of Pharmacy, London W.C.1.

Birmingham and Midland Eye Hospital.—Postgraduate course in industrial ophthalmology, 2–6 October. Details from Secretary, Industrial Ophthalmology Course, Research Department, Birmingham and Midland Eye Hospital, Church Street, Birmingham 3.

Societies and Lectures

For attending lectures marked ● a fee is charged or a ticket is required. Applications should be made first to the institution concerned.

Wednesday, 2 August

STOKE MANDEVILLE HOSPITAL.—12.15 p.m., Professor J. Chassar Moir: History of the Obstetric Forceps

Friday, 4 August

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. K. M. Citron: clinical demonstration.

Appointments

BIRMINGHAM REGIONAL HOSPITAL BOARD.— B. T. O'Connor, M.S., M.Ch.Orth., F.R.C.S., F.R.A.C.S, (whole-time consultant orthopaedic surgeon and director of clinical studies to the Robert Jones and Agnes Hunt Orthopaedic Hospital); A. M. Geddes, M.B., M.R.C.P.Ed. (whole-time consultant physician with experience in communicable diseases to the East Birmingham group); G. H. Davies, M.B., F.F.A. R.C.S. (joint appointment of maximum part-time consultant anaesthetist to the United Birmingham Hospitals and the Birmingham (Selly Oak) group); M. R. E. Dean, M.B., D.M.R.D. (whole-time consultant radiologist to the Shrewsbury group); M. L. Cox, M.B., M.R.C.O.G. (part-time consultant obstetrician and gynaecologist to the Coventry group).

EAST ANGLIAN REGIONAL HOSPITAL BOARD.—W. F. Kerr, M.B., F.R.C.S.Ed. (consultant cardio/thoracic surgeon—main centre, Norfolk and Norwich Hospital); J. F. Pereira, M.B., F.R.C.S.Ed., D.O. (consultant ophthalmic surgeon, West Suffolk area).

HOME OFFICE.—The following medical officers have been appointed to H.M. Prisons as indicated in parentheses: B. Klassnik, M.B., D.P.M. and N. M D. Murthi, M B., D.T.M.&H., T.D.D. (Birmingham); I. P. James, M.B., M.A.N.Z.C.P., D.P.M., and M. C. Mitcheson, M.B., D.P.M. (Brixton); W. P. Hurley, M.B., D.P.M., and G. D. Stewart, L.R.C.P.&S.Ed., D.P.M. (Grendon); S. P. C. O'Reagain, M.D. (Liverpool); Freda S. Reed M.B., D.P.M. (Maidstone); Mary C. Ahearne M.B. (Manchester); B. D. Cooper, M.B., D.P.H (Parkhurst); W. A. S. Grant, M.B. (Pentonville); H. O'B. Howat, M.B. (Wakefield); A. W. Griffiths, M.R.C.S., D.P.M. (Wandsworth); M. Dafashy, M.B., D.P.M. (Wormwood Scrubs); B. K. Banerjee, M.B., D.P.M., and L. J. Glancy, M.B., D.P.M. (Risley Remand Centre).

MANCHESTER REGIONAL HOSPITAL BOARD.—N. Berlyne, M.B., M.R.C.P.Ed., D.P.M. (whole-time or maximum part-time consultant psychiatrist Oldham and District group); R. A. C. Jones, M.B., F.R.C.S. (whole-time or maximum part-time consultant neurosurgeon, Salford group); W. G. Owen, M.B., M.C.Path. (whole-time or maximum part-time consultant pathologist (with special interest in histopathology), Preston and Chorley group); J. W. Warburton, M.D., D.P.M. (whole-time or maximum part-time consultant psychiatrist, South Cheshire group); D. N. Hutchinson, M.B., Dip.Bact. (whole-time consultant bacteriologist, Preston and Chorley group and the Public Health Laboratory at Preston Royal Infirmary (joint appointment)); H. L. Goldwater, M.B., F.F.A. R.C.S., D.Obst.R.C.O.G. (whole-time or maximum part-time consultant anaesthetist, North Manchester, and the Booth Hall and Monsall groups); R. S. Phillips, M.B., F.R.C.S.Ed. (whole-time or maximum part-time consultant traumatic and orthopaedic surgeon, North Manchester group); C. S. Mellor, M.D., D.P.M. (part-time consultant psychiatrist (3 half-days weekly), Alcoholism Unit, Springfield Hospital); M. S. Shaikh, M.B., M.R.C.P.Ed. (whole-time or maximum part-time consultant physician in geriatrics, Ashton, Hyde, and Glossop group); G. Birchall, M.B., M.C.Path., D.Obst.R.C.O.G. (whole-time or maximum part-time consultant pathologist (with special interest in haematology), North Lancashire and South Westmorland group); F. P. S. Marriott, M.B., F.R.C.S.Ed. (whole-time or maximum part-time consultant surgeon, Bolton and District group).

NATIONAL HOSPITALS FOR NERVOUS DISEASES.—D. B. Ellis, M.B., F.F.A. R.C.S. (consultant anaesthetist).

NEWCASTLE REGIONAL HOSPITAL BOARD.—D. G. A. Westbury, M.B., D.P.M. (consultant in forensic psychiatry, Durham); T. Dowell, M.B., F.F.A. R.C.S. (consultant in anaesthetics, Sunderland); E. T. Young, M.B., M.R.C.P. (consultant in geriatrics, Wansbeck); R. D. Peduzzi, M.B., F.R.C.S. (consultant in general surgery, East Cumberland); I. A. Fraser, M.B., D.P.H., D.C.H., D.P.M. (consultant in mental subnormality, Prudhoe); G H. Bevan, M.B., F.R.C.S.Ed., D.O. (consultant in ophthalmology, Newcastle)

NORTH-EAST METROPOLITAN REGIONAL HOSPITAL BOARD.—M. J. Harfst, M.B., D.P.M. (consultant in mental subnormality to South Ockendon Group of Hospitals); A. Pringle, M.B., M.R.C.P. (consultant physician in general medicine to Enfield Group of Hospitals); C. S. Ratnatunga, L.M.S., M.R.C.P. (consultant venereologist to Tottenham Group of Hospitals).

SOUTH-WESTERN REGIONAL HOSPITAL BOARD.—A. B. Herring, B.M., M.R.C.P (consultant neurologist, West Cornwall/Plymouth areas); J. A. C. Strachan, M.B., F.F.A. R.C.S (consultant anaesthetist (neurosurgery), Plymouth clinical area); R. A. Caldwell, M.D., M.R.C.P., M.C.Path. (consultant pathologist, Devon and Exeter clinical area (Exeter)); N. Edwards, M.B., F.R.C.S. (consultant ear, nose, and throat surgeon, Bristol clinical area); D. G. Calvert, M.B., F.R.C.S. (consultant in general surgery, North Gloucestershire clinical area); E. S. Lower, M.R.C.S., D.P.M. (consultant psychiatrist, Bristol clinical area); B. Murphy, M.B., M.C.Path. (consultant pathologist, Devon and Exeter clinical area (Torquay)).

Universities and Colleges

CAMBRIDGE

M.B.—Angela M. Birch (by proxy).

ST. ANDREWS

QUEEN'S COLLEGE, DUNDEE

At a Graduation Ceremonial on 4 July the following degrees were conferred:

M.D.—R. S. Bluglass.

PH.D.—*In the Faculty of Medicine*: D. Hopwood.

M.B., Ch.B.—[1]B. Gribbin, [2]Dorothy E. Roskell, [2]D. A. Newsome, [2]I. D. Duncan, [2]Diana F. Archer, [2]Margaret L. Elder, [2]Helen L. Dally, [2]J. H. Saywell, K. S. Aarnes, Elizabeth-Anne P. Adams, O. A. Afonja, K. J. Ball, J. R. Bell, D. H. Birrell, M. D. Blundell, D. T. Bunn, Catharine A. Ellis (or Chambers), D. Clish, T. D. Culshaw, D. G. Dalrymple, J. A. Davey, C. W. B. De Voil, V. U. Dewar, Marion M. Faulds, B. J. Green, R. W. Green, J. M. W. Grieve, A. J. L. Hart, A. Holme, M. A. King, A. G. Laing, B. E. Lambert, S. A. Lebeter, Anne G. Henderson (or Levison), A. M. McGregor, Alison L. Maitland, A. Mills, Claire V. Moore, H. G. Morton, D. J. C. Neilson, A. J. Ogilvie, K. M. O'Neill, Doreen G. Pae, K. Persad, B. B. K. Pirani, Clare A. Pirie, W. T. N. Pitkeathly, P. H. Robinson, J. T. S. Sadler, Diana M. Shelton, Patricia M. Skilling, J. G. Slessor, I. S. M. Smart, D. M. Smith, J. G. Spencer, R. R. Sturrock, Christine Starkie (or Taig), D. R. Taig, I. W. Taylor, S. Thornber, W. C. Wakefield, Sylvia N. Pegg (or Wood), B. G. Woodruff.

DIPLOMA IN INDUSTRIAL HEALTH.—J. H. Abhechand, S. K. Dallal, N. Frank, G. McHugh, R. B. MacLaren, W. M. Prentice, H. J. Royall, J. C. Talbot.

DIPLOMA IN PUBLIC HEALTH.—H. M. Abbas, A. M. Davidson, K. S. Dawoud, E. M. Elamin, W. Geddes, A. A. Ibrahim, A. A. Idris, J. E. Kahirimbanyi, P. Psaila-Savona, G. Reid.

CERTIFICATE IN INDUSTRIAL HEALTH.—E. Bougas, J. Nathan.

[1]With honours. [2]With commendation.

GLASGOW

M.B., CH.B.—*In absentia* by diploma: N. I. McPhail, Christine E. Robertson.

ABERDEEN

At Graduation Ceremonies on 6 and 7 July the following degrees were conferred:

HON. LL.D.—A Neuberger, M.D., Ph.D., F.R.S., professor of chemical pathology in St. Mary's Hospital, University of London, since 1955.

HON. D.D.—A. Craig, M.B., D.T.M., Church of Scotland Medical Missionary, Charteris Hospital, Kalimpong, since 1937

M.D.—[1]N. B. Bennett, [2]M. L. Diament, [2]W. McA. Easson (*in absentia*), R. A. Bennet, R. B. Gove (*in absentia*), Audrey Sutherland.

PH.D.—*In the Faculty of Medicine*: H. N. A. F. Fattah, J. H. Steyn.

M.B., Ch.B.—[1]Kathleen I. M. Watt (*née* Buchan), [1]Elizabeth S. Whiteford, [1]A. D. H. Wyllie, [2]Helen M. Adam, G. G. Aitken, R. M. L. Anderson, A. J. O. Antao, E. H. H. Austin, G. Barclay, J. A. G. Beattie, I. S. D. Begg, Mary R. Bell, Helen M. A. Birkbeck, H. T. Bruce, A. F. Chung, D. A. Cook, Diane P. Cramb (*née* Lawrie), A. E. Donaldson, C. G. Duncan, Elizabeth J. W. Duthie, H. McM. Dyer, I. H. Farquhar, H. G. M. Forsyth, B. Gill, J. F. Gordon, R. B. Gordon, R. W. Grant, W. F. D. Hamilton, F. B. A. Harhara, D. R. Harper, E. C. Jamieson, F. D. Johnstone, I. C. Keith, Frances Kelly, B. McCombie, Shina A. MacDonald, G. H. McIntosh, Doris M. McLean, A. Macmillan, J. W. McNab, I. D. McPherson, Elizabeth-Anne Marsh, J. Masing, D. G. Millar, A. H. Milne, G. T. Morrice, A. Munro, R. Murray, D. Pariente, Heather M. Petrie, M. A. Pratt, C. T. Preshaw, M. K. T. Puni, D. Reid, K. B. Ritchie, G. L. Robertson, D. G. Ross, Jill M. Savege, Lise Schirmer, M. McG. Scott, A. T. Shennan, Margaret E. Stephen, Helen M. R. Stirrat, I. W. Strang, I. A. Sutherland, J. R. Tallach, P. B. Taylor, Kathleen A. Tocher, J. F. Walker, I. C. F. Wisely, Susan E. Wood.

The following prizes and medals were awarded during the session 1966–7: *Anderson Medal and Prize in Clinical Medicine*, Kathleen I. M. Watt, (*Proxime accessit*) A. D. H. Wyllie. *Cash Medal for M.D. Thesis*, Audrey A. Dawson. *Chanock Medal in Anatomy*, and *Durno Prize in Anatomy*, G. P. M. Crawford. *Dyce Davidson Medal in Materia Medica*, and *Ogston Prize in Surgery*, G. R. D. Catto. *Matthews Duncan Medal in Obstetrics*, and *MacQuibban Prize in Surgery*, A. D. H. Wyllie. *Fulton Essay Prize in Neurology (1966)*, J. W. McNab. *Harry D. Griffith Prize in Medical Physics*, Leong Y. K. Leung Sui Fung. *Keith Medal in Surgery*, D. R. Harper. *Lizars Medal in Anatomy*, J. R. C. Logie. *McQuibban Prize in Medicine*, Kathleen I. M. Watt. *Faculty of Ophthalmologists' Prize*, Susan E. Ridley. *Shepherd Memorial Medal in Surgery*, Elizabeth S. Whiteford. *Davidson Smith Prize in Child Health*, Elizabeth J. W. Duthie, (*Proxime accessit*) A. D. H. Wyllie.

Appointments.—Dr. R. E. Mackie (senior lectureship, Department of Mental Health), Dr. M. G. Lyall, Dr A. B. Matheson (terminable lecturers, Department of Anatomy); Dr A Q Gardiner (terminable lecturer, Department of Mental Health).

[1]With honours. [2]With commendation.

EDINBURGH

At a Graduation Ceremonial on 19 July the following degrees were conferred:

M.D.—D. H. Clark, W. F. Coulson, [1]D. Doyle, J. S. Fleming, J. D. E. Knox, H. J. S. Matthew, [2]E. B. Ritson, [2]B. J. Wilken.

CH.M.—[2]J. A. Campbell, [1]B. H. Colman.

D.LITT.—D. J. Guthrie.

PH.D.—*In the Faculty of Medicine*: J. D. Cash, [2]D. C. Flenley, H. C. Guldberg, M. G. Mustafa.

M.B., Ch.B.—A. D. Adams, I. A. Archer, A. A. M. Aluaqi, A. S. Banks, A. R. Barlow, E. W. Barnes, R. D. Barnes, H. W. Bauld, E. I. Beckett, R. A. F. Bell, Hilda F. Bennett, D. B. Bennie, J. J. K. Best, A. B. Blyth, Susanne Boyce, W. B. Broadbent, J. V. Brooke, M. J. K. M. Brown, D. G. D. Campbell, Judith A. Campbell, Rosemary A. Cathels, W. B. Clark, Shirley Clarke, Affra M. V. Cocks, N. J. Cooke, A. Craig, Mary M. K. Craig, G. A. Crouch, D. C. Cumberland, J. A. G. da Costa, M. P. Daly, Pamela Davidson, J. M. M. Dey, R. A. Dickson, R. G. Donald, D. S. Dummer, R. A. Fawcitt, Jane E. Fleischmann, G. I. C. Fletcher, Margaret R. Flux, I. S. Fraser, J. French, H. M. Gilmour, K. A. Grant, [2]D. I. Grieve, Claire E. M. Guthrie, A. H. Habel, T. K. Hanid, A. D. B. Harrower, P. V. Harry, C. S. Haw, D. B. G. Hawker, P. C. Heaney, R. N. Hodges, R. Hodkinson, E. P. Hughes, Gwendoline Hughes, N. G. Y. Huseini, M. L. J. Jesudason, M. H. Kaufman, A. J. King, Jennifer A. King, Alison Leach, O. Ll. Lloyd, J. B. Loudon, Anne C. Lowe, R. A. A. Macaulay, J. M. F. McClemont, D. M. MacDonald, T. D. McGhee, Elizabeth H. M. McIntosh, G. B. McIntyre, M. J. McKitterick, E. H. McLaren, A. Macleod, R. S. Miles, Evelyn McK. Millar, A. W. Morrison, S. D. Moss, Frances M. C. Neilson, R. J. Nixon, O. A. Oyemade, A. C. Parker, W. D. Paterson, Cynthia G. Patient, Elaine Pemberton, C. W. G. Peterkin, G. N. Phillips, Sheila Picken, D. Poole, B. Rapoport, J. Rees, K. C. Riddell, A. W. Rifkind, Elizabeth M. S. Robertson, R. Robertson, Sheena S. Robertson, J. Robinson, M. E. Rodgers, Teng-Siam (née Cheah) Rodgers, P. Roscoe, M. J. Rowe, J. A. Russell, P. R. Samuel, P. J. Scott, F. R. Sharp, A. C. A. Smith, J. H. Spenceley, C. Thomson, I. M. G. Torkington, R. D. Turner, N. J. Vetter, T. A. Wadrop, S. A. Walker, J. M. Wallace, I. E. West, R. J. West, J. Whyte, S. R. Wild, D. N. Williams, J. B. Woolridge, W. S. Young.

Diploma in Medical Radiodiagnosis.—Valerie A. Briggs.

Diploma in Social Medicine.—Muriel I. K. Berkeley, J. D. Egdell, A. C. Irwin, W. B. C. Robertson, Elizabeth M. Russell, J. M. Tainsh.

Diploma in Tropical Medicine and Hygiene.—M. Hafezuddin, H. Kabir, M. O. Abdullah, A. A. Ali, A. S. M. M. Haque, M. M. Khakoo, A. W. Khalil, C. P. Kilala, E. N. Mngola, A. S. Nakadar, G. A. Noori, M. R. Qureshi, A. Rahman, T. B. Thapa, A Z. A. Zaidi.

The following Fellowships, etc., were awarded in the Faculty of Medicine: *Ettles Scholarship and Leslie Gold Medal in Medicine*, J. A. G. da Costa and Alison Leach (jointly). *Scottish Association for Medical Education of Women Prize, Mouat Scholarship in the Practice of Physic, Beaney Prize in Anatomy and Surgery, Dorothy Gilfillan Memorial Prize, Keith Memorial Prize in Systematic Surgery, 1936 Year Class Prize in Surgery, Annandale Gold Medal in Clinical Surgery*, Alison Leach. *Buchanan Scholarship in Obstetrics and Gynaecology*, I. S. Fraser. *James Scott Scholarship in Obstetrics and Gynaecology*, P. Roscoe. *Conan Doyle Prize*, B. Rapoport. *Lawson Gifford Prize in Obstetrics and Gynaecology*, R. Robertson. *Murdoch Brown Medal in Clinical Medicine*, D. N. Williams. *Graduate Research Fellowships*, Elizabeth Edmond, C. F. A. Whelan. *Graduate Research Scholarships*, R. N. Baird, R. A. Clark, B. Hawley, Jean C. MacPhail, Marie M. Ogilvie, I. R. Williams. *Graduate Travelling Scholarship*, F. W. Winton. *Lawrence Poole Prize in Rehabilitation after Poliomyelitis*, K. Vainio. *William Leslie Prize in Medicine*, I. M. L. Donaldson. *Chest and Heart Association Scottish Branch Undergraduate Prize*, B. Covell and M. J. Rowe (jointly).

Appointment.—Dr. E. R. Jay (lecturer, Department of Diagnostic Radiology).

[1]Commended for thesis. [2]*In absentia.*

DUBLIN

Trinity College, School of Physic

M.D.—R. Sinniah.

M.B., B.Ch., B.A.O.—B. W. Abbott, C. W. G. Angus, Edith S. M. J. I. Bacik, M. Blackman, J. R. Bradshaw, Jill Burland, R. L. Crowdes, T. E. B. Dane, C. N. O'N. Digges, R. J. R. Elmes, R. J. Fitzgerald, D. S. Freedman, G. F. Gervais, Kathleen A. Huey, Hung Soo Loh, Brigid J. McGinn, Frances P. M. Malone, J. S. Martin, P. E. Michael, F. R. I. Middleton, Jacqueline H. J. Milliken, Gillian J. Montgomery, C. C. M. Morrison, M. Mowbray, J. R. Nixon, T. H. Peirce, D. A. H. Rolfe, K. Sarda, R. G. K. Watson.

Diploma in Psychological Medicine.—*Part I:* Gladys M. Caskey, Jane A. Devitt, Mary Green, P. M. Kelly, Ruth Mitchell, D. M. Peppard, Mary E. T. Sheridan, M. J. Sweeney, M. M. Vanya, Joyce H. Weir. *Part II:* S. A. Ahmed, A. D. Duffy, A. Gravina, S. B. Sachs.

Diploma in Gynaecology and Obstetrics.—B. A. M. Al-Chalabi, B. Al-Niami, M. Khonji, S. Nizami, Q. Pabaney, S. T. Suhaly.

NEWCASTLE UPON TYNE

In Congregation on 1 July the following degrees were conferred:

M.D.—J. L. Gibbons.

Ph.D.—*In the Faculty of Medicine:* N. Bolton, P. G. Britton, M. Worsfold.

M.B., B.S.—A. O. G. Adeuja, S. K. Adjei, G. J. Aitken, Penelope E. M. Allan, S. F. Baker, Rosemary J. Berry, Alison M. Binks, F. D. Burke, R. H. Burr, Elizabeth A. Byers, Anne P. Charlton, R. J. Collingborn, D. B. Coltman, Wendy R. Cooper, Lesley Craft, Margaret C. Davison, A. M. Deall, D. S. Dry, W. A. Duke, S.-E. Ekeid, Elizabeth M. Foreman, R. Garry, R. F. Gillie, Anne H. Hagyard, D. G. Harle, P. Harrigan, Mary U. Hickey, P. S. Hogg, M. F. Humphreys, J. Hunton, Alexandra M. Hutson, H. U. Ihezue, S. T. R. Isherwood, Moira Johnston, T. Kelly, R. Y. Kendal, Susan H. Kinghorn, Elizabeth A. Lidster, D. T. Lord, Elizabeth G. Maddison, D. C. Marr, B. Marshall, W. M. Melrose, T. L. Moody, M. J. Mowbray, Dorothy M. Muir, J. M. Myers, Jennifer M. Naisbitt, Margaret Ormston, R. A. Pearson, Rosalind M. F. Sanderson, B. D. Shah, D. R. S. Smith, I. Stafford, P. J. B. Tilley, A. K. Vaid, Margaret Walton, C. L. Wheeler, M. Wilkinson, P. Willis, H. G. Wills, P. D. Wright.

LONDON

Dr. P. Curzen has been appointed to the readership in obstetrics and gynaecology tenable at Charing Cross Hospital Medical School.

Dr. Katharine G. Lloyd-Williams has been appointed a representative of the university on the council of the Royal Free Hospital School of Medicine.

The following have been recognized as teachers of the university in the subjects indicated in parentheses: *Institute of Child Health*, Dr. M. C. Berenbaum, Dr. J. F. Soothill (immunology), Dr. June K. Lloyd (paediatrics). *London Hospital Medical College*, Mr. J. P. Blandy (surgery), Dr. J. S. Pegum (dermatology). *St. Mary's Hospital Medical School*, Dr. C. A. Cheatle (anaesthetics), Mr. A. J. Harrold (orthopaedics), Dr. Doreen Rothman (obstetrics and gynaecology), Dr. P. H. Fentem (physiology), Dr. A. P. Fletcher (biochemistry). *Institute of Psychiatry*, Dr. W. G. Dewhurst, Dr. M. G. Gelder, Dr. M. Ll. Rutter (psychiatry), Dr. C. Rashbass (physiology). *Middlesex Hospital Medical School*, Dr. G. Farrer-Brown (pathology), Dr. C. B. Hobbs (chemical pathology). *Royal Postgraduate Medical School*, Dr. J. R. Hobbs (chemical pathology), Dr. R. H. Thomlinson (experimental pathology). *Institute of Orthopaedics*, Mr. H. B. Stafford Kemp (orthopaedics). *Royal Free Hospital School of Medicine*, Dr. M. R. Wills (chemical pathology). *St. Thomas's Hospital Medical School*, Dr. D. A. H. Yates (physical medicine). *Institute of Obstetrics and Gynaecology*, Dr. J. H. Smitham (radiology). *St. Bartholomew's Hospital Medical College*, Dr. G. H. Fairley (medicine).

M.D.—J. F. Arthur, D. J. Galton, H. Hunter.

M.S.—A. W. F. Lettin.

Ph.D.—*In the Faculty of Medicine:* Rosalind H. M. Ballin, D. F. Biggs, R. N. Boyes, H. G. Dixon, P. J. Holloway, J. F. Howes, G. A. Khan, A. Nasrallah, M. S. Starr, J. Thomas, R. O. Weller, J. E. Rees, A. R. Salim.

The following candidates at the London School of Hygiene and Tropical Medicine have been approved at the examinations indicated:

Ph.D.—*In the Faculty of Medicine:* M. F. Coldman, D. J. Ringshaw, H. O. Obianwu.

Academic Postgraduate Diploma in Public Health.—A. B. Allen, R. M. Badminton, *M. L. Burr, P. S. C. Cheh-Seeyave, P. N. Christie, P. J. Christopher, P. H. Cima, I. J. Cope, I. P. Crawford, S. Dharmavaratha, J. V. Earle, D. M. Fanning, A. M. M. Faris, A. Frame, W. L. R. Gibb, N. Govan, Ann B. Gray, D. W. K. Heendeniya, W. R. Henwood, Rosemary A. Hill, Vera M. C. B. P. Hollyhock, J. P. Hutchby, E. G. A. Jackson, E. Kangesu, H. G. Knox, K. Kooros, J. G. McL. Mortimer, S. A. Orzeszyna, Elizabeth J. Pritchard, *M. G. H. Rogers, A. V. Sheard, M. V. Smith, R. Sundaresan, Christine M. Thompson, Betty P. Westworth, M. C. T. Wilkes, D. S. Wright, C. Yoshida.

Academic Postgraduate Diploma in Tropical Public Health.—N. A. Atoot, M. M. Ayub, M. M. O. Beiram, B. C. Dando, Y. P. Cope, A. J. N. M. De Campos, Q. y A. Ferrer, A. Jamshidi, F. M. Khalifa, A. O. Marquez, A. D. Niazi, Q. M. Qhobela, Fidelina Regis, *Hilary M. Rowson, F. M. Shattock, S. Wongthai, *Yap Siew Khim.

Academic Postgraduate Diploma in Applied Parasitology and Entomology.—G. H. Dukes, H. N. Espinola, M. S. S. Gassouma, B. W. M. Gooneratne, S. L. Gorbach, Salome H. Gyaw, Z. G. Hayatee, L. Ilmolelian, J. M. R. Jjumba, Mary E. J. Mansfield, S. J. Mchinja, *Patricia M. Preston, N. T. Talbot, U. Winn, R. A. Ward.

Academic Postgraduate Diploma in Clinical Medicine of the Tropics.—S. A. Barnett, Y. D. Coble, P. T. Fox, S. E. Sama, M. G. Schultz, S. Shaikh, H. Sherief, E. B. Smith, P. Suntharasamai, M. S. Wolfe.

*Awarded a mark of distinction.

BIRMINGHAM

At a Degree Congregation held on 7 July the degree of D.Sc. *honoris causa* was conferred on Sir Derrick Dunlop, M.D., F.R.C.P.

The title of honorary research fellow has been conferred on Dr. B. H. B. Robinson (Department of Experimental Pathology) and Dr. C. I. Scott (Institute of Child Health) for the period of their work in the University.

Appointments.—Dr. J. A. Bushman (research fellow, Department of Anaesthetics); Dr. J. Herbert (lecturer, Department of Anatomy); Dr. A. Munro (senior lecturer and first assistant, Department of Psychiatry).

LIVERPOOL

M.D.—M. J. Brindle, G. J. Fairhurst, W. F. W. E. Logan, J. A. Wilson, P. J. J. Wren.

Ph.D.—*In the Faculty of Medicine:* A. B. E. Abdalla, D. J. Etherington, R. M. Green, R. Kellner, Elizabeth M. O'Ryan.

Ch.M.—P. T. Bruce, G. E. Dimopoulos, G. Sreēnevasan.

M.Ch.Otol.—W. Y. Nasser.

M.B., Ch.B.—[1,3,4]D. Owens, [1,4,5]Christine I. Riley, [2,5]Lydia A. Ellidge, [2,5]Jennifer Hughes-Nurse, [2,5]Valerie M. Inchley, [2,4]Rosalie P. Newsome, D. J. Allan, J. R. Allen, R. S. Arnold, K. G. Barrand, R. V. Brittain, R. M. Broadley, P. T. Bull, C. Bunting, N. R. Burford, P. L. Burke, R. Burrows, P. Buscombe, T. J. Butler, Jennifer M. Caile, Lesley J. Carter, J. J. Chambers, Cicely R. Chandler, J. S. Christie, J. E. Cleary, Christine M. Coates, A. I. M. Cook, D. J. Cooper, R. F. Dale, Patricia A. L. Denson, C. H. Dickie, P. J. Dixon, D. C. Egerton, A. G. England, Jane Flanagan, Wendy A. Freaker, V. N. L. Gohil, Margaret E. Green, M. G. E. Greensmith, Sandra L. Gregson, S. K. Hardy, D. S. Heath, Rosemary Henley, W. S. Henry, Adele M. Horley, J. R. Hughes, Doris K. Jagodzinska, J. T. Jenkins, D. Jenkinson, J. G. Jones, M. B. Jones, P. J. Lane, C. A. Lund, E. G. Lyon, Barbara M. McDougall, Catharine McGuire, G. S. Macmillan, Hilary J. Marcham, M. E. Mass, C. J. Molodynski, I. J. F. Morle, Valerie M. J. Muir, Edina M. Nakielna, C. W. Nicholls, Ruth D. Partridge, P. B. O. Pencharz, I. D. Plant, Celia M. Prinn, R. I. Pritchard, M. P. Quinlan, Winifred J. Robson, M. J. Rose, P. K. M. Rostron, K. Rowland, Carol J. Sage, A. W. Smerdon, S. L. Snowdon, C. W. Spencer, D. S. I. Taylor, A. Thomas, I. D. Tyson, [5]M. K. A. Varia, D. Vasey, D. M. Vickers, T. R. Watson, P. Webb, M. Weiner, P. A. Westwood, Elizabeth V. Williams, K. F. Woo, D. N. Yardley. *Passed in separate subjects:* A. G. Brown and A. J. May (medicine and obstetrics); J. J. Cockburn, M. Dalziel, J. R. Garcia-Valarino, and P. J. Gore (surgery and obstetrics); C. J. Hope (medicine and surgery).

Appointments.—Dr. D. V. Roberts (senior lecturer, Department of Physiology); Dr. K. Lubkiewicz (lecturer in child health); Dr. K. N. Brown, Dr. A. A. Deutsch, Dr. I. H. Emery, Dr. T. P. E. Nener (demonstrators in anatomy).

[1]With first-class honours. [2]With second-class honours. [3]Passed with distinction in medicine. [4]Passed with distinction in surgery. [5]Passed with distinction in obstetrics and gynaecology.

LEEDS

M.B., Ch.B.—[1]N. C. Barraclough, [1,2,3]J. C. Cawley, [1]D. F. Chapman, [1]R. Dakin, [1]Jean M. Graveney, [1]Rosemary A. Hoar, [1,3]Carolyn E. M. Jones, [1]V. K. Modgill, [1,2]G. J. S. Parkin, [1]M. R. Warren, [1,2]R. Wray, Susan J. Allan, D. W. Allen, F. Allenby, M. R. Banks, R. M. Barr, Jane L. Baxter, J. Bentley, Diana E. Brice, Jane E. Burrell, Gladys M. Cammish, Hazel P. Compton, J. S. Donohue, Sheila M. Donohue, S. W. Farrar, J. D.

Fenwick, J. A. Finnegan, M. C. Galvin, G. C. Goodman, G. P. Hall, J. L. Hancock, K. Hutchinson, Cathleen M. Jennings, Lucia A. Jones, Angela L. King, K. Liddell, R. W. Lodge, K. C. MacIntosh, A. R. MacKay, N. R. Matthews, M. H. Mehta, Mary S. Morris, P. M. Norton, J. V. Parkin, H. I. Rein, M. E. T. Roberts, G. B. Sacks, P. A. Shand, S. H. Shaw, Jennifer E. Storer, S. G. Tan, R. C. True, D. F. Wigglesworth, B. D. Willis.

D.P.M.—J. L. Barton, Beryl M. Bromham, A. K. Choudhuri, W. Galley, M. A. Hill, C. R. Samanta, Jenifer A. Shaw.

[1] With honours. [2] With distinction in medicine. [3] With distinction in obstetrics and gynaecology.

SHEFFIELD

Titles conferred.—Dr. J. K. A. Beverley (reader in medical microbiology); Dr. V. Dubowitz (reader in child health).

Appointments.—Mr. D. C. A. Bevis (full-time senior lecturer in obstetrics and gynaecology); Dr. I. B. Pearson (full-time lecturer in psychiatry); Dr. J. R. Cox (part-time clinical teacher in medicine); Mr. I. Hopper (part-time honorary clinical tutor (ear, nose, and throat)); Dr. P. G. Small (part-time honorary clinical tutor (radiology); Dr. R. S. Smith (part-time honorary lecturer (haematology) within the Department of Pathology); Mr. D. F. L. Watkin (part-time honorary clinical tutor (surgery)).

QUEEN'S UNIVERSITY OF BELFAST

M.D.—[3]S. S. A. Fenton, W. B. Loan, R. A. McNeill, R. H. McNeilly, W. W. Ramsay, T. J. Robinson, J. O. Woods.

PH.D.—*In the Faculty of Medicine:* D. W. Barron, J. S. Chopra, P. Froggatt, A. G. Garg, A. H. M. Lutfi, S. P. Parbhoo, [3]M. N. Rashad.

M.B., B.CH., B.A.O.—[1]P. Kennedy, [2]Helen Mawhinney, [2]J. S. Robinson, I. O. Achike, N. A. Akingbehin, L. L. Bailie, P. J. S. Baker, J. D. Boyd, D. A. Boyle, S. Brown, Elizabeth M. Bryars, P. O. Burton, J. G. Camblin, Ruth E. Carson, Frances Chambers, W. J. Charles, M. J. Cinnamond, P. F. Crowe, Judith A. Dennis, R. E. Dibble, Mary E. C. Donnelly, R. K. Eccles, F. R. Elder, Margaret E. L. Elliott, Mary E. B. Elliott, F. B. T. Forbes, J. H. Gaston, D. H. M. Groves, B. D. Hanna, J. R. W. Harris, T. W. Hayes, Mary J. Hollinger, Eileen A. Irwin, R. G. G. James, H. A. Jefferson, H. C. Johnston, J. E. Johnston, P. G. M. Kelly, Barbara E. Kernohan, A. R. F. Kerr, Barbara Leitch, A. G. Leonard, W. D. McCallum, R. J. McClelland, Margaret E. McCrory, R. McK. Martin, R. Millar, T. D. Miller, Jennifer A. Milligan, Margaret R. Mitchell, R. C. Montgomery, B. J. F. Morgan, [3]T. C. M. Morris, C. K. Munro, Rosemary J. Orr, J. R. Palmer, F. Patterson, Josephine M. Patterson, B. Peoples, M. R. Phillips, G. F. W. Price, H. C. Ramsey, J. W. Richardson, Joan A. Russell, [3]S. M. Then, Elizabeth R. Trimble, S. Z. H. Wafa.

[1] First-class honours. [2] Second-class honours. [3] *In absentia.*

BRISTOL

M.B., CH.B.—[1] [2]Elizabeth J. Leese, [1]Barbara R. A Maddox, [1]I. M. Vickery, C. Adey, G. A. J. Appleby, A. F. Avery, A. A. J. Barros D'Sa, R. E. Barry, A. F. Boyles, B. J. Burke, Prunella E. Caville, S. K. M Chan, Margaret C. Clark, P. B. Clark, A. G. Clarke, D. F. Cochrane, Yahia F. Dajani, Maureen I. Delves, D. W. Felce, Susan Gage, D. W. R. Gibson, T. J. Hamblin, W. A. V. Henderson, Vivien M. Hesketh, J. D. L. Holroyd, Margaret S. Jones, Sandra E. Mooney, W. J. Moore, J. F. Morris, H G. Oon, D. Poole, M. B. Roberts, M. J. Y. Ruck, [2]G. B. Salmon, Rosemary J. Simpson, D. J. T. Webster. *In Section I only:* R. M. Gannaway. *In Section II only:* A. J. Brown, B. J. W. Pingree.

M.D.—Bimla Arora, June M. Brown, P. F. Harris, E M. Sedgwick, I. Surveyor.

CH.M.—R. A. Sellwood.

PH.D.—*In the Faculty of Medicine:* L. M. Silverstone.

Appointments.—Dr. J. D. M. Blayney, Dr. A. E. B. Giddings (demonstrators in anatomy); Dr. J. Gough (lecturer in pathology); Dr. P. S. Hasleton, Dr. D. Robertson, Dr. M. R. Thompson (demonstrators in pathology); Dr. D. J. Moffatt (lecturer in anatomy).

[1] With second-class honours. [2] With distinction in public health.

ROYAL COLLEGE OF SURGEONS OF ENGLAND

On 6 July Mr. H. Osmond-Clarke (London Hospital) and Mr. Robert V. Cooke (Bristol Royal Hospital) were re-elected and Mr. George Qvist (Royal Free Hospital) was elected Members of the Council of the College.

ROYAL COLLEGE OF SURGEONS OF EDINBURGH

At a recent meeting of the College the following candidates having passed the requisite examinations were admitted ordinary Fellows:

S. M. Aga, A. U. Ahmed, S. H. Aiyar, S. T. Al-Mufti, Md. N. Amin, M. Anwar, C. K. Asavanich, Min Aung, P. S. Bajaj, M. R. Baylis, R. Buntwal, A. F. G. Campbell, C. L. Chakrabarty, T. D. Chatterjee, K. A. Ul H. Cheema, F. Chi-Yan Cheng, J. F. Clegg, B. K. Devgan, W. A. Downie, M. S. H. El-Sawah, T. A. H. English, B. O. Fasehun, C. B. D'A. Fearn, F. Fleming, J. B. McG. Fleming, M. V. L. Foss, P. V. Godbole, J. H. Goldin, J. M. T. Griffiths, D. H. Gudgeon, S. S. Guindi, Om-Prakash Gupta, J. G. Guy, A. Hai Khan, K. A. Haq, K. P. Hardas, S. M. Hasan, A. I. Hasham, N. Hazari, A. D. Heath, K. M. Helmi, L. Henkel, D. A. W. Hopkinson, I. Hopper, M. J. S. Hubbard, A. K. C. Hui, J. O. Ikpeme, R. R. Ingle, S. Iskander, M. R. Islam, E. A. Jangda, P. J. E. Johnson, R. H. Johnson, V. K. Kak, V. K. Kapur, A. B. Kargbo, S. J. Karran, S. P. Kaushik, A. S. M. Abdul Khaleque, A. M. Khan, A. A. Kiely, A. K. S. Koh, A. D. W. Maclean, V. I. McCusker, J. J. Maeda, G. Mah, F. Mahmood, (Mrs.) Sabiha Mahmood, B. J. Masakorala, I. A. Miller, A. G. Mina, B. N. Misra, D. K. Mukherjee, D. K. Murray, M. R. Nicoll, J. N. Norman, K. D. Okey, D. F. Omalley, J. R. Pandey, (Miss) Naima S. Panow, J. D. Patel, R. Plotkin, B. J. Preston, (Miss) Zarina S. Qureshi, K. K. Ramalingam, M. H. Randhawa, M. J. Rao, M. K. Sahasrabuddhe, S. L. Sandhir, R. N. Sapsford, T. G. G. Scott, R. A. Sells, N. Selvarajah, R. P. Sengupta, P. H. Shah, G. Sham Sunder, J. D. Shaw, D. C. Shove, S. K. Sil, D. J. Simon, M. L. Singh, P. Singh, G. J. A. Siriwardena, C. L. K. Ssali, P. Y. F. Taikie, T. A. Talaat, R. K. Thakore, R. Thammari, J. Thomas, S. Venugopalan, T. R. Verma, A. Wahab, J. R. Wambwa, J. G. Wheeler, A. R. B. El Zawawi, A. F. M. Zuaiter.

At a recent meeting of the College the Honorary Fellowship was conferred upon Sir David Cuthbertson.

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

At a meeting of the College held on 3 July J. R. Ayers was admitted *in absentia* Fellow *qua* Surgeon.

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

At a meeting of the College held on 2 June the following were admitted to the Fellowship:

R. H. Bland, W. H. Hood, W. M. O. Purcell, J. C. McGoldrick, L. G. McElearney, M. D. Joyce, A. J MacDonald.

The following were admitted to the Membership:

F. R. B. Brown, A. T. Carty, E. B. Casey, Hean-Tat Goon, D. M. McCarthy, G. H. Tomkin, R. P. Towers.

At a meeting of the College held on 30 June the President, Professor Alan Thompson, admitted the following to the Licence in Medicine and Obstetrics:

W. T. Bishop, J. M. Blankson, S. Bokhary, S. A. Boodoosingh, R. A. Bourke, A. A. Bulbulia, M. A. H. Coovadia, S. Covenden, K. Dansoh, L. S. Dassama, R. Doraisamy, H. G. Falkenberg, I. R. Ghelani, R. A. Gorczak, M. S. Haffajee, R. F. Harrison, P. R. Hosein, C. F. E. Hudson, G. D. Hurley, P. J. Johnson, R. A. Joseph, Z. K. Kalapesi, R. Kānapathipillai, J. B. Kelly, M. Khan, M. A. Khan, M. Kirwan, J. A. Kirkby, M. M. Lee Chong Ken, M. H. Lokhat, G. R. R. Maharaj, J. D. G. Malone, K. P. Manning, I. S. Mebitaghan, J. A. Milne, M. Minty, E. M. Moola, A. K. Mula, S. L. B. Musani, M. B. McGill, H. C. O'Neill, O. O. K. Oye, F. M. Panchbhai, H. D. Patel, V. C. Patel, R. Ramdenee, R. N. Ramgoolam, R. K. Rattan, R. Ryan, J. O. Sehindemi, M. A. Shah, F Shannon, B. O. Soyemi, P. S. Tilluckdharry, Olu-Olusanya, L. Tunwashe, N. K. Whelan, Wong Peng Chee.

ROYAL COLLEGE OF SURGEONS IN IRELAND

On 5 July the Final Fellowship in Otolaryngology was conferred on the following candidates:

L. R. C. Bain, A. G. Evans.

On 7 July the Fellowship in Ophthalmology was conferred on the following:

F. L. Lavery, P. A. Tan.

COLLEGE OF PATHOLOGISTS

The following founder members have been promoted to Fellows:

M. K. Alexander, S. S. Alexander, B. E. Andrews, K. C. Basu Mallik, Isobel P. Boswick, R. P. Bradshaw, J. C. Burne, H. Caplan, H. R. Colquitt, I. M. P. Dawson, J. C. Edozien, A. H. Emslie-Smith, A. W. H. Foxell, R. K. Gadgil, N. R. Grist, W. A. Harland, W. G. Henderson, R. A. Holman, J. B. Howie, M. S. R. Hutt, K. G. Irving, H. C. Jeffrey, W. J. Jenkins, A. Kertesz, M. B. King, J. Kohn, C. J. P. La Touche, J. K. Lucas, R. H. McInroy, T. Manners, A. K. Mant, C. E. Marshall, K. M. Mattocks, M. S. Millard, D. L. Mollin, B. P. L. Moore, R. A. Neely, R. C. B. Pugh, S. S. Raphael, D. S. Ridley, G. B. S. Roberts, F. J. C. Roe, P. B. Schofield, G. B. D. Scott, J. G. Selwyn, J. A. Shrigley, D. R. Smith, P. B. Stones, A. D. Thomson, R. P. Towers, K. A. D. Turk, S. O. Waller, J. B. Walter, G. K. Welch, J. P. Whitehead, K. M. Win, L. Wolman, R. C. Woodcock, V. Wynn, A. Wynn-Williams, F. Fulton, Doris C. Peiris.

Deaths

Hutt.—On 8 July 1967, in St. Bartholomew's Hospital, London, Charles Wayte Hutt, M.B., B.Chir., of Minster, Isle of Sheppey, Kent, aged 56.

Kirkham.—On 16 July 1967, at his home, 59 Knowle Avenue, Ainsdale, Southport, Arthur Welsby Kirkham, M.B., Ch.B., aged 71.

MacDonald.—On 18 July 1967, in hospital, Donald Alexander MacDonald, M.B., Ch.B., of Chadwell Heath and Romford, Essex.

Corrections

Allopurinol.—We regret that the mention of allopurinol in the Today's Drugs article on "Hazards of Drug Prescribing in Pregnancy" (22 July, p. 220) was inaccurate.

Allopurinol acts by inhibiting xanthine oxidase and it is a valuable and relatively safe drug for use in gout and in some other conditions of hyperuricaemia. Thus allopurinol has been used as an adjunct in cancer chemotherapy to diminish hyperuricaemia and to improve the chemotherapeutic index of 6-mercaptopurine, which is oxidized by xanthine oxidase. The toxicity to the host of this combination is not necessarily increased to the same degree as is toxicity to the tumour. Allopurinol has not been shown to be teratogenic in man, neither is it mainly used in cancer treatment. The sentence in the article should therefore have read: "Apart from thalidomide, these are drugs mainly used in the treatment of cancer—antimetabolites (such as methotrexate and 6-mercaptopurine), alkylating agents (such as chlorambucil), and antibiotic substances (such as actinomycin D)."

Cyclandelate.—The manufacturers of Cyclospasmol have drawn attention to the article on cyclandelate in Today's Drugs, 3 June, p. 622. A starting dose of 100 mg. three times daily was recommended. Cyclospasmol is no longer manufactured in 100-mg. tablets, and the manufacturers recommend a starting dose of 200 mg. four times a day, which may be raised to 1,600 mg. daily if necessary. The recommended maintenance dose is 200 mg. b.d.

We regret that the name of the publisher, Butterworth & Co. Ltd., London, was omitted from the review of *Clinical Surgery: Abdomen and Rectum and Anus*, edited by Professor Charles Rob, Mr. Rodney Smith, and Sir Clifford Naunton Morgan (22 July, p. 224).

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON W.C.1. TELEPHONE: 01-387 4499. TELEGRAMS: *Aitiology, London W.C.1.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs.

ADVERTISEMENT AND SUBSCRIPTION ORDERS should be addressed to The Manager at B.M.A. House, London, or at 415 Bourke Street, Melbourne, Victoria, Australia.

MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the British Medical Association, B.M.A. House, London, or to the Scottish Secretary, B.M.A. Scottish Office, Drumsheugh Gardens, Edinburgh.

BRITISH MEDICAL JOURNAL

LONDON SATURDAY 5 AUGUST 1967

Pointers

Common Market: Movement of doctors (p. 326).

Food-vending Machines: Public health aspects (p. 325).

Chest Pain after Myocardial Infarction: Patients with left chest pain with or without angina had highest neuroticism scores, according to Professor R. R. H. Lovell and Dr. A. Verghese from Melbourne, Australia (p. 327). Leader this page.

Measuring Iron Absorption: Three radioisotope techniques compared by Dr. J. A. Lunn and colleagues (p. 331).

Squint: Demographic and social factors in Manchester patients surveyed by Drs. A. M. Adelstein and J. Scully (p. 334). Leader at p. 324.

Hormones and Breast Cancer: Dr. B. A. Stoll discusses role of progestins in management of postmenopausal patients (p. 338).

Chronic Heart Block: In a post-mortem study by Drs. M. J. Davies and colleagues, this was associated with coronary artery disease in only eight out of 53 specimens (p. 342).

"Instant" Urine Culture: Drs. D. Guttmann and G. R. E. Naylor report satisfactory results using a dip-slide technique (p. 343).

Hazard of Peritoneal Dialysis: Sodium uptake may account for acute heart failure in hyponatraemic patients, reports Dr. J. D. Swales (p. 345).

Thalassaemia and Hydrops Foetalis: Dr. D. Todd and colleagues relate hydrops foetalis with homozygous thalassaemia in Hong Kong Chinese (p. 347).

Short Reports: Study of virus antibodies in subacute sclerosing panencephalitis (p. 350). Diffuse systemic sclerosis with abnormal liver and gall bladder (p. 353).

Rise of Pathology: Professor C. H. Browning tells how pathology became a career (p. 359).

Protein Metabolism: Meeting at R.C.P. (p. 362).

Canadian Medical Association: Scientific sessions at Centenary Annual Meeting (p. 364).

M.R.C. Report: £12.8m. for research (p. 366).

Adder Bite: Its management (p. 367).

Cannabis: Trepanning experiments (p. 367).

Geriatric Patients: Co-ordination of services is "long overdue" (p. 367).

Abortion Bill: Amended in the Lords; Bill's future (p. 380).

G.M.S. Committee (Scotland): Report of meeting, *Supplement* (p. 109).

Chest Pain after Infarction

Chest pain is common among patients who have had a myocardial infarct. In the first few days after the infarct pericarditis is usually responsible, but arrhythmias may bring on ischaemic pain. More rarely pain in the first week heralds rupture of a papillary muscle or of the interventricular septum, though then severe dyspnoea and shock predominate. Pulmonary embolism becomes more frequent in the second week, and it may be confused with the post-myocardial infarction syndrome, which begins to occur at this time. Angina pectoris usually becomes evident as the patient starts to return to normal activity, though it may be felt earlier. These and other extra-cardiac causes need consideration before recurrent chest pain is attributed to extension of infarction, a diagnosis which is usually wrong.

Later in their convalescence patients may continue to feel pain of various kinds. Most experience at least transient discomfort,[1] and pains are often of more than one type. Angina pectoris is the most frequent of those which become established, though there are few systematic surveys of its incidence. In one series[2] about half the patients with no previous angina had developed the symptom when examined two to five years after their infarct. J. H. Palmer[3] found it in about 60% of patients after recovery from infarction (half of these had experienced it before their infarct). The most important feature in the diagnosis of this pain is its relationship to factors which precipitate or relieve it.

It has been estimated[4] that the post-myocardial infarction syndrome complicates 3–4% of cases of myocardial infarction. The complete syndrome is a triad of pericarditis, pleurisy, and pneumonitis, and it is most frequent two to six weeks after the infarct, though it may appear earlier or several months later. It is characterized by prolonged and recurrent chest pain and fever and by a strong tendency to relapse. Typically the pain is pleuropericardial, aggravated by breathing or change in posture. A pericardial friction rub is heard in 80% of patients with the syndrome, and pleural and pericardial effusions are common. The syndrome appears to be the result of an autoimmune response to injured myocardium and thus to resemble the post-cardiotomy syndrome. It is self-limiting and often requires no treatment apart from reassurance and relief of pain. Corticosteroids lead to dramatic improvement, but relapse often follows their withdrawal. Anticoagulants are dangerous and are contraindicated.

Professor R. R. H. Lovell and his colleagues in Melbourne have recently interested themselves in chest pain following myocardial infarction. During a follow-up period of between six months and three years 38% of their patients developed angina.[1] The next most common symptom was a pain in the left chest, which occurred, without angina, in 9% of the patients. Other authors[4 5] have commented on the occurrence of left chest pain after infarction and have found a similar incidence. This pain sometimes seems to upset patients more than does angina pectoris, which is more

© *British Medical Journal*, 1967. All reproduction rights reserved.

predictable. It is usually described as being of a steady dull aching character and of mild to moderate intensity. It is not directly related to exertion but tends to occur towards the end of the day and often seems to come on when a patient has exerted himself rather more than he feels he ought to have done. It is frequently affected by movement of the body, and many patients have areas of localized tenderness over the chest.[6]

The mechanism of this left chest pain remains uncertain. It is unlikely to be ischaemic in origin, and has been likened to the pain of Da Costa's syndrome. It appears to be correlated with responsiveness of the sympathetic nervous system,[7] and Professor Lovell and Dr. A. Verghese show in their paper published this week in the *B.M.J.* at page 327 that it is also linked with neuroticism. They find in addition that patients with left chest pain tend to be long and narrow in body build and to be less fat than others. The authors indicate that these features have been shown to be linked with constitutional neuroticism and suggest that it might be worth trying to identify early in convalescence patients likely to develop these pains. Some of the disabling features of the pain might then be prevented. Once anxiety about it has been met with adequate reassurance and explanation the pain usually disappears or at least ceases to worry the patient.

Left chest pain has also been compared with the "frozen shoulder" and "shoulder-hand" syndromes, usually attributed to reflex muscular spasm and disturbances of sympathetic innervation. Disuse also is probably important, and these conditions are seen less frequently now that early mobilization after infarction is encouraged. They had previously been described as occurring in 10–20% of patients. Persistent pain may develop in one or both shoulders, usually with tenderness and limitation of movement.[8] Sometimes there is wasting of the shoulder muscles. In a minority of patients the hands are also affected, with stiffness, pain, swelling, and discoloration.[9] Dupuytren's contracture and other trophic changes are described. The pain can persist for many months, and may recur. Physiotherapy often helps, and infiltration with procaine or hydrocortisone may also do so.

Any pain in the chest or arm which occurs after the pain of myocardial infarction is commonly taken by the patient to indicate serious cardiac disease. The doctor too may misinterpret its significance or unintentionally transmit anxiety to the patient. Rehabilitation is then often held up without need, and A. J. Goble and his colleagues[10] have given a dramatic description of the incapacity which may ensue. It is the doctor's task to prevent this.

[1] Verghese, A., and Lovell, R. R. H., *Brit. med. J.*, 1966, **2,** 1102.
[2] Solem, J. H., Helle, I., and Jörgensen, W., *Acta med. scand.*, 1963, **174,** 315
[3] Palmer, J. H., *Quart. J. Med.*, 1937, **6,** 49.
[4] Dressler, W., *Arch intern. Med.*, 1959, **103,** 28.
[5] Edwards, W. L. J., *Amer. Heart J.*, 1955, **49,** 713.
[6] Prinzmetal, M., and Massumi, R. A., *J. Amer. med. Ass.*, 1955, **159,** 177.
[7] Nestel, P. J., Verghese, A., and Lovell, R. R. H., *Amer. Heart J.*, 1967, **73,** 227.
[8] Ernstene, A. C., and Kinell, J., *Arch. intern. Med.*, 1940, **66,** 800.
[9] Johnson, A. C., *Ann. intern. Med.*, 1943, **19,** 433.
[10] Goble, A. J., Adey, G. M., and Bullen, J. F., *Med. J. Aust.*, 1963, **2,** 975.

Risky Grandmothers in Rh Disease

Red blood cells from a foetus can pass through the placenta into the mother's blood stream, and most of this leak occurs during labour. It is this leak that sensitizes an Rh-negative mother who has an Rh-positive foetus, so that Rh-antibodies are produced by the mother's immunological system. When the mother becomes pregnant again she already has some Rh antibodies in the blood stream, and they can pass the placenta and affect the red cells of an Rh-positive foetus.

But often this sensitization does not occur. Figures vary from 1 in 19 to 1 in 23 of expected pregnancies, so that the incidence of children with erythroblastosis is much less than theoretically expected.[1] One of the attempts to explain the deficit has involved the role of the grandmother of the affected child—that is, the mother of the Rh-negative woman who has an Rh-positive child. It is sometimes not realized that maternal red blood cells can pass the placenta into the circulation of the foetus. R. R. Race and Ruth Sanger show from published reports that this can happen in 1 in 6 pregnancies or even more often.[1] Two theories about the effect of this maternal invasion have been proposed. One theory suggests that the passage of maternal cells may induce immunological tolerance in the foetus; the other theory is directly opposed and suggests that the passage of maternal cells increases the liability of the child to respond to Rh stimulation in later life.

Jane F. Taylor,[2] of Columbus, Ohio, has set out to investigate which of these theories is likely to be correct. She has done this by examining a series of families each consisting of a grandmother, her Rh-negative daughter, and the daughter's children. When ABO blood groups of mother and child are incompatible, foetal Rh-positive cells that cross the placenta may be destroyed before they are able to induce sensitization in the Rh-negative mother; consequently such families where this might occur were not included in the trial. She also eliminated any mothers who had been transfused, and did not include any non-white families. With these limitations, 157 out of the original 236 families were included in her trial and they were derived from two groups: families in which the mother had had a child affected by erythroblastosis in any pregnancy, and families referred for routine prenatal testing in which the mother had had at least three Rh-positive children none of whom had developed erythroblastosis. The grandmothers, the mothers, and the children all had their ABO and Rh groups determined, and erythroblastosis was diagnosed on clinical evidence and the occurrence of a positive direct antiglobulin test with the child's red cells and the presence of Rh antibodies in the mother's serum.

The results showed a statistically significant excess of Rh-positive grandmothers in the families who had an erythroblastotic child. In families with Rh-positive grandmothers 79% of the children had erythroblastosis, whereas in the families with Rh-negative grandmothers 60% of children were affected. By an ingenious calculation Taylor showed that the effect of the Rh-positive grandmother was equivalent

[1] Race, R. R., and Sanger, R., *Blood Groups in Man*, 1962, 4th ed., p. 387. Oxford.
[2] Taylor, J. F., *New Engl J. Med.*, 1967, **276,** 547.

to one Rh-positive pregnancy. Consequently Taylor firmly supports the view that the passage of maternal cells from an Rh-positive mother to her Rh-negative female foetus means that when the daughter bears children in her turn she will be more, not less, liable to have an affected child if her husband is Rh-positive. And the risk of erythroblastosis occurring in the daughter's children is about equivalent to one Rh-positive pregnancy.

Taylor also cites data which suggest that for the majority of Rh-negative women who have Rh-positive husbands the first child to be affected is most likely to be that of the third pregnancy. But the data from the examination of grandmothers suggest that if the woman has an Rh-positive grandmother the first affected child may well come from the second pregnancy. However, mothers in these circumstances should not receive too gloomy a prognosis from their medical advisers, because the rule still applies that only about 1 in 20 pregnancies that might result in a child affected by erythroblastosis actually does so.

Disorders of Defaecation in Children

Disorders of bowel habit in children are notoriously difficult to manage. To the mother failure in toilet training is considered to be a reflection upon herself, and she may make strenuous efforts to conceal the evidence of faulty control of the bowel in her child from relatives, friends, and doctors.

In considering the problem of abnormal bowel habits in children a clear distinction must be made between organic and "functional" disease. Apart from anatomical deformities such as anal stenosis, Hirschsprung's disease is the most important organic condition which must be considered. Symptoms of this disease are invariably present from the neonatal period, with prolonged periods without a bowel motion and accompanied by extreme gaseous distension of the abdomen or actual intestinal obstruction. The infrequent stools are small and "rabbity" in type, but occasionally an infant may present with severe diarrhoea. Thus any disorder of bowel habit with infrequent stools which comes on after a period of months or years of normal defaecation is almost certainly not due to Hirschsprung's disease.

In infancy, however, the passage of hard stools is not uncommon and may cause an anal fissure, with a resulting fear of defaecation. This may ultimately lead to voluntary retention of the faeces, which in turn become hard and painful to pass. A vicious circle may then be set up, which may last for many weeks or months. In the older child, on the other hand, faecal soiling is more difficult to evaluate. A detailed history will usually show whether the soiling is due to leakage of soft faecal material through the anal sphincter, or whether it is due to an involuntary or voluntary act of defaecation which is inappropriate in time and place. Constant faecal soiling is due to the softening of impacted faeces in the rectum and anal canal or to mucus and faeces leaking round a firm faecal mass. There is usually a history of a normal bowel habit until a period of constipation which is followed by faecal soiling: the cycle may be ended by the passage of a very large motion often described in revealing terms,[1] after which the sequence will be repeated. The circumstances which set off this dismal story can often be easily identified. A period of mild dehydration with constipation may accompany a febrile illness, a spell of hot weather, a long car journey, or a summer holiday—or an admission to hospital for a minor operation, or starting school, may be the initial cause. There is obvious perianal soiling, the anal sphincter is lax, and firm faeces fill the anal canal. There is no question of voluntary defaecation in such cases; the child may spend long periods attempting unsuccessfully to defaecate. Management is not easy in long-established cases; enemas and wash-outs should be avoided unless other measures fail, and most children will respond to the use of liquid paraffin initially followed by carefully regulated doses of proprietary senna preparations. A full explanation to both parent and child is essential. Nevertheless, relapse is common, and it is difficult to avoid the conclusion that in many instances there is an underlying emotional disorder in child or parents, or both, which prevents the re-establishment of a normal bowel habit.

Margit Bellman[2] in Stockholm has recently conducted a survey into "encopresis." Most of the children in this group had either never gained normal bowel control ("primary encopresis"), or had broken down after a period of normal control ("secondary encopresis"). Constipation did not play an important part in the troubles of these children, who seem to constitute a separate group from those with chronic constipation and faecal soiling. Dr. Bellman's findings are of interest. The condition was commoner in boys, and of the whole series encopresis was mentioned in the school record card in only 11%. The mothers of affected children tended to be over-anxious, and coercive pot-training was common. "Accidents" were punished severely, and yet at other times the mother was indulgent. The children were lacking in self-assertion and rarely had the normal period of defiance at the age of 2–3 years. Happily the majority had lost their bowel symptoms by the age of 10 years. Thus the conclusions of this interesting study seem to justify the introduction in 1925 of the distinctive term "enkopresis" by C. Pototsky.[3]

---

[1] Gairdner, D., *Brit. med. J.*, 1965, 2, 91.

[2] Bellman, M., *Acta paediat. scand.*, 1966, Suppl. No. 170.

[3] Pototsky, C., *Die Enkopresis*; in Schwarz, O., *Psychogenese und Psychotherapie körperlicher Symptome*, 1925. Wien.

Musculo-skeletal Disorders after Renal Transplantation

A variety of skeletal and muscular disorders have been described after renal transplantation. They fall into three main categories: complication of high doses of corticosteroids, consequences of inadequate renal function, and changes in parathyroid function.

It is often necessary to treat patients with transplants with very high doses of corticosteroids, rising to as much as 200 mg. of prednisone a day during rejection crises. In addition to the usual features of Cushing's syndrome, demineralization of the bones may result in renal stones and pathological fractures. If the high corticosteroid dosage needs continuing it can stunt the growth of children. Arthropathy resembling gout can follow renal transplantation.[1] However, chemical analysis of the periarticular deposits shows high concentrations of calcium and phosphorus, with negligible amounts of urate. The joint surfaces themselves are not involved, and the lesions are probably due to a crystal-induced arthropathy which has been called pseudogout.[2] It has been reported in patients on chronic intermittent dialysis[3] and is probably due to insufficient dialysis, while in patients with renal transplants it is almost certainly due to poor function in the transplant.

Secondary parathyroid hyperplasia is a common sequel to long-standing renal disease. J. J. McPhaul and colleagues[4] described the development of autonomous hyperparathyroidism after restoration of renal function by a transplant. After transplantation there was marked hypophosphataemia, phosphaturia, hypercalciuria, and hypercalcaemia. Patients with this syndrome may require removal of the parathyroid glands to prevent formation of stones and decalcification of the bones.

J. F. Bravo and colleagues[5] have reviewed 60 long-term surviving patients with renal transplants, the mean follow-up being 491 days from operation. Of these patients 38% had one or more clinical signs of connective-tissue disorder, apart from muscle weakness, skin diseases, osteoporosis, or neuropathy. Five patients suffered from avascular necrosis of the bone, five from synovitis, thirteen from arthralgia, and ten from diffuse musculo-skeletal pain. Anti-gammaglobulin activity against human globulin was found between the second and twenty-eighth weeks after operation in 93% of cases regardless of the presence or absence of rheumatic disorders. Antibodies to deoxyribonucleic acid and ribonucleic acid were found in 40% and 28% respectively. These workers were unable to detect antibodies to specific constituents in synovial membranes, skeletal muscle, blood vessels, liver, or kidney. Determination of plasma lipids[5] showed fluctuating abnormalities in free and esterified cholesterol, phospholipid, triglycerides, non-esterified fatty acids, and total lipid levels. The synovial fluid consistently showed both intracellular and extracellular refractile, oval, lipid-staining particles varying from less than 1 to over 25 μ in diameter. Bravo and colleagues suggest that the aberrations of lipid metabolism may be secondary to corticosteroid therapy. The very high incidence of the rheumatoid factor in the serum in patients with transplants is of interest, though the mode of production of these antibodies is at present unknown. Humoral antibodies were not found in transplants between twins.

It would seem likely from the work of Bravo and colleagues that all patients with renal homografts from donors other than twins would eventually develop rheumatoid factor in the serum, but there was no apparent relationship of the appearance of the rheumatoid factor to the pathogenesis of the connective tissue disorders, since the activity appeared regardless of the presence or absence of rheumatic complaints. The severity of rheumatic disturbances was not related to variations in dosages of immunosuppressive drugs. However, J. P. Jones and colleagues[6] found evidence of fat emboli after rapid reduction of corticosteroid therapy, and fat embolism could be a cause of avascular necrosis of bone.

It is most important that evidence of muscular and skeletal disorders after kidney transplantation should be sought continuously, since early treatment may prevent disastrous consequences, particularly in hyperparathyroidism, when surgery can be entirely effective. There would seem to be a need for caution in suddenly changing corticosteroid doses, and no patient should be kept on high doses longer than is absolutely necessary. If good transplant function can be maintained, the pseudogout arthropathy will not develop.

---

[1] Calne, R. Y., Loughridge, L., MacGillivray, J. B., and Swales, J. D., *Brit. med. J.*, 1966, **2**, 1345.

[2] McCarty, D. J., jun., Kohn, N. N., and Faires, J. S., *Ann. intern. Med.*, 1962, **56**, 711.

[3] Caner, J. E. Z., and Decker, J. L., *Amer. J. Med.*, 1964, **36**, 571.

[4] McPhaul, J. J., McIntosh, D. A., Hammond, W. S., and Park, O. K., *New Engl. J. Med.*, 1964, **271**, 1342.

[5] Bravo, J. F., Herman, J. H., and Smyth, C. J., *Ann. intern. Med.*, 1967, **66**, 87.

[6] Jones, J. P., jun., Engleman, E. P., and Najarian, J. S., *New Engl. J. Med.*, 1965, **273**, 1453.

Dangers of Squint

The harmful effects that a squint may have on visual function are not always realized, so that delay in diagnosis, and hence of treatment, is of more frequent occurrence than it should be. The condition is fairly common in children. In fact the clinical study carried out in Manchester and Salford by Drs. A. M. Adelstein and John Scully reported at page 334 of the *B.M.J.* this week showed that over 4% of 6-year-old children had it.

The most serious sequel of untreated squint is amblyopia of the affected eye due to suppression of part of the vision, and it may eventually go on to loss of useful sight in that eye. It is by this process that a child with a squint may overcome the diplopia and confusion which tends to occur when the eyes are constantly looking in different directions. On the other hand a child with a squint may attempt to co-ordinate the function of both eyes by using the fovea centralis of the fixing eye in conjunction with an eccentric point on the retina of the squinting eye. This may operate only when both eyes are open, the squinting eye rapidly resuming foveal fixation if the other eye is covered. It is known as "anomalous retinal correspondence." However, if this abnormal association between the two eyes becomes more stable, the squinting eye may still tend to view a fixation object eccentrically in spite of the other eye being occluded, though the fovea maintains its normal directional value. Such eccentricity of viewing may later give way to "eccentric fixation," in which the eccentric point of fixation becomes relatively stabilized and assumes the principal visual direction of that eye. Eccentricity of fixation is in most cases associated with considerable amblyopia in the squinting eye, and prolonged treatment is usually required to overcome it. It is only in a squint freely alternating from eye to eye or an intermittent squint that really good vision is retained in each eye.

Statistical evidence in Adelstein and Scully's paper shows that the percentage of children with non-central viewing increases as the interval between onset of squint and its diagnosis (and effective treatment) increases. Furthermore it is most frequent in those children who start squinting early in life and less frequent when the squint starts later. This emphasizes the need to refer a doubtful case of squint immediately to an ophthalmologist, so that early treatment can be undertaken. Though a squint of large degree is more likely to attract attention than one of small degree, the adverse affect on visual function may be just as serious in the latter. Every clinician should be familiar with the method of diagnosis of squint by means of the cover test.[1]

Adelstein and Scully have also shown that the longer the interval of time between onset of squint and diagnosis the greater the percentage of children showing non-central viewing. Non-central viewing was most frequent in those who developed a squint at an early age, and the frequency decreased progressively as the age of onset increased, but the trend of decrease was not shown in the group of cases showing the longest interval of time between onset and diagnosis. They also found that a difference in refractive power between the two eyes of two or more dioptres predisposed towards eccentric viewing, and that it was proportionately slightly more frequent in boys than in girls. Furthermore, there was also a tendency for the onset of squint to be commonest in the winter months, with a peak in January.

---

[1] Wybar, K., in *Child Care*, p. 223. 1966. British Medical Association, London.

Although in Manchester and Salford the percentage of cases of squint diagnosed within a year of its onset was about 80–90% in children who began to squint between the ages of 2 and 6, it was considerably lower among those who began to squint at an age of under 1 year, indeed only about 50%. This is no doubt due to the old-fashioned idea that very young infants are too young for diagnosis and treatment. No infant is too young for examination and diagnosis nor for treatment by occlusion (if indicated). In some cases, for instance those of freely alternating squint, the early management may, in the absence of relevant errors of refraction, merely consist in periodic and careful observation. Moreover, the clinician must always bear in mind that a squint may be the outward sign of some serious ocular disease or may be paretic in nature and due to some underlying neurological disorder necessitating further investigation.

It is not always realized that a constant unilateral convergent squint which might otherwise end in a relatively blind eye may, as a result of timely occlusion, become converted into one of freely alternating convergent squint. This will ensure that both eyes keep good vision, and subsequently if the squint is controlled by correction of the refractive error or by surgery and orthoptic treatment or both the child may attain binocular single vision or, failing that, some useful form of binocular association. The development and preservation of good vision in each eye of a young child is a duty which every ophthalmologist must accept, but in order to discharge this duty he must rely on the early referral of all cases of squint by general practitioners, paediatricians, doctors in infant welfare clinics, health visitors, and others, but perhaps above all on its early recognition by parents and relatives, especially when there is a family history of squint. Delay in diagnosis and treatment is dangerous.

Fall-out and Strontium

After the explosion of the first hydrogen bomb in 1954 radioactive contamination of the environment and of human tissues reached measurable levels in many parts of the world. The long-term significance of fall-out is linked with deposition of strontium-90, a radioactive isotope with a half-life of 28 years. Because of its chemical affinity with calcium, this material is deposited in the skeleton, where it may be detected by chemical treatment and radioactive assay of bone samples obtained post mortem.

Work of this sort began in Great Britain in 1955[1] and is now conducted by two groups (one at the Capenhurst laboratories of the United Kingdom Atomic Energy Authority and one in Glasgow), who analyse more than 400 bone samples a year. The concentration of strontium-90 in bone is greater in children than in adults. The level of contamination rose to a peak in 1959 and declined slowly for three years before rising to another maximum in 1964 and 1965. The latest report[2] from the Medical Research Council, covering the first half of 1966, shows that levels of strontium-90 in bone continue to decline slowly, though remaining higher than at any time before 1964.

Arrangements for the analysis of human bone samples in the United Kingdom have been altered in a small but significant way. Until now the femur has been used in the British programme, but vertebrae have been analysed in most other countries. The difference is not important for infants, children, and adolescents, for whom little variation has been found in strontium-90 levels among the bones of the skeleton. In adults, however, the concentration of strontium-90 in vertebral bone is two to three times greater than in the femur. It has now been decided that the United Kingdom Atomic Energy Authority team (who receive an appreciable number of samples from adult subjects as well as from infants and children) will use vertebrae for analysis. The Glasgow group, whose work is confined mainly to study of samples from subjects under 5 years of age, will continue to analyse femora.

For the present, levels of strontium-90 in human bone do not give cause for serious anxiety in regard to radiation hazards, but valuable information is beginning to emerge from the study of the long series of results now available and from comparisons with other countries, where diet and weather conditions lead to differences in uptake of radioactive fall-out.

---

[1] Bryant, F. J., Chamberlain, A. C., Morgan, A., and Spicer, G. S., *Radiostrontium in Soil, Grass, Milk and Bone in the United Kingdom, 1956, Results* (A.E.R.E. HP/R 2533). 1957. H.M.S.O.

[2] Medical Research Council Monitoring Report No. 14, *Assay of Strontium-90 in Human Bone in the United Kingdom—Results for 1966*, part 1. 1967. H.M.S.O.

Coin-operated Vending Machines

The coin-operated vending machine answers a demand for quick meals and drinks at any hour of the day or night. Labour is minimal, being required only for maintenance and supplies. The machines are filled by the occupant of the land or premises on which they stand or by the company operating them. They may be either hired or purchased. If hired their maintenance is the responsibility either of the company loaning the machines or of those hiring them. Vending machines may be found in factories, hospitals, offices, and air, rail, or sea terminals, garages, sports grounds, exhibition halls, and also in streets and arcades of towns and cities. The food sold ranges from hot meals and sandwich or pie snacks to hot or cold drinks of many varieties.

The food is stored in an enclosed system, so that a simple cleaning process is essential to avoid the accumulation of stale food, particularly in powdered form, or liquid in parts of the machine invisible to the public eye. Many of the cold foods are perishable—for example, meat sandwiches, pies, and sausage rolls. Thus the temperature of storage is important and also the length of time the foods are held in the machine. The Food Hygiene Code of Practice No. 7,[1] of which M. Parry[2] has discussed the background, recommends a temperature of storage in accordance with the Food Hygiene Regulations[3]—that is, below 10° C. (50° F.) or above 62° C. (145° F.)—though these regulations apply only to food for immediate consumption in catering establishments. The Code of Practice gives no recommended time of storage for perishable products in vending machines, which in fact are acting as domestic refrigerators and should be operated at the appropriate temperature of 3–5° C. (37–41° F.). It has been reported[4] that machines vending perishable foods in the U.S.A. are required to hold those foods under refrigeration or alternatively above 140° F. (60° C.). In one district perishable foods and sandwiches with perishable fillings are required to be marked with the date of manufacture and permitted only 24 hours' storage in the machine. Perishable foods vended in the U.K. might be marked with the date of manufacture or a statement giving the final date for consumption. Machines should be sited away from the direct rays of the sun or suitable protection provided,[5] and only heat-treated milk should be used in vending machines.

---

[1] *Hygiene in the Operation of Coin-operated Food Vending Machines*, Food Hygiene Code of Practice No. 7, 1967. H.M.S.O.

[2] Parry, M., *Publ. Hlth Inspect.*, 1967, **75**, 369.

[3] Statutory Instruments (1960), *The Food Hygiene (General) Regulations*, 1960, Cmnd. 1601. H.M.S.O.

[4] Hughes, H. L., *Munic. Engng. Lond.*, 1967, **144**, 926.

[5] Skinner, W. E. D., *Roy. Soc. Hlth J.*, 1967, **87**, 19.

[6] Bailey, C. A., *Publ. Hlth Inspect.*, 1967, **75**, 306.

[7] Gibson, H. G., ibid., 1966, **75**, 121.

It is important that foods intended to be eaten hot should be maintained at temperatures above 145° F. (62° C.), as recommended in the Code of Practice. H. L. Hughes[4] reports that in the U.S.A. a microwave oven may be included in the range of vending machines to allow quick cooking of small articles of food provided by other machines. C. A. Bailey[6] describes incidents of chemical poisoning from vended fruit juices and recommends that occasional checks should be made for the metallic content of fruit juice vended from machines.

In the interests of public health there would seem to be need for close co-operation between the various sections of the food industry engaged in packaging and automatic vending and the public health authorities.[7] Moreover, as a precautionary measure firms intending to buy vending machines might be well advised to dismantle and reassemble the apparatus to check that it can be operated and cleaned in an efficient manner.

One Step Nearer?

According to the Treaty of Rome its provisions were to come into effect not later than 12 years from the signing of it in 1957. The treaty provides for free movement of doctors within the countries of the Common Market. The articles which deal with the matter are mainly article 48, which covers freedom of movement, and article 57, which refers to directives about mutual recognition of diplomas, certificates, and other qualifications, and the progressive removal of restrictions. To put these articles into effect certain adjustments in the conditions of practice and educational systems of the member countries will be required.

The Permanent Medical Committee of the European Economic Community, which, as previously explained,[1] was formed in 1956 with representatives from national medical associations of the member States and is a purely advisory body with no executive power, has made recommendations on these matters. These recommendations have been presented to the Commission—the standing administrative body of the European Economic Community—and last month the appropriate working party of the Commission met in Brussels to draft a directive on the subject. The working party, which is composed of civil servants, is also concerned with other professions—such as law, engineering, and architecture—and its directive should embody the plans for free movement of these as well as the medical profession. A draft should be presented by the end of the year to the Commission, whence it will go to the Council of the Ministers of the Six next year. It has to be unanimously approved by the Council and the European Parliament in Strasbourg and will then be referred back for ratification in the respective Parliaments of the member States. It could become implemented by January 1969.

The Permanent Medical Committee does not believe that this programme will give enough time. It thinks there is need for a delay of about five years to allow the various problems to be solved satisfactorily. In its view there are two major stumbling-blocks. Firstly, although some agreement has been reached in principle on the medical curricula of the member countries, there is a considerable difference in length and type of training for both graduation and specialization in each of the countries of the Six. Secondly, the social security systems in each country will require some harmonization. The medical administration of each country is closely linked with its social security system, and modifications may not be simple.

Opinion in Brussels is optimistic that Britain's entry to the Six may become a reality in about two years. Since new entrants are required to go through a transition period before full integration with the European Community, doctors here will have the opportunity of observing how matters are working out for their colleagues on the Continent, if the timetable envisaged by the Community's civil servants is fulfilled.

---

[1] Hendry, N. G. C., *Brit. med. J.*, 1967, 2, 431.

Elusive Popliteal Pulse

Fortunately in the majority of sites where we wish to determine the existence of an arterial pulse the vessel is near both to the surface and to the underlying bone. Thus the detection of the carotid, subclavian, brachial, radial, femoral, and foot pulses is easy. It is not so with the popliteal pulse. It is often essential to know whether the popliteal pulse is present or absent—for example, to distinguish a block of the lower femoral artery from one of the popliteal artery—yet many students, some of them postgraduate, have been heard to say that they have never felt it.

R. Ger[1] points out that the lower half of the popliteal artery is nearest to bone and skin as it lies behind the head of the tibia, and that this should be the standard point for palpating it. In fact there are three methods of palpating this artery, and the clinician may have to try them all before being sure that the pulse is absent. The commonest method is to grasp the upper end of the tibia with both hands—thumbs in front, fingers behind—with the knee slightly flexed. If the fingers are then moved from side to side they slip over the neurovascular bundle, which, once identified, can be fixed between the fingertips and compressed back against the bone. Occasionally it is easier to feel the artery higher up, behind the lower end of the femur, by hyperextending the knee joint with one hand pushing backwards on the patella, and placing the fingers of the other hand between the popliteal fossa and the bed. Both of these methods may be ineffectual in an obese person.

Probably the best and most certain way to feel the popliteal pulse is to have the patient in the prone position. The whole length of the popliteal fossa can then be palpated with the tips of the fingers of both hands. A pulse that cannot be felt in this way is surely absent. As with all clinical techniques, success comes from constant practice and, in the matter of palpating the popliteal pulse, self-discipline. A quick feel behind the knee is of no value. The approach must be slow, deliberate, and painstaking.

---

[1] Ger, R., *Surgery*, 1966, 60, 615.

Papers and Originals

Personality Traits Associated with Different Chest Pains after Myocardial Infarction

R. R. H. LOVELL,* M.D., F.R.C.P., F.R.A.C.P. ; A. VERGHESE,* M.D., B.SC., D.P.M.

Brit. med. J., 1967, 3, 327–330

Most patients who have had an acute myocardial infarction later experience pain in the chest of one sort or another. Angina pectoris is the commonest pain, and one in or including the left anterior chest is the next commonest single entity. The factors which determine post-infarction pain are complex. Clinical observation suggests that they include mental ones. Angina pectoris is often induced by emotion, and left chest pain in patients with heart disease has long been associated with anxiety. If mental factors associated with pain after myocardial infarction could be defined, more might be learnt of the mechanisms causing the pains and it might be possible to prevent some of them.

The first difficulty faced in trying to relate mental factors to chest pains is that clinical judgements regarding the diagnostic category to which a pain belongs are often unreliable. This difficulty can be overcome if precise criteria are laid down for specified pain entities, and these criteria are sought by using standard questions which avoid the influence of the observer's bias. On this basis Rose (1962) proposed criteria for diagnosing angina pectoris in epidemiological studies. Extending this approach, we have recently classified pains occurring after myocardial infarction and have shown the reliability of the pain questionary on which the classification was based (Verghese and Lovell, 1966).

The second difficulty arises from the fact that clinical judgements about mental traits are no more reliable than they are about the nature of chest pain, and similar problems of definitions exist (Carstairs, 1963). Cattell and Scheier (1961) have commented: "Theory and therapy are in a confused state essentially because one cannot be quite sure what another is talking about when he says 'anxiety' or 'neurosis,'" and they see as an answer to this the placing of instruments for meaningful and exact measurements in the hands of the clinician. Various attempts have been made to develop such instruments, including personality inventories and methods for measuring physiological and biochemical reactions to standard stressful situations. We have recently described the use of the latter method in a study in which catecholamine excretion and sympathetic nervous responses after a standard mental stimulus were compared in patients who, having had a myocardial infarction, had been classified according to their subsequent experience of chest pain (Nestel *et al.*, 1967). We now describe attempts to measure personality traits in these patients.

Methods

The patients studied were those whose pain experience we have described previously (Verghese and Lovell, 1966). They were Australian- or British-born men, with an average age of 56, who had been in hospital with acute myocardial infarction. On discharge from hospital they had been admitted to a controlled trial of long-term treatments with anticoagulants. The diagnostic criteria for admission to the trial and the clinical characteristics of patients admitted have been reported elsewhere (Lovell *et al.*, 1964).

The main group of 106 patients was derived from 121 admitted consecutively to the trial, of whom three died before they could be studied, one was too muddle-headed, and 11 were missed because their clinical attendances did not coincide with questionary sessions.

With the use of the questionary appended to the previous report (Verghese and Lovell, 1966), all these patients were classified with regard to their pain experience after an interval of between six months and three years from their myocardial infarction and before other measurements were made. The pain categories defined were: angina pectoris, either as the only pain recognized or with additional pain ; left chest pain ; other pains ; and no pain.

All these patients were designated for measurements of personality traits. For this purpose two questionaries were used, the Eysenck Personality Inventory (E.P.I.) (Eysenck and Eysenck, 1964) and the Cornell Medical Index Health Questionnaire (C.M.I.) (Brodman *et al.*, 1949).

The E.P.I. consists of 57 questions and is intended to measure two dimensions of personality, neuroticism–stability and introversion–extroversion. According to Eysenck (1959) the dimension of neuroticism measures people's emotional stability. Neuroticism is the "general emotional lability of a person, his emotional over-responsiveness, and his liability to break down under stress." The dimension of introversion–extroversion measures people's sociability along a continuum from an extreme extrovert position reflecting a maximum degree of "outgoing, uninhibited social proclivities" of a person to an extreme introvert position reflecting a minimum of such proclivities. The inventory is designed so that neuroticism–stability and introversion–extroversion are measured as separate dimensions. This is confirmed in large-scale studies where the correlation coefficients between extroversion and neuroticism scores are found to be negligible.

The C.M.I. consists of 195 questions in 18 sections and was designed for use as an adjunct to the medical interview. The first 12 sections (A–L) are intended to reveal somatic symptoms, and the last six sections (M–R) are intended to reflect mood and feeling A high M–R score is said to discriminate neurotic patients from normals (Culpan *et al.*, 1960).

The following scores were calculated: (1) the neuroticism score (N score) from the E.P.I., (2) the extroversion score (E score) from the E.P.I., and (3) the number of "yes" responses in sections M–R of the C.M.I. (M–R score).

---

* University of Melbourne Department of Medicine, the Royal Melbourne Hospital Post Office, Victoria, Australia.

The patients were given the E.P.I. and C.M.I. forms together with a stamped addressed envelope when they paid a routine visit to the clinic. They were all aware that the clinic was concerned with research and they were told that their replies might help us to learn more about their diseases.

One of the designated patients died before he could be studied. From the remaining 105, 97 completed forms were received. Of the remaining eight, six were in the no pain group and two in the angina pectoris group.

Since physical constitution has been related from time immemorial to mental traits, some physical dimensions were measured in a subgroup of these patients. The subgroup was selected from among patients in the main group, on the basis that a comparison would be attempted between 10–15 patients in the angina pectoris only, the left chest pain, the other pains, and the no pain groups. All 10 patients in the left chest pain group agreed to participate in this extended study and four of the 12 in the other pains group refused. Of the first 15 patients in the angina pectoris group, designated by their consecutive attendances at the clinic, one refused and two were not used because they were thought to be too senile to take part in a mental-stress test associated with this part of the study (Nestel *et al.*, 1967). Of the first 14 patients similarly designated in the no pain group, one also refused and one was thought too senile. Thus there were 42 patients in the subgroup. The physical dimensions measured were: height, transverse chest diameter, weight, and the skinfold thickness at three sites. The transverse chest diameter was taken at the fourth intercostal space, midway between inspiration and expiration, by means of an obstetrics pelvimeter. From the chest diameter and the height the Rees–Eysenck body index was obtained, a nomogram (Hamilton, 1950) being used. The sites for the measurements of skinfold thickness were left subscapular, left triceps, and left umbilical, and from these the total body fat was calculated, the formula proposed by Edwards and Whyte (1962) being used.

Finally, in the subgroup of 42 patients, a clinical interview was conducted. Neither the pain categories to which the patients belonged nor their scores on the personality inventories were known by the interviewer at the time of the interview. The interview was of an ordinary psychiatric kind, the patients being encouraged to talk freely without much interruption. An item sheet was used, but only as a guide to direct the interview and to permit classification of the findings which emerged from it.

Results

Table I shows the number of patients in the different pain categories and their personality inventory scores.

TABLE I.—*Personality Inventory Scores*

Pain Category	No. of Patients	Scores (Standard Deviations)		
		E.P.I.		C.M.I. M–R
		E	N	
Angina pectoris only	28	9·6 (3·4)	10·7 (5·8)	8·9 (3·3)
Angina plus another type of pain ..	9	8·0 (4·3)	14·3 (4·6)	10·4 (8·3)
Left chest pain ..	10	11·6 (5·1)	14·2 (5·5)	11·3 (11·1)
Other pains	12	8·8 (3·9)	8·8 (4·6)	5·1 (4·3)
No pain	38	10·9 (4·1)	7·6 (4·2)	4·3 (4·5)

The mean E scores did not differ significantly between the groups. The N and M–R scores were highest in the patients with left chest pain and in those with angina who recognized more than one type of pain. The scores of those who recognized angina as their only type of pain, though not so high, were also greater than those of the other pains and no pain groups. Differences between means which were significant are given in Table II.

Scores reported for normal working-class and neurotic patient groups are shown for comparison in Table III. The mean N scores of the patients with left chest pain, of those with angina who recognized more than one type of pain, and of the neurotic patients were practically the same, while the mean N scores of the other pains, no pain, and normal groups were also very similar to each other. The same groups resembled each other in M–R scores also.

TABLE II.—*Difference in Scores Between Groups Which Were Significant*

Scores	Comparison	Difference Between Means	Significance
N	Left chest pain *v.* no pain	6·6	P < 0·01
	„ „ „ *v.* other pains	5·4	P < 0·05
	Angina only *v.* no pain	3·1	P < 0·05
	„ plus another type of pain *v.* no pain	6·7	P < 0·001
	„ „ „ „ „ „ *v.* other pains	5·5	P < 0·02
M–R	Left chest pain *v.* no pain	7·0	P = 0·05
	Angina plus another type of pain *v.* no pain	6·1	P < 0·05

TABLE III.—*Personality Inventory Scores of British Normal Working class and Neurotic Patient Groups**

Group	Scores (Standard Deviations)				
	E.P.I.			C.M.I.	
	No.	E	N	No.	M–R
British normal working-class	85	11·2 (4·4)	7·8 (4·8)	48	2·8 (3·4)
British neurotic patient	61	10·0 (4·3)	14·4 (5·5)	46	14·1 (10·0)

* The British normal working-class and neurotic patient groups were ones whose N and E scores were reported by Eysenck and Eysenck (1964) and others whose M–R scores were reported by Culpan *et al.* (1960).

Table IV shows the Rees–Eysenck index, the total body fat, and the ratio weight: height for the different pain categories. Differences between means which were significant are given in Table V. The left chest pain group had the highest and the angina group had the lowest Rees–Eysenck body index: that is to say, the former tended to be relatively narrow-chested in relation to their height. For total body fat and weight: height ratio the angina group had the highest and the left chest pain group had the lowest means.

TABLE IV.—*Body-build Indices*

Pain Category	No.	Means (Standard Deviations)		
		Rees–Eysenck Body Index	Total Body Fat in kg.	Weight (lb.) / Height (in.)
Angina pectoris*	12	94·8 (4·0)	21·0 (5·7)	2·56 (0·35)
Left chest pain	10	99·7 (5·5)	14·2 (4·1)	2·12 (0·27)
Other pains	8	95·7 (5·2)	19·8 (2·9)	2·40 (0·20)
No pain	12	94·7 (5·2)	19·1 (3·8)	2·37 (0·20)

* Recognizing only one type of pain.

TABLE V.—*Difference in Body-build Indices Between Groups Which Were Significant**

Indices	Comparison	Difference Between Means	Significance
Rees–Eysenck body index	Left chest pain *v.* angina pectoris ..	4·9	P < 0·05
	„ „ „ *v.* no pain	5·0	P < 0·05
Total body fat	„ „ „ *v.* angina pectoris ..	6·8	P < 0·01
	„ „ „ *v.* no pain	4·9	P < 0·01
	„ „ „ *v.* other pains ..	5·6	P < 0·01
Weight / Height	„ „ „ *v.* angina pectoris ..	0·44	P < 0·01
	„ „ „ *v.* no pain	0·25	P < 0·05
	„ „ „ *v.* other pains ..	0·28	P < 0·02

* The angina patients are those recognizing only one type of pain.

Table VI compares the indications of neurosis extracted from clinical interview data for each of the groups. A history of items such as marital disharmony, psychiatric illness in the family, unsatisfactory parent–child relations, and frequent change of jobs was found most commonly in the left chest pain group. Patients in this group also more commonly exhibited behaviour traits found in neurotic subjects. The total number of these indicators recorded in the left chest pain group was found to be significantly higher than in each of the other groups.

TABLE VI.—*Clinical Interview : Number of Patients in Each Pain Group Showing the Item Listed*

Items	Pain Category			
	Angina Pectoris	Left Chest Pain	Other Pains	No Pain
Parental lack*	4	5	1	5
Unsatisfactory parental relationship†	1	4	1	2
Psychiatric illness in the family	1	3	2	1
Marital disharmony	1	4	3	1
Position in school (studies) below average	2	3	1	1
Frequent change of jobs	1	3	0	1
Not satisfied with work	2	4	2	1
Perfectionistic	4	6	2	2
Cannot sit down and relax when there is no work	5	7	2	2
Fussy about tidiness and discipline	3	5	1	1
Not easy-going in everyday life	2	7	1	1
Clinical impression of being tense	2	4	0	1
Total items	28	55	16	19
No. of patients in each group	12	10	8	12

* Dead, separated for more than one year, or habitually absent from home.
† Relationship with one or both parents not happy.
Significant differences between numbers of items among patients in each group, tested by χ^2:
Left chest pain *v.* no pain ($P < 0{\cdot}001$).
,, ,, ,, *v.* other pains ($P < 0{\cdot}001$).
,, ,, *v.* angina pectoris ($P < 0{\cdot}001$).

Discussion

In interpreting these findings, the possibility that factors associated with the original acute episode of myocardial infarction may have varied between the groups, and perhaps have influenced the indices subsequently measured, merits consideration. There is no evident variation in such factors in this study. All the patients were men admitted to the same hospital with an acute illness fulfilling strict criteria of myocardial infarction, and subsequently supervised by the same small group of doctors in the same clinic. Furthermore, the severity of the acute myocardial infarction, as measured by laboratory indices and by the number of days spent in hospital (average 20), did not differ between the groups.

The inferences to be drawn from the findings must depend on the meaning of N and M–R scores in the situations in which they were measured and especially on the extent to which they may be influenced by physical illness. The E scores raise no problem in interpretation, since the groups did not differ in this trait.

The E.P.I. was developed from results of studies in clinically normal population groups. The N score has been conceived as an index of constitutional neuroticism, and a high score is found in neurotic patients (Eysenck and Eysenck, 1964). In normal subjects the N score appears relatively stable, the correlation coefficient of scores tested and then retested after 8 to 12 months being over 0.8 (Eysenck and Eysenck, 1964). However, the finding of Knowles and Kreitman (1965) that in neurotic patients the high N scores fell somewhat after treatment suggests that they may be influenced by environmental factors. The finding of McGuire *et al.* (1963), using the Maudsley Personality Inventory (M.P.I.) from which the E.P.I. was developed, that N scores did not differentiate neurotic from psychotic patients also suggests that the N score cannot be regarded simply as an index of constitutional neuroticism.

The possibility that N scores may be modified by physical illness has not been critically tested. Sainsbury (1960) found that patients attending a general hospital with a variety of physical illnesses had raised N scores as measured by the M.P.I. He interpreted the findings as showing an association between neuroticism and certain so-called psychosomatic conditions. Among these, coronary disease was listed as psychosomatic and herniated disc as possibly psychosomatic. He did not discuss the possibility, with which his findings are consistent, that certain sorts of physical diseases may themselves cause the N scores to rise. This possibility cannot be ignored in interpreting N scores in ill people.

Unlike the E.P.I., the M–R section of the C.M.I. was designed to reveal mood and feeling patterns in people attending for a medical interview. Its use in clinics dealing with organic diseases has been more extensively reported (Brodman *et al.*, 1949 ; Leigh and Marley, 1956 ; Culpan *et al.*, 1960), and the possibility that the emotional disturbances due to the nature of some physical symptoms may account for high M–R scores has been mentioned (Culpan *et al.*, 1960). Using a modified C.M.I., Rawnsley (1966) found that in physical disorders both physical and psychological mean symptom frequencies are raised.

High Neuroticism Scores

Our results show that after myocardial infarction patients who have left chest pain and also those who experience angina with some additional type of pain which is not necessarily in the left chest have, on two independent ratings, the highest scores for neuroticism. Their N scores are as high as those which have been found in neurotic patients (Eysenck and Eysenck, 1964 ; Knowles and Kreitman, 1965). Comparably high M–R scores are also found in neurotics (Leigh and Marley, 1956 ; Culpan *et al.*, 1960 ; McDonald and Mowbray, 1967). The finding of these high scores in the left chest pain group accorded with the finding in them on clinical interview of the frequent occurrence of features commonly found in neurotic patients. It also accords with the widely held clinical impression that patients who consult doctors complaining of this sort of pain are neurotic (Conner, 1930 ; Bourne, 1937 ; Wittkower, 1937 ; Schnur, 1939 ; White, 1951 ; Wood, 1956). The fact that the left chest pain group had features of body build which have been shown to be associated with the trait of neuroticism (Rees, 1944 ; Eysenck, 1947 ; Parnell, 1957) suggests that in them the trait is constitutional and was already present when they had their myocardial infarction. We lack information on body build in the patients with angina plus some other sort of pain, but their very high N or M–R scores suggest that they may fall in this same category.

The interpretation of the findings in the group whose only recognized pain was angina pectoris is more difficult. Their scores for neuroticism, while not as high as those of patients with left chest pain and angina plus some other sort of pain, were nevertheless above those of the no pain group. However, they did not differ significantly from the no pain group in features of neuroticism detected on clinical interview and they lacked somatic features associated with constitutional neuroticism, tending to be fat and heavy in proportion to their height.

The fact that the N and M–R scores of the other pains group did not differ from those of the no pain group shows that experience of chest pain is not inevitably associated with rises in these scores. However, some findings are consistent with the possibility that the scores may be influenced by the duration and frequency of pain experience. In the angina pectoris only group we found that the N and M–R scores of the patients whose pain had started before their infarct tended to be above those of the patients whose angina followed it, though the differences between the means of 1.5 and 2.5 respectively could have occurred by chance. The average frequency of the experience of pain was greater in the angina pectoris group (5 times a week) than in the other pains (1.9 times a week) and left chest pain (1.8 times a week) groups. The angina pectoris group were also apparently " iller " in the sense that a greater proportion of them had been prescribed drugs for treatment of cardiac failure or hypertension. The possibility is not therefore excluded that the raised N and M–R scores in the angina pectoris only group are consequences of the type, severity, and duration of the particular symptoms which they experienced.

An alternative possibility is that the angina pectoris only group had a higher than average degree of constitutional neuroticism before their infarcts and that the expected accompanying features of body build, evident in the left chest pain group, were absent perhaps because of a strong association between angina and mesomorphism. This possibility gains support from the finding of Ostfeld *et al.* (1964), in a prospective study, that indices of personality in men who later developed angina differed from those of men whose coronary disease presented as myocardial infarction. Ostfeld *et al.* found that the men developing angina had shown relatively high scores for traits of emotional lability and suggestibility.

Difficulties in Interpretation

The difficulties in interpreting the findings in the angina group reflect the need for further evaluation in ill people of methods currently used for measuring personality traits. But in whatever way the results of these attempts to study personality traits associated with chest pains are interpreted, it is clear from them that studies of mental factors in coronary disease must take account of the different pain experience of different patients. Coronary disease is not to be regarded as a single entity.

From the practical point of view we have been impressed with the frequency with which unnecessary invalidism after myocardial infarction tends to be associated with experience of left chest pain and of multiple chest pains. By the time patients actually complain of these pains they are often depressed. The findings reported here suggest that it might be worth while trying, early in convalescence, to identify patients with the high degrees of neuroticism which are associated with these particular pains. If the doctor responsible for guiding the patient's return to active life were forewarned, some of the disabling features of these pains might be prevented or at least recognized early and mitigated.

Summary

Ninety-seven men who had had a myocardial infarction were classified according to their subsequent experience of chest pain, in the following groups: angina pectoris, left chest pain, other pains, and no pain. Personality traits were measured in them by means of the Eysenck Personality Inventory for extroversion and neuroticism, and the M–R section of the Cornell Medical Index for neurotic symptoms. Indices of body build were measured in 42 of the patients who were also examined in an ordinary psychiatric interview.

Patients in the left chest pain group and those who experienced angina together with some additional type of chest pain had the highest neuroticism scores. The left chest pain group tended to be long and narrow in body build and to be the least fat. Patients recognizing angina as their only pain also had higher neuroticism scores than did the other pains and no pain groups, but in body build they tended to be fatter and relatively heavy for their heights. The other pains and no pain groups did not differ in any indices measured.

Because the left chest pain group had physical features recognized as being associated with constitutional neuroticism, this trait is regarded as constitutional in them, and its early recognition in the hope of preventing unnecessary invalidism is advocated.

The significance of the raised scores in patients with angina is discussed.

This study was supported in part by a grant from the National Heart Foundation of Australia and was made possible by the collaboration of the staff of the Royal Melbourne Hospital. We are indebted to Professor Brian Davies and Dr. Robert Mowbray for helpful comments.

REFERENCES

Bourne, G. (1937). *Brit. med. J.*, **1**, 695.

Brodman, K., Erdman, A. J., Lorge, I., and Wolff, H. G. (1949). *J. Amer. med. Ass.*, **140**, 530.

Carstairs, G. M. (1963). "Standardization of Psychiatric Judgements," in *Epidemiology: Reports on Research and Teaching*, edited by J. Pemberton. London.

Cattell, R. B., and Scheier, I. H. (1961). *The Meaning and Measurements of Neuroticism and Anxiety.* New York.

Conner, L. A. (1930). *J. Amer. med. Ass.*, **94**, 447.

Culpan, R. H., Davies, B. M., and Oppenheim, A. N. (1960). *Brit. med. J.*, **1**, 855.

Edwards, K. D. G., and Whyte, H. M. (1962). *Clin. Sci.*, **22**, 347.

Eysenck, H. J. (1947). *Dimensions of Personality.* London.

—— (1959). *The Manual of the Maudsley Personality Inventory.* London.

—— and Eysenck, S. B. G. (1964). *Manual of the Eysenck Personality Inventory.* London.

Hamilton, M. (1950). *J. ment. Sci.*, **96**, 540.

Knowles, J. B., and Kreitman, N. (1965). *Brit. J. Psychiat.*, **111**, 755.

Leigh, D., and Marley, E. (1956). *J. psychosom. Res.*, **1**, 128.

Lovell, R. R. H., Denborough, M. A., Nestel, P. J., and Goble, A. J. (1964). *Arch. intern. Med.*, **113**, 267.

McDonald, C., and Mowbray, R. M. (1967). *Aust. N.Z. J. Psychiat.* In press.

McGuire, R. J., Mowbray, R. M., and Vallance, R. C. (1963). *Brit. J. Psychol.*, **54**, 157.

Nestel, P. J., Verghese, A., and Lovell, R. R. H. (1967). *Amer. Heart J.*, **73**, 227.

Ostfeld, A. M., Lebovits, B. Z., Shekelle, R. B., and Paul, O. (1964). *J. chron. Dis.*, **17**, 265.

Parnell, R. W. (1957). *Brit. med. J.*, **1**, 1485.

Rawnsley, K. (1966). *J. psychosom. Res.*, **10**, 84.

Rees, W. L. (1944). *Proc. roy. Soc. Med.*, **37**, 635.

Rose, G. A. (1962). *Bull. Wld Hlth Org.*, **27**, 645.

Sainsbury, P. (1960). *J. psychosom. Res.*, **4**, 261.

Schnur, S. (1939). *Amer. Heart J.*, **18**, 153.

Verghese, A., and Lovell, R. R. H. (1966). *Brit. med. J.*, **2**, 1102.

White, P. D. (1951). *Heart Disease*, 4th ed. New York.

Wittkower, E. (1937). *Lancet*, **2**, 665.

Wood, P. (1956). *Diseases of the Heart and Circulation*, 2nd ed. London.

Comparison between Three Radioisotope Methods for Measuring Iron Absorption

J. A. LUNN,* M.B., CH.B., M.R.C.P.ED. ; JOHN RICHMOND,† M.D., F.R.C.P.ED., M.R.C.P.
J. D. SIMPSON,‡ PH.D., B.SC. ; JOAN D. LEASK,§ B.SC. ; PETER TOTHILL,|| PH.D., B.SC., F.INST.P.

Brit. med. J., 1967, 3, 331–333

The present methods for determining iron absorption from the alimentary tract depend on the measurement by radioisotope techniques of iron retained in the body after oral administration. They vary in convenience and complexity, and sometimes require assumptions about iron metabolism for their interpretation.

The first, the "faecal recovery" method, was introduced by Dubach *et al.* (1948). In this method after a dose of iron-59 has been given by mouth the patient's stools are collected for several days until the excretion of radioactivity has stopped. The most important criticism of the faecal method is the difficulty of ensuring absolutely complete stool collections even from the most intelligent patients and in the best hospital circumstances.

The second, the "double isotope method" first described by Saylor and Finch (1953), makes use of two isotopes of iron, iron-55 and iron-59, which can be measured separately because of the different energies of their radiation. One isotope is given by mouth (iron-59) and simultaneously the other (iron-55) is bound to the patient's plasma protein and injected intravenously. After a suitable interval the ratio of the two isotopes in a blood sample gives a measure of absorption. It is necessary to assume that absorbed iron and parenterally administered iron are handled by the body in exactly the same way through the whole spectrum of iron disorder from iron deficiency to iron overload. Moreover, the separation of iron-59 and iron-55 demands very careful preparation and concentration of samples and complicated counting equipment.

The third, the "whole-body-counting" technique, has been applied by several workers (Price *et al.*, 1961, 1962 ; van Hoek and Conrad, 1961 ; Callender *et al.*, 1966). In this method iron-59 is given by mouth, and shortly afterwards the amount given is determined by external whole-body counting of radioactivity. After 10 to 14 days, when unabsorbed iron has been excreted, the amount of iron retained is determined by a further external whole-body measurement. Of the three methods this can be seen to be much the most convenient for the doctor and the patient. However, it is necessary to consider the possible change of efficiency of counting between the first and the last measurement. In the first, the "100% measurement," the iron is mainly in the alimentary tract, but in the second there might be considerable variation in its distribution in the body, being mainly in the circulating blood in a patient with severe iron deficiency or mainly in the body stores in a patient with refractory anaemia. The whole-body counters employed for this type of study have usually been expensive instruments of high sensitivity and low background, designed to measure levels of natural radioactivity and small burdens of accidental contamination.

These three main radioisotope measurements of iron absorption have been compared simultaneously in a series of patients. No attempt has been made to evaluate the amount of iron absorption in relation to other aspects of iron metabolism, but rather to see what correlation existed between the three methods over a range of haemoglobin level, serum iron, and stainable marrow iron. The main purpose of the present study was to assess a simple and inexpensive apparatus of low but adequate sensitivity for whole-body counting.

Material and Methods

Iron absorption was measured in 17 patients. They were inpatients in the Royal Infirmary, Edinburgh, and at the time of the study they all had normal bowel function and none showed occult bleeding from the alimentary tract. The patients were in wards where collection of excreta is standard practice for metabolic studies, and the need to be most careful in the complete collection of stools was emphasized to the patients and nursing staff for this particular investigation.

Routine examination of peripheral blood was by methods described by Dacie and Lewis (1963). Serum iron levels and total iron-binding capacity were determined as described by Ramsay (1957). The iron content of sternal marrow aspirate was assessed by a staining technique ; the method is given by Richmond *et al.* (1956). The amount of iron has been recorded as absent (O) or present in the range one plus to three plus (+ to + + +). During each study all stools collected were examined for blood by the Haematest method.

Measurements of Iron Absorption

The first five patients (Cases 1–5) were given 10 μCi of iron-59 orally in the form of ferric chloride (specific activity in the range 3–15 μCi/μg.) in a standard breakfast (Pirzio-Biroli *et al.*, 1958) containing 7.5 mg. of food iron. The remaining 12 (Cases 6–17) received the same amount of iron-59 in the fasting state, together with 10 mg. of carrier iron and 50 mg. of ascorbic acid. The conditions of administration of iron were changed to produce a wider range in the amount of iron absorbed for the purposes of comparison between the methods.

Iron-55 (specific activity in the range 1–4 μCi/μg.) was incubated with the patient's plasma or donor plasma as described by Veall and Vetter (1958), and 60 to 90 minutes after the iron-59 had been taken orally iron-55-labelled plasma containing approximately 20 μCi of iron-55 was injected intravenously.

Faecal Recovery Method

Measurements of stool radioactivity were made in a counter consisting of a ring of Geiger–Müller tubes. Some stool samples were also assayed with a scintillation counter and good agreement was obtained.

---

* Now Bahamas Government Medical Officer. Formerly Bahamas Government Fellow.
† Senior Lecturer, Department of Medicine.
‡ Senior Physicist, Department of Medical Physics.
§ Physicist, Department of Medical Physics.
|| Principal Physicist, Department of Medical Physics.
Royal Infirmary and University of Edinburgh.

Double Isotope Method

Blood samples taken at intervals of three to four days and on the same day as the final whole-body measurements were used to determine the ratio between the orally and intravenously administered isotopes. Iron was extracted from the washed red cells (W. N. M. Ramsay *et al.*, to be published) and electroplated on copper discs for counting.

Isotope separation was achieved by the use of two counters. Firstly, the radioactivity of iron-55 was measured by a xenon-filled proportional counter fitted with a beryllium window (Twentieth Century Electronics Ltd., Type PX 130/Xe), which largely absorbs the iron-59 β-rays but admits a reasonable proportion of the low energy *x* rays from the iron-55. Pulse height analysis enabled the iron-55 to be counted with an estimated efficiency of 6% and only 0.2% efficiency for iron-59; the background count rate was in the range of 0.3 to 0.7 count per second.

The radioactivity of iron-59 was then measured with an end-window Geiger–Müller counter in an anti-coincidence shield (Panax type LC/5). A platinum filter 0.015 mm. thick reduced the effect of the *x* rays of iron-55 to give counting efficiencies of 5.3% for iron-59 and 0.001% for iron-55. The background count rate was approximately 0.04 count per second.

The absorption of orally administered iron-59 was then calculated as follows:

$$\% \text{ absorption} = \frac{{}^{59}\text{Fe activity in blood}}{{}^{59}\text{Fe activity administered orally}} \times \frac{{}^{55}\text{Fe activity administered i.v.}}{{}^{55}\text{Fe activity in blood}} \times 100$$

To reduce statistical errors to a minimum long counting-times were necessary with both techniques. With the proportional counter, counting for 1,000 seconds gave approximately 10,000 counts, while counting for about 60 minutes was necessary to achieve a similar number of counts with the end-window counter. A separate standard for each isotope was prepared by adding known amounts of radioactivity to a sample of haemolysed red cells taken from the subject before the test. The standard red cells were then digested and electroplated in the same way as the blood samples.

The accuracy of the measurement depended on the similarity of recovery of radioactive iron for each standard. The quantitative recovery of added iron is easier than that of haemoglobin iron, and this consistency was checked in supplementary experiments.

Isotopic contamination of the solutions administered was found to be negligible.

Whole-body Counting Method

Whole-body iron-59 radioactivity was estimated with a single sodium iodide crystal, 12.5 cm. in diameter and 9 cm. in depth. The background count rate was reduced by means of a 2.5-cm. thick lead shield. This consisted of a plate 30 cm. long and 27 cm. wide, through which the crystal protruded, and sides 16 cm. high, forming an inverted U-shape. The shield was designed to accept radiation from the whole body without interference and to provide the maximum reduction in background count rate for a given amount of lead. At the energies used with the iron-59 studies the background count rate was approximately halved.

Measurements were made under integral bias conditions above 1 MeV to include both the 1.1 and 1.3 MeV photopeaks of iron-59; this gave a background count rate of approximately 50 counts per second. Counting was performed in two ways: firstly, with the patient in a sitting position in a reclining chair, and, secondly, with the counter placed at different points over the patient lying on a horizontal couch.

Measurements over the couch were made with a crystal-to-couch distance of 50 cm. and with the crystal vertically above positions 25, 75, and 125 cm. from the top of the head in each case. Counts were repeated in both the supine and the prone positions with the arms held by the sides. The sum of the six counts was then used as an estimate of the total body radioactivity. After a dose of 9 μCi the mean count rate in these six positions was approximately 360 counts per second, and a total patient counting-time of 600 seconds was used.

Only one 200-second count was required when using the chair geometry, in which the subject reclined with the chest at about 17 cm. from the nearest part of the crystal and with most of the body, except the head and the lower parts of the legs, positioned roughly in a 40-cm. arc around the centre of the crystal. A corresponding count in this arrangement after a 9 μCi dose gave approximately 650 counts per second.

The initial count on each patient was made four hours after the administration of iron-59, and this result was taken as the 100% retention value. The final absorption was estimated by re-counting between 14 and 20 days after the initial count, at which time the retention has reached a constant level (Schiffer *et al.*, 1964); this observation was verified on several patients by making serial measurements. To allow for any variation in counter sensitivity, a standard iron-59 source in a 5-litre polyethylene container was counted before and after each set of measurements. As the patient himself may modify the background count rate a count was made with him in position before the administration of the isotope, so that subsequent background measurements could be corrected for this.

The main advantage of the couch geometry is that it minimizes the effects of isotope distribution in the body on the efficiency of counting. These effects were studied by measuring the response of the counter to a small source as it was moved in different positions in a tank of water 20 cm. deep. Results showed that the effect of distance of the source from the crystal could be almost eliminated by counting from both sides of the tank and adding the two count rates. Allowance was made for the effect of isotope distribution in the patient by counting in both the prone and the supine positions.

Results

The main haematological data and the estimation of iron absorption obtained by the three methods in each of the patients are summarized in the Table.

Routine Haematological Data and Iron Absorption

Case No.	Haemoglobin (g./100 ml.)	Mean Corpuscular Haemoglobin Concentration (%)	Serum Iron (µg./100 ml.)	Total Iron-binding Capacity (µg./100 ml.)	* Marrow Iron	Iron Absorption Per Cent. Administered			
						Faecal Recovery y_2	Whole Body Counting		Double Isotope x
							Lying y_1	Sitting	
1	14·6	35·0	115	—	+ + +	22	0	0	0
2	7·1	33·4	267	—	+ +	12	0	0	0
3	5·3	31·6	85	—	+	10	0	0	0
4	10·6	31·8	78	212	+	28	1	1	1
5	5·0	25·1	5	345	0	25	13	9	8
6	—	—	60	134	—	82	78	96	73
7	14·2	—	—	—	—	39	25	27	12
8	7·0	28·9	200	246	+	73	65	66	57
9	14·6	33·0	—	—	—	50	12	10	5
10	7·3	25·0	50	594	0	97	93	117	93
11	6·9	25·3	44	582	0	91	85	109	86
12	10·8	31·0	39	522	0	91	74	90	79
13	5·1	30·5	—	—	+ +	44	31	32	28
14	9·9	33·5	95	360	0	37	15	17	11
15	6·1	24·8	27	412	0	57	43	44	55
16	8·6	27·0	28	307	0	85	—	87	78
17	8·3	31·8	160	343	+	34	13	15	13

*Arbitrary scoring of marrow iron: 0, + + + + + + (—, result not available).

Though a good correlation was obtained in the whole-body counting method between the sitting and lying positions ($r = +0.994$, $P < 0.001$, $n = 16$), the estimate of absorption for the sitting posture was much higher than for the lying position in four patients and exceeded 100% in two.

There was a high correlation ($r = +0.987$, $P < 0.001$, $n = 16$) between percentage iron absorption measured by whole-body counting in the lying position (y_1) and the double isotope method (x); these data are shown in Fig. 1. The regression equation of y_1 on x is given by $y_1 = 1.02x - 2.41$. The slope of this is not significantly different from 1.00 and the intercept is not significantly different from zero—that is, the regression line is not significantly different from the line of identity.

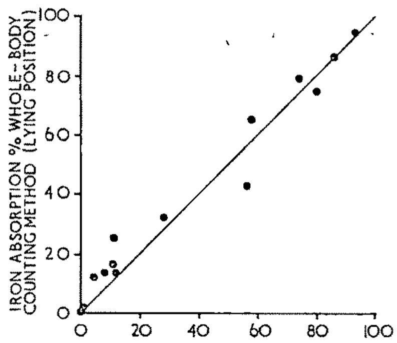


FIG. 1

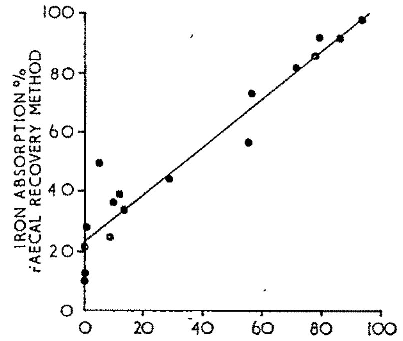


FIG. 2

FIG. 1.—Relation between iron absorption as measured by the double isotope method and the whole-body counting method (lying position). FIG. 2.—Relation between iron absorption as measured by the double isotope method and the faecal recovery method.

The correlation ($r = +0.961$, $P < 0.001$, $n = 17$) between the results of the faecal recovery method (y_2) and the double isotope method (x) was also good (Fig. 2). However, the regression equation for y_2 upon x is given by $y_2 = 0.798x + 23.5$. The regression coefficient of this line is significantly different from 1.00 ($0.001 < P < 0.01$) and the intercept is significantly different from zero ($P < 0.001$). Hence this regression line differs significantly from the line of identity.

Discussion

It is shown that the whole-body counter used with couch geometry gave results in good agreement with those from the double isotope technique. The sitting position led to rather poorer agreement, presumably owing to redistribution effects.

There was considerable discrepancy between the faecal recovery method and the other two methods, especially at the lower levels of iron absorption. This difference is believed to be due to incomplete faecal collections, despite full co-operation from nursing staff and patients. A similar result was obtained by Pitcher *et al.* (1965). Callender *et al.* (1966), in comparing results obtained by the whole-body counting method and faecal recovery method, believed that stools were lost by 16 of their 54 patients.

Callender *et al.* (1966) concluded that a whole-body counting technique with the use of a double detector system and travelling motor-driven couch was a very reliable and convenient way of measuring iron absorption. The present study, in which a very simple whole-body counting system was employed, confirms this view. Counts made in three positions from each side of the patient are combined, and this seeems to overcome inaccuracies from redistribution of isotope. Each measurement of whole-body radioactivity took about 15 minutes; a further 15 minutes was required for the counting of background radioactivity and a standard. The apparatus cost approximately £750, excluding the scaler.

Summary

A simple inexpensive whole-body counting technique for iron absorption in which radioactivity was measured in three positions with the patient prone and supine is described. It gave results which correlated well with the double isotope method in 16 patients who showed a wide range of haemoglobin level, serum iron, and stainable marrow iron.

Only two measurements on the patient were required, each taking about 15 minutes.

The faecal recovery method for iron absorption, which was used simultaneously, showed poor agreement with the whole-body counting and double isotope techniques. The discrepancy was believed to be due to incomplete stool collections, despite attempts to avoid this.

We wish to thank Dr. D. L. Gardner for estimation of marrow iron and Dr. W. N. M. Ramsay for assistance and advice and the determinations of serum iron. We are grateful to Miss A. A. McKay, Miss I. Martin, and Miss M. McArthur for their technical assistance.

Requests for reprints to be addressed to John Richmond, M.D.

REFERENCES

Callender, S. T., Witts, L. J., Warner, G. T., and Oliver, R. (1966). *Brit. J. Haemat.*, **12**, 276.
Dacie, J. V., and Lewis, S. M. (1963). *Practical Haematology*, 3rd ed. London.
Dubach, R., Callender, S. T. E., and Moore, C. V. (1948). *Blood*, **3**, 526.
Pirzio-Biroli, G., Bothwell, T. H., and Finch, C. A. (1958). *J. Lab. clin. Med.*, **51**, 37.
Pitcher, C. S., Williams, H. S., Parsonson, A., and Williams, R. (1965). *Brit. J. Haemat.*, **11**, 633.
Price, D. C., Cohn, S. H., Wasserman, L. R., Reizenstein, P. G., and Cronkite, E. P. (1962). *Blood*, **20**, 517.
—— Reizenstein, P. G., Cohn, S. H., Cronkite, E. P., and Wasserman, L. R. (1961). *Clin. Res.*, **9**, 165.
Ramsay, W. N. M. (1957). *Clin. chim. Acta*, **2**, 214.
Richmond, J., Gardner, D. L., Roy, L. M. H., and Duthie, J. J. R. (1956). *Ann. rheum. Dis.*, **15**, 217.
Saylor, L., and Finch, C. A. (1953). *Amer. J. Physiol.*, **172**, 372.
Schiffer, L. M., Price, D. C., Cuttner, J., Cohn, S. H., and Cronkite, E. P. (1964). *Blood*, **23**, 757.
van Hoek, R., and Conrad, M. E. (1961). *J. clin. Invest.*, **40**, 1153.
Veall, N., and Vetter, H. (1958). *Radioisotope Techniques in Clinical Research and Diagnosis*. London.

Epidemiological Aspects of Squint

A. M. ADELSTEIN,* M.D., D.P.H.; JOHN SCULLY,† M.B., CH.B., D.P.H., D.O.M.S.

Brit. med. J., 1967, 3, 334–338

This paper deals with squint in children diagnosed in two clinics—the Manchester Royal Eye Hospital and the Ophthalmic Clinic of the Health Department, Salford—discusses some demographic and social factors associated with squint and particularly with non-central viewing. It also confirms the observations of Scully and Naylor (1961)—namely, that non-central viewing occurs frequently (in about 22% of cases of squint); that it is more prevalent in younger children, particularly in those who have remained untreated for long periods; and that it appears very commonly in children with a high degree of anisometropia. We are now more confident about the estimates of these interrelationships because of the larger sample of cases we are able to present. Non-central viewing is shown to be more common in boys; and the possible associations between squint, season of onset, and recent infection are discussed.

The records presented are of children between the ages of a few months and 10 years examined by one of us (J. S.) at the above-mentioned clinics during the period October 1960 to March 1965.

Patients at the Manchester Royal Eye Hospital are referred by doctors in the area of the Manchester Regional Hospital Board. However, it is not possible to define the population from which patients would necessarily be referred. Patients at the Ophthalmic Clinic of the Health Department, Salford, are referred by the Maternal and Child Health Service and the School Health Service of Salford and also by practitioners. We are confident that very few cases in Salford came from other clinics, and we can therefore use these data to estimate rates of squint in the community.

The method of examination has already been described (Scully, 1961a). The history, taken from the parent or other informant, includes date of birth, family history, date when the squint began, and possible precipitating factors. The physical examination includes ocular movements, cover test, refraction, examination of fundus, and estimation of fixation with aid of the visuscope.

Presentation of Figures

In the papers already mentioned it has been shown that the time which elapses between the onset of the squint and its ascertainment was related to non-central viewing. Hence, mothers of all the patients referred to in this paper have been carefully questioned regarding the date of onset of the squint. The age at onset or the interval between onset and ascertainment is given in the Tables as one factor. We realize that memory and observation will sometimes be at fault and that the time when a squint began may not be easy to define; nevertheless, age at onset and time between onset and ascertainment are useful criteria. Because of the inevitable error introduced by relying on the observations and memory of the mothers we also refer to the age at examination. However, in a few of these cases the information was destroyed, and some Tables therefore show slightly smaller numbers.

Incidence of Squint

Table I shows the numbers of boys and girls diagnosed with squint in each year of age at the two clinics. Boys outnumber girls slightly. Since there is no defined group of people from which this hospital draws its patients it is not possible to calculate rates of squint. But if we assume that age does not determine whether a case will be referred here or elsewhere we can examine the relative incidence at various ages. The trend of distribution by age is similar in boys and girls. The highest incidence is at age 2 years, followed by ages 3, 4, 1, and 5 years successively.

TABLE I.—*Number of Cases of Squint by Age at Ascertainment, Sex, and Place of Examination*

Place of Examination	Sex	Age at Examination (years)							Total
		<1	1–	2–	3–	4–	5–	6+	
Manchester Royal Eye Hospital	Boys	47	211	365	315	222	115	91	1,366
	Girls	38	201	308	284	206	108	104	1,249
	All	85	412	673	599	428	223	195	2,615
Salford Health Department Clinic	Boys	10	49	54	40	54	37	41	285
	Girls	5	25	56	52	44	37	34	253
	All	15	74	110	92	98	74	75	538

Table II shows the cases of squint in boys and girls according to age at onset. The distribution of cases by age at onset is, of course, different from that of age at ascertainment, though in both categories the highest numbers are of children aged 2 years. However, about 16% of the squints are reported to have begun in the first year of life and relatively few after the fifth year.

Interval Between Onset and Examination of Squint

We have examined the distribution of intervals between onset and ascertainment in categories of three months, but for purposes of discussion we include in Table II the proportion of cases ascertained within one year. In the Manchester data, for both boys and girls, the smallest percentage and therefore the longest average delay occurs when the age of onset is

TABLE II.—*Number of Cases of Squint and Percentage Ascertained within One Year After Onset (in parentheses) by Age at Onset, Sex, and Place of Ascertainment*

Place of Ascertainment	Sex	Age at Onset (Years)							Total
		<1	1–	2–	3–	4–	5–	6+	
Manchester Royal Eye Hospital ..	Boys	229 (53·7)	303 (71·3)	340 (85·0)	261 (83·5)	169 (88·2)	60 (81·7)	42 (85·7)	1,404 (76·9)
	Girls	203 (44·8)	266 (78·2)	299 (82·6)	239 (91·6)	162 (90·7)	66 (90·9)	59 (89·8)	1,294 (79·2)
Salford Health Department Clinic..	Boys	36 (58·3)	53 (88·7)	64 (68·8)	47 (72·3)	40 (80·0)	26 (80·8)	22 (86·4)	288 (75·7)
	Girls	22 (45·5)	47 (68·1)	49 (83·7)	56 (80·4)	41 (87·8)	24 (91·7)	18 (83·3)	257 (78·2)

---

* Senior Lecturer, Department of Social and Preventive Medicine, University of Manchester.

† Senior Hospital Medical Officer, Manchester Royal Eye Hospital.

under 1 year. The percentage of cases ascertained within one year of onset tends to rise as the age at onset increases, and after the age of 2 years more than 80% of cases are ascertained within one year. In the data from Salford the trend of the length of interval between onset and ascertainment is much the same as in the Manchester data, though somewhat irregular owing to relatively smaller numbers.

The differences between the sexes with respect to the interval between onset and ascertainment may now be considered. The Manchester data show that when the age at onset is under 1 year a higher percentage of boys than of girls are ascertained within one year, and when the age at onset is after 1 year the girls have the shorter interval—that is, the percentage of girls ascertained is higher than that of boys within one year of onset for each age except for age 2. The differences, however, are small and attain statistical significance ($P<0.05$) in only one age group. The Salford data show the same trends except that in boys ascertainment is quicker when onset is in the first two years, and only later is the position reversed.

Type of Squint

The number of cases diagnosed in the Manchester Royal Eye Hospital according to the type of squint and the percentage of each type at each age group of onset are shown in Table III. (The number of children at Salford was too small for meaningful examination in these categories.)

TABLE III.—*Number of Cases by Type of Squint, and Percentage of Each Type by Age at Onset (Manchester)*

Type of Squint	Age at Onset (years)								No.
	<1	1–	2–	3–	4–	5–	6+	All Ages	
Right convergent squint	22·7	32·5	33·9	44·0	39·9	40·5	46·5	35·2	950
Left „ „	31·3	40·4	43·5	37·6	48·6	41·2	33·7	40·0	1,078
Alternating „ „	37·7	22·2	18·8	15·2	10·0	15·1	15·8	20·5	553
Right divergent „	2·5	1·2	0·8	0·2	—	0·8	—	0·9	25
Left „ „	1·9	1·6	1·4	1·0	0·6	—	3·0	1·3	36
Alternating „ „	3·9	2·1	1·6	2·0	0·9	2·4	1·0	2·1	56
Total number	432	569	639	500	331	126	101		2,698

The overall total shows that convergent squint is more common on the left side than on the right (40% and 35.2% respectively). As the age of onset increases the percentage of alternating squints diminishes—from 38% when the onset is in the first year to about 15% after the age of 3.

TABLE IV.—*Percentage of Children with Non-central Viewing According to Age at Onset, Interval Between Onset and Ascertainment, and Sex. (The Number of Children with Squint in Whom a Diagnosis of Fixation was Made is Shown in Parentheses)*

	Months Between Onset and Ascertainment	Age at Onset of Squint (years)			
		<2	2+3	4+	All Ages
		Manchester Royal Eye Hospital			
Boys ..	0–6	26·7 (101)	22·7 (379)	14·4 (195)	20·9 (675)
	7–24	39·2 (153)	31·6 (152)	31·3 (64)	34·7 (369)
	25+	45·1 (71)	51·7 (29)	50·0 (12)	47·3 (112)
	All intervals	36·6 (325)	26·6 (560)	19·9 (271)	27·9 (1,156)
Girls ..	0–6	16·5 (97)	14·9 (349)	8·6 (220)	13·1 (666)
	7–24	26·9 (104)	21·1 (114)	26·7 (60)	24·5 (278)
	25+	28·1 (64)	43·5 (23)	66·7 (6)	34·4 (93)
	All intervals	23·4 (265)	17·7 (486)	13·6 (286)	18·0 (1,037)
		Salford Health Department Clinic			
Boys ..	0–6	23·3 (30)	23·7 (59)	9·4 (53)	18·3 (142)
	7–24	38·9 (18)	40·6 (32)	19·4 (31)	32·1 (81)
	25+	66·7 (9)	80·0 (10)	66·7 (3)	72·7 (22)
	All intervals	35·1 (57)	34·7 (101)	14·9 (87)	27·8 (245)
Girls ..	0–6	11·1 (18)	21·3 (61)	9·7 (62)	14·9 (141)
	7–24	40·0 (10)	22·2 (18)	10·5 (19)	21·3 (47)
	25+	45·5 (11)	40·0 (10)	33·3 (3)	41·7 (24)
	All intervals	28·2 (39)	23·6 (89)	10·7 (84)	19·3 (212)

Central Viewing According to Age at Onset, Interval Between Onset and Diagnosis, and Sex of the Child

When the child does not co-operate a decision on central viewing cannot be made, and it is not surprising that the proportion of cases in which no decision is arrived at is larger in younger children. Among the Manchester children whose squint began in the first year of life 47% of boys and 44% of girls could not be diagnosed for fixation. Most of these children were, of course, examined before the age of 2. The proportion of cases not diagnosed for fixation diminishes as the age of onset increases, and when the onset occurs after the age of 4 hardly any cases remain undiagnosed.

Table IV shows the percentage of children with non-central viewing (among those cases in which a decision on central viewing could be made) according to age of onset, interval between onset and diagnosis, and sex. The association of each of these factors with non-central viewing can be examined independently.

Data from Manchester

Non-central Viewing and Interval Between Onset and Diagnosis.—The percentage of children with non-central viewing increases as the interval between onset and diagnosis increases; the trend is present in each age of onset and in both sexes.

Fixation and Age at Onset of Squint.—This relation is best examined among those children in whom the interval between onset and ascertainment was less than six months—that is, those represented in the first row for each sex in Table IV. These include most of the cases of squint, and the distribution of delay is likely to be similar within each group by age at onset. Among these children non-central viewing is most frequent in those with the youngest age at onset, and the rate decreases progressively as the age at onset increases. In each section of the Table there is a clear difference between the group with the youngest onset age and that with the oldest. When the delay between onset and ascertainment is 7 to 24 months the gradient of the percentage of non-central viewing is not distinct in each of the two rows, but there is a clear difference in proportion of non-central viewing between the children with the youngest and those with the oldest age at onset. This trend of decrease of non-central viewing with increasing age at onset does not emerge in the group showing the longest interval between onset and ascertainment—more than 25 months. However, it seems reasonable to suppose that the different trend has arisen because in this group there is a considerable difference between the average intervals in the three groupings of age at onset; of those children whose onset age is below 2 some have had a comparatively long delay, whereas in those in whom the age at onset is over 4 years the interval is short. The cases are too few in number for a more detailed analysis of this open-ended category.

Non-central Viewing According to Sex.—The boys have a higher proportion with non-central viewing than the girls in each category of age at onset and in each category of interval between onset and diagnosis (except one in which the numbers are small). Thus, on examining the column which refers to onset under 2 years of age and comparing the data of the boys with those of the girls, in each category of interval we have the following comparisons of pairs of percentages: 26.7, 16.5; 39.2, 26.9; and 45.1, 28.1. In general the Salford data follow the same pattern, though there are exceptions which are to be expected because of small numbers. Table IV presents the cases according to age at onset, and, since they are actually examined at varying times after onset, the data are presented in Table V with age at diagnosis as the variable in place of age at onset. This Table shows that two factors—interval after onset and sex—are, as shown previously, independently related to the frequency of non-central viewing. However, age at ascertainment, unlike age at onset, is not related to the frequency of non-central viewing.

TABLE V.—*Percentage of Children with Non-central Viewing According to Age at Diagnosis, Interval Between Onset and Ascertainment, and Sex. (The Number of Children with Squint in Whom a Diagnosis of Fixation was Made Shown in Parentheses)*

	Months Between Onset and Ascertainment	Age at Diagnosis of Squint (years)			
		<2	2+3	4+	All Ages
		Manchester Royal Eye Hospital			
Boys ..	0–6	21·7 (69)	23·4 (359)	16·7 (228)	20·9 (656)
	7–24	34·2 (38)	38·8 (188)	30·1 (133)	35·1 (359)
	25+	— —	37·0 (46)	53·8 (65)	46·8 (111)
	All intervals	26·2 (107)	29·3 (593)	26·5 (426)	28·0 (1,126)
Girls ..	0–6	14·8 (61)	15·3 (327)	9·9 (253)	13·1 (641)
	7–24	28·1 (32)	22·4 (134)	24·5 (106)	23·9 (272)
	25+	— —	25·6 (39)	40·7 (54)	34·4 (93)
	All intervals	19·4 (93)	18·0 (500)	17·7 (413)	18·0 (1,006)
		Salford Health Department Clinic			
Boys ..	0–6	24·0 (25)	21·6 (51)	14·3 (63)	18·7 (139)
	7–24	50·0 (6)	43·5 (23)	30·8 (52)	35·8 (81)
	25+	— —	66·7 (6)	75·0 (16)	72·7 (22)
	All intervals	29·0 (31)	31·3 (80)	28·2 (131)	29·3 (242)
Girls ..	0–6	— (11)	21·3 (61)	12·1 (66)	15·2 (138)
	7–24	33·3 (3)	42·9 (14)	10·7 (28)	22·2 (45)
	25+	— —	50·0 (4)	40·0 (20)	41·7 (24)
	All intervals	7·1 (14)	26·6 (79)	16·7 (114)	19·8 (207)

Anisometropia

The meridian with the greatest refractive error in each eye was considered and three categories are described: (1) patients with less than one degree of difference between the greatest meridian of the two eyes, (2) those with one to two degrees, and (3) those with more than two degrees of difference.

There is no indication of the frequency trend of these categories of anisometropia by sex or age at onset, the overall figures being 82% with less than one degree, 13% with 1–2 degrees, and 5% with more than two degrees among the 2,698 children examined at the eye hospital, and 82, 11, and 7% respectively at Salford.

Anisometropia and Non-central Viewing.—The relation between these attributes can be seen in Table VI for those cases in which fixation was determined. There is a regular increase in the percentage of children with non-central viewing from those with less than one degree of anisometropia (23% in boys and 13% in girls) to those with two or more degrees of anisometropia (70% in boys and 60% in girls).

TABLE VI.—*Number of Boys and Girls with Squint by Category of Anisometropia, Showing the Percentage of Non-central Viewing in Each Category*

Sex	Category of Anisometropia	No. of Children	Percentage with Non-central Viewing
Boys ..	No anisometropia	938	23·4
	1+ degrees	158	39·2
	2+ „	61	70·5
	Total	1,157	27·9
Girls ..	No anisometropia	846	13·5
	1+ degrees	133	28·6
	2+ „	58	60·3
	Total	1,037	18·0

Social Class

An attempt was made to classify the children according to the social classes defined by the Registrar General and from the fathers' occupation. However, entirely suitable data are not available against which to compare the findings, since the social class distribution of children need not be similar to that of adults (depending on the marriage and fertility rates of their parents), and because we do not know the population at risk with reference to the Manchester Royal Eye Hospital. In addition we are not confident that the records are accurate regarding some subdivisions of occupations.

Bearing in mind these problems, we have calculated the expected number of children in the various social classes by using as the basic distribution the married women of the South-east Lancashire conurbation as shown in the report of the 1961 Census, and have adjusted these by the fertility rates. In both the Salford clinic and the Manchester Royal Eye Hospital there is a relative shortage of managerial and professional classes, except that in Manchester Royal Eye Hospital employed professional workers are in excess of those self-employed. These findings may be explained if more of the affluent classes are referred to private consultants, with the exception of workers in medical institutions whose children tend to be referred to the Manchester Royal Eye Hospital.

The other large disparity between the expected and observed numbers concerns the class of unskilled workers (socio-economic group II). About 11% of the children in the eye hospital are to be expected from this group, but there are 19%; in the Salford clinic the respective figures are 13.6 and more than 27%. In both samples the distribution differs significantly from the expected.

Season of Onset and Infections

The numbers of cases according to the month in which the squint appeared, as stated by the mothers, are shown in Table VII. The mean number per day in each month allows for difference in the length of month. A seasonal pattern emerges with a high peak of onset in January and a trough in June. The difference between the observed and expected numbers of cases, if there were only chance differences between the months, are highly significant (P<0.001).

TABLE VII.—*Frequency Distribution of Squint by Month of Onset (as Reported) Compared with Expected*

Month of Onset	No. of Cases		
	Observed	Expected	Mean per Day, Observed
June	221	259·1	7·37
July	233	267·8	7·52
August	250	267·8	8·06
September	221	259·2	7·37
October	270	267·8	8·71
November	258	259·1	8·60
December	305	267·8	9·84
January	389	267·8	12·55
February	269	241·9	9·61
March	289	267·8	9·32
April..	224	259·1	7·47
May	224	267·8	7·23
Total..	3,153	3,153 0	8·64

$\chi^3 = 93{\cdot}61$. d.f. = 11. P < 0·001.

These figures suggest that the squints tend either to occur or to be noticed for the first time during January and December, or that the informants (and the doctors) are more inclined to choose January or December. If illness plays a part in the presentation of squint or in noticing it, the figures could be explained by the increase of upper respiratory infections during these months. We were unable, however, to find any association between the particular seasons involved and the epidemics of measles in Manchester.

In each case of squint a question was asked about the occurrence of an illness in the four weeks preceding the onset. About 9% (230) reported that the child had measles, and an additional 15% (399) reported some other type of infection. Among those cases with a history of infection there is a similar increased incidence of squints in January as there is among the children with no history of infection.

Discussion

There are noticeable differences between published estimates of the incidence of squint (Nordlöw, 1964), and for a number of reasons some degree of variation is to be expected. There is evidence that squint is related to the development of the foetus and infant. Thus brain injury, spasticity, prematurity, mental deficiency, and other factors identified with social class have been shown to be relevant (Miller *et al.*, 1960 ; Nordlöw, 1964 ; Chief Medical Officer of the Department of Education and Science, 1966). If comparisons of incidence between populations are made, variations between these factors must be considered. In addition, the method by which the squints are ascertained may vary. For example, the data may be derived from routine medical services or from special surveys. If the data depend on routine services they will reflect variations of local practice, particularly in the delay between onset and ascertainment. Prospective studies would yield the most accurate estimates of rates of onset of squint by age, because retrospective methods rely on the observations, memory, and attitudes of the mothers. The only reasonably extensive prospective study of which we are aware is part of the well-known study of child development in Newcastle upon Tyne (Miller *et al.*, 1960), which revealed 40 cases of squint. This number represented 4.7% of all children up to the age of 5 years, and the authors quoted another survey showing 5% prevalence among children entering school in Newcastle between 1947 and 1952.

Nordlöw (1964) published a comprehensive survey of routinely ascertained cases in a defined area in Sweden. He estimated that a cohort of nearly 6,000 children at birth would develop, by the age of 6 years, 242 cases of squint—that is, 4.03% (or 2.6% of constant divergent squints). Let us consider our data from the Salford clinic as though they were almost complete ascertainment ; by adding the mean annual incidence rates of squints ascertained during each year of age-grouping we reach an approximate prevalence rate of a particular age. This works out as 4.3% at the age of 6, and is expected to be a slight underestimation of the actual state, since a small number of children would be referred elsewhere.

The assessment of the relative incidence of squint by age at onset is also variable. Nordlöw states that "retrospective information would be influenced if a long time elapsed between the onset of the squint and the initial examination." He found 52% with histories of less than one year, whereas in our data more than 75% are in this category. Comparison of the rate of onset by age shows that the pattern in his data differs from ours. Nordlöw reported that approximately 38% of the squints began in the first year of life, and in the ensuing consecutive years the percentages were 20, 14, 16, 7, 1, and 1 ; thus the highest proportion is in the first year, and then there is a decline year by year. In our data (similar in Manchester and Salford) the largest number of cases are reported to have begun in the third year of life (23.7% in Manchester), and slightly lower numbers in the second and fourth years (21.1% and 18.5%) ; then follow the first year, the fifth year, and the sixth year, after which hardly any cases occur.

In this respect the data from Newcastle—which, as mentioned above, have been gathered prospectively—resemble our data much more than Nordlöw's. In essence the survey method in the Newcastle study comprised regular visiting of a representative group of families. The percentages year by year were 5, 27, 25, 25, and 17. (The sampling errors are considerable.)

The surveys mentioned, and others, as pointed out by Nordlöw, divide into two characteristic patterns of distribution by age at onset of squint. First, those such as ours, in which the onset is most frequent between the ages of 1 and 4 years ; and those, such as Nordlöw's, in which the onset is commonest in the first year and then diminishes progressively. Even allowing for the fact that different surveys adopted different definitions of squint these patterns are quite distinct.

In attempting to explain the difference between the two patterns of incidence of onset of squint, a number of factors can be invoked, but they would hardly seem to be sufficient. Important differences between surveys, in addition to the variations between definitions of what constitutes a squint and its beginning, are possibly due to selection of cases ; in some instances those with an early onset, being younger, may be referred to one type of clinic and those with late onset to another. Selection may involve cases with associated defects such as brain injury or subnormality. Our data do not include certain categories of handicapped children, and therefore the percentage of squints which began in the first year of life would be deficient in our figures ; but this could by no means account for the large disparity in patterns of onset.

Another possible cause for the difference is that in those populations with a higher incidence the excess might occur in one particular age rather than another. For instance, if, say, in Manchester the overall rate of squints at 6 years of age was 5% and in Sweden 3%, the excess 2% if distributed mainly in the second to fourth years could account for the different patterns of onset described.

Non-central Viewing

Non-central viewing is a serious consequence of squint. In previous papers Scully (1961a, 1961b) has pointed out the association between non-central viewing and age at onset, interval between onset and ascertainment, and degree of anisometropia. We confirm these associations.

The influence of the time interval after the onset is particularly marked, so that when the delay is more than two years rates of non-central viewing are high, reaching even 70% among this group of boys in Salford. High degrees of anisometropia also are associated with non-central viewing, those children with more than two degrees of anisometropia having more than 60% with non-central viewing.

A surprising finding is that boys have more non-central viewing than girls in each category defined by age and interval and also in each category of anisometropia. In the Manchester data the boys have 27.9% and the girls 18% of non-central viewing, overall. We have no explanation for this difference between the sexes. It is not apparent that this difference could arise because parents delayed medical care for boys, and, in addition, subsequently volunteered a spuriously shorter history. This is unlikely, since the actual distribution of cases by age at examination is alike for each sex ; and in Salford most of the cases do not depend entirely on the mother's intervention, but are referred by the School Health Service or the Maternal and Child Health Service. The differences in the frequency of non-central viewing between the sexes must be taken as found. The fact that the proportion of children with non-central viewing diminishes as the age at onset increases suggests that non-central viewing may be a failure of integration of the various components of vision, since these would tend to improve with age. There are other functions which show higher rates of failure in boys ; for example, boys have higher rates of enuresis and of dyslexia. Dyslexia has been shown by Birch and Belmont (1966) to be associated with auditory-visual integration.

Season

The seasonal pattern of onset is quite distinct ; we have discussed some sources of possible error, but do not think that this clear pattern could be due to these errors. Since the pattern is similar among children who are reported to have had no infection and those who have had infections in the four weeks before the alleged onset, overt infection does not explain the trend. We can only speculate on factors such as subclinical infections, or length of daylight.

Summary

We report an analysis of 3,243 cases of squint examined at a health department clinic and an eye hospital. The estimated prevalence of squint at the age of 6 years is 4.3%, similar to estimates in other surveys in England. Incidence of onset is highest in the third year of life, and, if this distribution reflects the incidence in the community, it represents one characteristic pattern of distribution. Another pattern has been described in which the highest rate of onset is in the first year and diminishes rapidly thereafter. Non-central viewing occurs in 23% of the cases of squint in which this function could be assessed. Non-central viewing is much more frequent in boys, in children in whom the onset is early, in those who have had the squint for a longer period, and in those with high degrees of anisometropia. There is evidence that squints begin more often in winter, with a peak incidence in January.

We are indebted to Mrs. Anne Fish for her painstaking and careful handling of the data, and to Professor C. I. Phillips for his advice. We wish to thank the surgeons at the Manchester Royal Eye Hospital for making available for examination cases under their care.

REFERENCES

Birch, H. G., and Belmont, Lilian (1966). *E.E.N.T. Digest*, vol. 28, No. 12, p. 47.
Chief Medical Officer of the Department of Education and Science (1966). *The Health of the School Child*. H.M.S.O., London.
Miller, F. J. W., Court, S. D. M., Walton, W. S., and Knox, E. G. (1960). *Growing Up in Newcastle-upon-Tyne*. London.
Nordlöw, W. (1964). *Acta ophthal. (Kbh.)*, 42, 1015.
Scully, J. (1961a). *Brit. med. J.*, 2, 1610.
—— (1961b). *Brit. J. Ophthal.*, 45, 741.
—— and Naylor, E. J. (1961). *Brit. med. J.*, 2, 81.

Progestin Therapy of Breast Cancer: Comparison of Agents

BASIL A. STOLL,* M.R.C.S., F.F.R.

Brit. med. J., 1967, 3, 338-341

Over recent years many synthetic orally active progestational agents have been introduced to clinical practice. The multiplicity of such agents presents a problem of choice to the clinician considering progestin therapy in breast cancer. A similar problem applies also to uterine cancer. Various authors, each using a different progestin, have reported their results in small series of breast cancer cases (Jonsson *et al.*, 1959 ; Lewin *et al.*, 1959 ; Douglas *et al.*, 1960 ; Baker and Kelley, 1960 ; Jolles, 1962 ; Bucalossi *et al.*, 1963 ; Stoll, 1965). The trials are summarized in Table I, and from the results it is obvious that there is a place for progestin therapy in breast cancer. To our knowledge no basis has yet been shown for statements that the presence of breast cancer contraindicates the use of progestins because they may possibly stimulate the tumour (Klawans, 1965).

TABLE I.—*Reports of Clinical Response in Breast Cancer After Progestin Administration*

Author	Progestin	Clinical Response in
Jonsson *et al.* (1959) ..	Bromoketoprogesterone	7 of 34
Lewin *et al.* (1959) ..	Norethindrone	5 ,, 22
Douglas *et al.* (1960) ..	Norethisterone oenanthate	1 ,, 12
Baker and Kelley (1960) ..	Norethynodrel	4 ,, 20
Jolles (1962)	Hydroxyprogesterone caproate	3 ,, 9
Bucalossi *et al.* (1963) ..	Medroxyprogesterone	11 ,, 30
Stoll (1965)	Norethisterone acetate Medroxyprogesterone	3 ,, 16

Nevertheless, there still remains the evaluation of the most efficacious agent and the most suitable stage of the disease for its administration. The choice of suitable agent is made more difficult by differences in side-effects, particularly in the incidence of gastrointestinal upset, biochemical evidence of liver damage, and signs of masculinization after prolonged use. For this reason it was thought valuable for one observer, using standardized criteria, to compare examples of each class of progestin in the treatment of advanced breast cancer. This report is of a limited pilot trial of this nature.

Material

A total of 72 postmenopausal women with advanced breast cancer were treated by synthetic oral progestins selected to represent the three major groups in use—that is, 19-nortestosterone derivatives, 17α-hydroxyprogesterone derivatives, and the testosterone derivatives. The initial daily dosage given was in general six times that used in oral contraceptive practice and is noted in Table II. Cases were not randomized, but were allocated on a chronological basis as agents became available for trial.

As well as objective evidence of tumour regression, special note was taken of side-effects from each drug—mainly the immediate ones, but also in a few cases the long-term ones. Special investigations carried out in the majority of patients included liver-function studies and serial cytohormonal assessment of the vaginal smear, both before and during treatment. In some of the later cases glucose-tolerance tests were carried out after at least four weeks of hormone treatment.

All 72 patients had undergone either a natural menopause or castration. They were suffering from advanced breast cancer, beyond the control of both surgery and radiotherapy. All patients had measurable evidence of progressing soft-tissue lesions regularly measured, and photographed when appropriate. Simultaneous treatment of the part under observation was not permitted by any method except local dressings. Patients were selected for drug trial only if the disease was progressing in activity as recorded in serial observations. Previous hormone therapy had been discontinued for at least two months and castration carried out at least six months previously.

Nathanson's (1952) classical criteria of objective response from hormone therapy in breast cancer were used. A response indicates observation of at least 50% regression in size of accessible lesions, while, at the very least, all existing inaccessible lesions remain static in activity and no new lesions appear. Of the 72 patients, there were 65 who received the hormones for two months or longer and were assessed for tumour regression. The patients who discontinued the drugs before completion of two months' treatment are excluded from the analysis as having had insufficient trial. As this was regarded essentially as a screening trial, only patients who showed tumour regression at two months were continued on drug therapy. The earliest macroscopic regression could be identified at four weeks after starting treatment. It was maintained for periods of up to eight months when the drug was continued. Details of response for each patient are shown in Table II, and for each group in Table III.

---

* Cancer Institute, Melbourne, Australia. Address requests for reprints to 54 Princes Park Avenue, London N.W.11.

TABLE II.—*Details of 65 Patients with Advanced Breast Cancer Assessed for Clinical Response to Progestin Therapy*

Case No.	Age	Postmenopausal (Years)	Previous Response to		Progestin and Daily Dose	Response to Progestin	L.F.T. Change	Vaginal Smear		Response to Other Progestins
			Androgens	Oestrogens				Initial	Later	
1	54	4		+	Norethisterone acetate 60 mg.	−		A		
2	69	17		+	,, ,,	−		I		
3	75	29	−		,, ,,	−		A		
4	71	23		−	,, ,,	−		I		
5	60	10	−	−	,, ,,	−		?		
6	81	40		+	,, ,,	+		I		
7	68	17	+	−	,, ,,	−		I		
8	54	3	−		,, ,,	−		A		
9	48	2	+	+	,, ,,	+		I		
10	48	1	−		,, ,,	−		A		
11	29	3	−	−	,, ,,	−		I		
12	44	1	+	−	,, ,,	−		I		Medroxy-progesterone −
13	52	5	−		Lynoestrenol 30 mg.	+	−	I		Lyndiol +
14	49	1			,, ,,	−	+	I		
15	65	20			,, ,,	−	+	A	I	Melengestrol −
16	48	1			,, ,,	−	+	I	I	
17	48	2			,, ,,	−	−	I		Megestrol +
18	62	9		−	,, ,,	−	−	I		Dimethisterone +
19	53	10			,, ,,	−	−	I		
20	44	1	−	−	Medroxy-progesterone 200 mg.	−		I		Norethisterone −
21	40	1		−	,, ,,	−		?	I	
22	72	24			,, ,,	−		A		
23	81	30			,, ,,	−		?		
24	48	2			,, ,,	+		I	I	
25	71	18			Medroxy-progesterone 400 mg.	−	−	I	I	Lyndiol −
26	76	26		−	,, ,,	+	−	I	I	
27	75	31		−	,, ,,	−	−	A	A	Lyndiol − Dimethi-sterone −
28	82	40		+	,, ,,	−	−	A	A	
29	69	21			,, ,,	−	−	A	A	Megestrol −
30	44	2			,, ,,	−	−	I	I	
31	66	18		−	,, ,,	−	−	I	A	Lyndiol −
32	66	21			Melengestrol 120 mg.	−	−	A	A	Lynoestrenol −
33	57	6		−	,, ,,	−	−	I	I	Lyndiol −
34	59	14		−	,, ,,	+	−	I	I	,,
35	84	33		−	,, ,,	−	−	I	I	
36	64	8		−	,, ,,	−	−	?	I	
37	71	26		−	Megestrol 30 mg.	−	−	I	A	
38	76	30		−	,, ,,	−	−	A	A	Dimethi-sterone −
39	81	40		+	,, ,,	−	−	?	I	Medroxy-progesterone −
40	48	2			,, ,,	+	−	I	I	Lynoestrenol −
41	57	11		−	,, ,,	−	−	A	A	Lyndiol +
42	45	10	−		,, ,,	+	−	I	I	
43	68	18			,, ,,	−	−	I	I	
44	68	22		+	,, ,,	−	−	I	I	
45	76	26			,, ,,	−	−	A	I	Lyndiol −
46	55	9			,, ,,	−	−	A	A	Dimethi-sterone − Lyndiol −
47	59	10			,, ,,	−		I		Dimethisterone +
48	71	33		−	Dimethisterone 300 mg.	Partial	−	A	A	
49	53	2			,, ,,	−	−	I	I	
50	57	15		−	,, ,,	+	−	I	I	Lyndiol +
51	62	9		−	,, ,,	+	−	I	I	Lynoestrenol −
52	42	3			,, ,,	Partial	−	A	A	Lyndiol −
53	54	8			,, ,,	,,	−	A	A	Megestrol—
54	67	17		−	,, ,,	,,	−	I	I	
55	76	30		−	,, ,,	,,	−	A	A	Megestrol −
56	45	5	−		,, ,,	+	−	A	A	
57	43	1			,, ,,	−	−	I	I	Lyndiol −
58	52	7		−	,, ,,	Partial	−	A	A	Lyndiol −
59	54	5		−	,, ,,	−	−	I	I	
60	48	1			,, ,,	Partial	−	I	I	
61	53	8			,, ,,	,,	−	I	I	Lyndiol −
62	68	24		−	,, ,,	−	−	I	I	
63	75	31		−	,, ,,	−	−	A	I	Medroxy-progesterone − Lyndiol −
64	71	25	−		,, ,,	−		?		
65	59	10		−	,, ,,	+		I		Megestrol −

A = Atrophic. I = Intermediate. ? = Inflammatory.
L.F.T. = Liver-function tests.

TABLE III.—*Agents and Dosage Used in this Trial and Clinical Response of Breast Cancer*

Progestin	Daily Oral Dose	Clinical Response in	Group Response	Significance
19-Nortestosterone Derivatives				
Norethisterone acetate	60 mg.	2 of 12	3 of 19 = 16%	Not significant
Lynoestrenol	30 ,,	1 ,, 7		
17α-Hydroxyprogesterone Derivatives				
Medroxyprogesterone ..	200–400 mg.	2 of 12	5 of 28 = 18%	
Melengestrol	120 mg.	1 ,, 5		
Megestrol	30 ,,	2 ,, 11		
Testosterone Derivative				
Dimethisterone ..	300 mg.	4 of 18	= 22%	

Results

Objective response as defined above was noted in 12 of the 65 patients. It was seen in 3 out of 19 cases on the 19-nortestosterone derivatives, in 5 out of 28 on the 17α-hydroxyprogesterone derivatives, and in 4 out of 18 on the testosterone derivative. In the last group there were 8 additional cases where the observed lesions showed regression but less than 50% reduction in size. There is no statistically significant difference in tumour response rate between the groups (Table III). However, the selected example of the testosterone derivatives (dimethisterone) differs in one respect from the other groups in that it yields a high proportion of patients with partial response, similar to that seen from corticosteroid administration (Stoll, 1963). The dose level selected for dimethisterone appears to be near its minimum effective level, as shown in four of these patients where the dosage was halved when the disease appeared to be partially under control. In two of these patients with nodular infiltration of the chest wall the symptoms of itching and tightness, which had eased at full dosage, reappeared at half dosage, but eased again when full dosage was reinstituted.

Of the 65 patients assessed for tumour response on progestins, 40 had undergone a previous trial of oestrogen or androgen therapy (Table IV). When comparing patients previously responding with those not responding to oestrogen or androgen therapy there is no statistical difference in the proportion of progestin responders (Table IV). Of eight progestin responders who had received a previous trial of oestrogens or androgens, only two had responded to these agents. It has also been reported (Stoll, 1966) that 3 out of 10 patients failing to show tumour regression on 15 mg. of stilboestrol daily did show such a regression when progestins were added. It appears, therefore, that there is no obvious correlation between tumour response to progestins and response to previous sex hormone therapy. It seems likely that progestin responders do not belong to the same group of patients as those who respond to the conventional sex hormones.

TABLE IV.—*Response to Progestins in Relation to Previous Hormonal Response*

Previous Hormone Response	Subsequently Responding to Progestins	Significance
Response to oestrogens or androgens ..	2 of 9 (22%)	Not significant
No response to oestrogens or androgens ..	7 of 31 (22%)	

Side-effects

In the total series of 72 cases, side-effects necessitated stopping therapy in seven cases, found only in the first two groups. Severe nausea and vomiting or abdominal pain accounted for five cases; in one case the complaint was of severe mental depression and in another of irritability. Minor side-effects overcome with persistence included nausea, constipation, and backache. Breakthrough bleeding was noted in only three cases in the total series on high doses of progestins.

Unusual side-effects were noted with the selected example of the testosterone derivatives (dimethisterone). Gross increase in appetite, generally associated with a gain in weight, was mentioned by 7 of the 18 patients. In addition, four of the patients in the group noted an improvement in mood in the form of tranquillization. In two cases in this group taking the hormone for longer than five months it caused long-term side-effects in the form of puffiness of the face and hypertrichosis of the face and chin. Segaloff (personal communication, 1965) noted a Cushingoid effect from prolonged therapy with a 17α-hydroxyprogesterone derivative.

Biochemical and histological evidence of liver damage after the administration of oral progestins and oral contraceptives has been reported (Eisalo *et al.*, 1964; Stoll *et al.*, 1966). Total serum bilirubin and serum aspartate aminotransferase levels were assessed fortnightly in 45 cases in the present series. Only in the 19-nortestosterone group were abnormal changes seen in the aminotransferase levels, the first rise appearing after two weeks' drug administration. Liver biopsy carried out in one of the cases showed evidence of parenchymal cell necrosis with accumulation of lipofuscin (Stoll *et al.*, 1966). In the present series there were no cases with clinical signs of jaundice or a raised bilirubin level.

Glucose-tolerance tests were carried out in eight cases after at least four weeks' drug administration. Abnormally high blood glucose levels after one hour were noted in one of the eight cases (compared with three of four cases in a similar therapeutic trial of Lyndiol (Stoll 1967a)). The liver-function tests showed no gross abnormality in the patients with abnormal blood glucose levels.

Pretreatment Vaginal Smear

The adrenal cortex secretes androgens throughout life in the female. In addition, the secretion of oestrogens and progesterone does not cease with atrophy of the ovary at the menopause, as breakdown products of both these corticosteroids have been shown in the urine in postmenopausal women (Klopper *et al.*, 1955; Nissen-Meyer and Sanner, 1963). The major part of these corticosteroids originates in the adrenal cortex and their circulating levels are reflected in the vaginal smear. It should be noted that the distribution of vaginal smear patterns in postmenopausal patients suffering from breast cancer is no different from that of a control group of normal postmenopausal women of the same age group (Struthers, 1956; Finkbeiner, 1960).

Cytohormonal assessment of the vaginal smear was carried out before initiating treatment in all but one of the patients. After the menopause two main smear patterns are observed, an atrophic pattern and an intermediate pattern. The former indicates a complete absence of sex-hormone stimulation. The latter pattern reflects a response to adrenal hormones, but cytologists disagree on whether it reflects oestrogenic or androgenic substances or a mixture of the two.

The pretreatment vaginal smears were classified by the cytologist as atrophic if over 80% of the cells were parabasal in type, and intermediate if over 80% of cells were of the intermediate type. It is shown in Table V that whereas only 5% of patients with an atrophic smear responded to progestin therapy, 29% of patients with an intermediate smear responded. The difference is statistically significant ($P<0.03$). The pretreatment smear can therefore be used to select patients for progestin therapy in the same way that the "discriminant factor" is used before adrenalectomy or hypophysectomy in advanced breast cancer (Atkins, 1966). It is interesting that in our experience the pre-treatment vaginal smear cannot be correlated with the likelihood of a response either to oestrogens or to androgens (Stoll, 1967b).

TABLE V.—*Clinical Response to Progestins (Described in This Paper) in Relation to Initial Vaginal Smear. Parallel Figures for Lyndiol (Stoll, 1967a) for Comparison*

Hormone Therapy	Proportion of Cases Responding if Initial Vaginal Smear		Significance
	Intermediate	Atrophic	
Progestins ..	11 of 38 (29%)	1 of 21 (5%)	$P<0.03$
Lyndiol ..	8 „ 20 (40%)	1 „ 16 (6%)	$P<0.03$

Effect of Progestins on the Vaginal Smear

The 19-nortestosterone derivatives used in this trial are norethisterone acetate (17α-ethynyl derivative) and lynoestrenol (17α-ethynyl-3-deoxy derivative). Some members of this group show oestrogenic properties and, in addition, the group tends to be androgenic in experimental animals.

The 17α-hydroxyprogesterone derivatives used in this trial are medroxyprogesterone (6-methyl derivative), megestrol (6-dehydro-6-methyl derivative), and melengestrol (16-methylene derivative of megestrol). The testosterone derivative used was dimethisterone (6α,21-dimethylethisterone). These latter two groups of compounds are said to possess no inherent oestrogenicity and no significant androgenic activity in the experimental animal (Goldzieher, 1964).

Serial vaginal smear tests were carried out at two-weekly intervals during progestin therapy in 42 cases. In 16 of these patients who showed a pre-treatment atrophic pattern there was a change to the intermediate pattern in only three after the administration of progestins. One case was recorded in each of the groups—that is, the 19-nortestosterone derivatives, the 17α-hydroxyprogesterone derivatives, and the testosterone derivatives. This picture presumably reflects some degree of inherent oestrogenicity or androgenicity in the compounds involved (Table II).

Discussion

By definition, a progestational agent is one which causes a secretory response in the uterine lining after oestrogen priming. The many synthetic orally active progestational agents available have marked qualitative differences in their oestrogenicity, androgenicity, and metabolic activity. We prefer to use the term "progestins" rather than "progestogens" or "progestational agents," because their major clinical use in recent years has not been for assistance in the initiation of pregnancy. The mode of action of progestins in breast cancer may be by:

1. *Effect on Anterior Pituitary Secretion.*—There is conflicting evidence concerning the effect of progestins on total gonadotrophin excretion (Brown *et al.*, 1964). Nevertheless, it is possible that a decrease in the luteotrophin secretion alone may be the effect common to these agents (Diczfalusy, 1965). They are also said to stimulate release of mammotropin from the pituitary (Kim, 1965).

2. *Conversion of Progestins to Another Active Steroid—such as Androgen or Oestrogen.*—It is believed that some of the 19-nortestosterone derivatives have both androgenic and oestrogenic metabolites. Our vaginal smear observations suggest that this may be true of some members of the other groups also.

3. *Local Effect on the Breast Tumour.*—The possibility of a local effect by progestins on the tumour is shown by Kim's (1965) observation that in the hypophysectomized animal there is a growth-promoting effect on hormone-sensitive mammary cancer by the combined administration of oestradiol and progesterone, but not from oestrogens alone.

Recent experimental reports suggest a fourth possible mode of action. Huggins *et al.* (1962) reported a hormone-sensitive chemically induced mammary cancer in female rats. They reported that oestradiol 20 μg. daily will depress tumour growth, but its combination with 4 mg. of progesterone daily will actually ***extinguish*** tumour growth in the majority. Young *et al.* (1963) noted that the administration of oestradiol after oophorectomy causes tumour reactivation in less than 50% of such rats, but the addition of progesterone causes reactivation in 95% of cases. Similarly, though Sterental ***et al.*** (1963) showed no reactivation of the experimental cancer by oestrogen administration after hypophysectomy, Kim (1965) noted that the combination of oestradiol and progesterone has a very potent growth-promoting effect in the hypophysectomized animal.

All these observations can be interpreted as suggesting a fourth possible mode of action of progestins in breast cancer. It is possible that progesterone acts by sensitizing experimental mammary cancer in rats to the action of oestrogens, whether in the form of stimulation or of depression of tumour growth. If this applies to man one would not expect to obtain significant response of breast cancer to progestin therapy in the absence of oestrogens. This may account for the very poor response rate seen in patients with an atrophic vaginal smear, as such a smear indicates a complete absence of oestrogen stimulation in the postmenopausal woman.

A previous paper (Stoll, 1967a) reported the effect on advanced breast cancer of Lyndiol, a commercially available oral contraceptive containing lynoestrenol, a progestin of the 19-norsteroid group, combined with the oestrogen mestranol. The proportion of responders was similar to that noted in this paper for progestin-treated cases (Table V). The addition of oestrogen (in the form and dose found in Lyndiol) does not seem to increase the response rate in the patient with an atrophic vaginal smear.

There may be some selectivity of action by particular progestins. There were five patients to whom dimethisterone was given after failure of previous progestins, and in two of them tumour response (by full criteria) was noted. However, dimethisterone given to five patients after failure of Lyndiol gave no response. It is suggested that the metabolism of different progestins might be investigated in breast cancer patients by the administration of radioactively tagged progestins. This would establish whether there is indeed a direct effect on the target organ cells. In addition, the distribution of the radioactive hormone in the tumour could be estimated by autoradiography, since localization is probably not uniform and depends on vascularity, patchy necrotic changes, or other factors.

Summary

The effect of representatives of the three major groups of progestins is compared on metastatic soft-tissue growth of breast cancer in postmenopausal women.

Objective regression of soft-tissue tumour was noted in 12 out of 65 patients treated for two months or longer. Differences in side-effects and liver toxicity between the groups are noted. In addition, a corticosteroid-like effect of one agent on breast cancer is noted.

It is possible to differentiate patients with a 29% likelihood of response from those with only a 5% likelihood of response by cytohormonal examination of the postmenopausal vaginal smear before therapy.

The possible mode of action of progestins in breast cancer is discussed.

My thanks are due to Dr. W. J. Moon for many stimulating discussions in the course of this project.

References

Atkins, H. (1966). *Ann. roy. Coll. Surg. Engl.*, **38**, 133.
Baker, W., and Kelley, R. (1960). In *Biological Activities of Steroids in Relation to Cancer*, edited by G. Pincus and E. P. Vollmer. New York.
Brown, P. S., Wells, M., and Cunningham, F. J. (1964). *Lancet*, **2**, 446.
Bucalossi, P. Dipietros, S., and Genneri, L. (1963). *Practitioner*, **191**, 702. (Abstract.)
Diczfalusy, E. (1965). *Brit. med. J.*, **2**, 1394.
Douglas, M., Loraine, J. A., and Strong, J. A. (1960). *Proc. roy. Soc. Med.*, **53**, 427.
Eisalo, A., Järvinen, P. A., and Luukkainen, T. (1964). *Brit. med. J.*, **2**, 426.
Finkbeiner, J. A. (1960). *Acta cytol.*, **4**, 121.
Goldzieher, J. W. (1964). *Med. Clin. N. Amer.*, **48**, 529.
Huggins, C., Moon, R. C., and Morii, S. (1962). *Proc. nat. Acad. Sci. (Wash.)*, **48**, 379.
Jolles, B. (1962). *Brit. J. Cancer*, **16**, 209.
Jonsson, U., Colsky, J., Lessner, H. E., Roath, O. S., Alper, R. G., and Jones, R. (1959). *Cancer (Philad.)*, **12**, 509.
Kim, U. (1965). *Cancer Res.*, **25**, 1146.
Klawans, A. H. (1965). *Presbyterian-St. Luke's Hosp. med. Bull.*, **4**, 63.
Klopper, A., Michie, E. A., and Brown, J. B. (1955). *J. Endocr.*, **12**, 209.
Lewin, I., Spencer, H., and Herrmann, J. (1959). *Proc. Amer. Ass. Cancer Res.*, **3**, 37.
Nathanson, I. T. (1952). *Cancer (Philad.)*, **5**, 754.
Nissen-Meyer, R., and Sanner, T. (1963). *Acta endocr.*, **44**, 325.
Sterental, A., Dominguez, J. M., Weissman, C., and Pearson, O. H. (1963). *Cancer Res.*, **23**, 481.
Stoll, B. A. (1963). *Brit. med. J.*, **2**, 210.
—— (1965). In *Recent Advances in Ovarian and Synthetic Steroids*, edited by R. P. Shearman, pp. 147–155. Sydney.
—— (1966). *Med. J. Aust.*, **1**, 331.
—— (1967a). *Brit. med. J.*, **1**, 150.
—— (1967b). *Cancer (Philad.)*. In press.
—— Andrews, J. T., and Motteram, R. (1966). *Brit. med. J.*, **1**, 960.
Struthers, R. A. (1956). Ibid., **1**, 1331.
Young, S., Cowan, D. M., and Sutherland, L. E. (1963). *J. Path. Bact.*, **85**, 331.

Heart Block and Coronary Artery Disease

M. J. DAVIES,* M.B., B.S.; D. REDWOOD,† M.A., M.B., B.CHIR., M.R.C.P.; A. HARRIS,† M.B., B.S., M.R.C.P.

Brit. med. J., 1967, 3, 342–343

Acute heart block is an uncommon but serious complication of myocardial infarction, though survivors usually return to sinus rhythm.

Chronic heart block associated with Stokes–Adams attacks is also often assumed to be ischaemic in origin. Some clinical reviews have, however, stressed the high incidence of "primary" heart block (Zoob and Smith, 1963; Johansson, 1966). Initial studies from this hospital suggested that significant coronary artery disease was not present in most cases of chronic heart block and that pathological changes were often confined to the conduction system (Portal *et al.*, 1962).

A detailed post-mortem study of both acute and chronic heart block has now been carried out to define the part played by coronary disease in the production of complete heart block.

Material and Methods

The material comprised the hearts from 14 cases of atrioventricular (A-V) block associated with acute myocardial infarction and 53 cases of chronic complete heart block. Many of the hearts from cases of acute infarction were received as post-mortem specimens from other hospitals. The majority of cases of chronic heart block had Stokes–Adams attacks and had been referred to this hospital for pacing. The average age at death for this group was 62. A control series of 35 hearts obtained from routine necropsy material was studied in an identical manner. The control subjects were over the age of 50 at the time of death and had had a normal electrocardiogram in the last three months of life.

Post-mortem examination of the hearts included coronary angiography (Crawford *et al.*, 1961) and serial sections of the coronary arteries at 5-mm. intervals. The degree of atherosclerosis in the coronary arteries was assessed by scoring the degree of stenosis in each of 16 segments, after the method of Eusterman *et al.* (1962). The entire conduction system was studied by use of a serial histological section technique (Davies, 1967).

Results

Acute Infarction.—In 9 of the 14 cases of acute infarction there was thrombotic occlusion of a dominant right coronary artery which supplied the posterior wall of the heart and ultimately the A-V node. In four cases there was occlusion of a dominant left circumflex artery supplying the posterior wall of the heart and A-V node. These 13 cases showed recent posteroseptal infarction. In the remaining patient there was occlusion of the anterior descending coronary artery with a large anteroseptal infarct involving both bundle branches. The site of damage to the conduction system in acute infarction is shown in Table I. Pathological changes in the conduction system with the usual posteroseptal infarct were often relatively minor. If major damage occurred the changes were found in the bundle branches.

2. *Chronic Heart Block.*—The lesions in the conduction system responsible for chronic heart block in 53 cases are shown in Table II. Coronary disease was the cause in only eight and was associated with destruction of both bundle branches in the scarring of old septal infarction. In five of the eight cases this was posteroseptal and in three anteroseptal. Severe atherosclerosis was present in all cases, and recanalized or old occlusions were demonstrable in the coronary arteries in relation to the areas of old infarction. The commonest cause of chronic complete heart block was bundle-branch fibrosis, which accounted for 21 cases. Loss of conduction fibres had occurred in the upper two-thirds of both bundle branches. The immediately adjacent myocardium was normal. The coronary arteries in this group showed no significant degree of atheroma and did not differ from the control group when scored for coronary artery disease, the method devised by Eusterman *et al.* (1962), with serial (5-mm.) sections of the coronary arteries, being used. Focal myocardial scarring was increased compared with the controls, but major pathological changes were more or less confined to the conduction system.

TABLE I.—*Pathology of the Conduction System in 14 Cases of Acute Infarction and Complete Block*

Lesions		No.	Site of Infarction
Normal conduction system		4	Posteroseptal
Focal necrosis in A-V node	Minor pathological changes	3	,,
Partial necrosis of left branch		4	,,
Total necrosis of left branch		1	,,
Complete necrosis of both branches		2	One posteroseptal, one anteroseptal

TABLE II.—*Aetiology of 53 Cases of Chronic A-V Block at Necropsy*

Bilateral bundle branch fibrosis	21 (40%)
Coronary artery disease	8 (15%)
Cardiomyopathy	8
Calcification of valve rings	4
Active myocarditis	2
Rheumatic myocarditis	2
Collagen disease	3
Congenital lesion	1
Aneurysm of membranous septum	1
Amyloidosis	2
Transfusion siderosis	1

Discussion

This paper is concerned only with the relation of coronary artery disease to complete heart block. Detailed analysis of other and more common causes of heart block are reported elsewhere (Davies, 1967).

In the majority of patients who develop complete heart block as a complication of myocardial infarction the conduction disturbance is transitory. This feature has been stressed in clinical reviews, and few survivors need long-term pacing (Penton *et al.*, 1956; Gilchrist, 1958; Harris and Bluestone, 1966). Even in those who die major structural damage to the conduction system is found in only a minority. In most cases it is therefore reasonable to presume that heart block is due to anoxia of the A-V node secondary to an occlusion of the dominant coronary artery, usually the right, which supplies the node. In a minority with acute infarction major damage is found to involve the bundle branches, and only if both branches are totally destroyed will block be permanent.

In the eight cases of chronic heart block due to coronary artery disease, comprising only 15% of those with chronic A-V block, there was destruction of both bundle branches in

---

* Department of Pathology, St. George's Hospital Medical School, London S.W.1.

† Department of Cardiology, St. George's Hospital Medical School, London S.W.1.

areas of old infarction. This figure is in close agreement with that of Johansson (1966), who, on clinical criteria, suspected that only 24 out of 142 cases (17%) of chronic heart block were ischaemic in origin. He offered no pathological explanation for 64 out of 142 cases (45%) which were classified as "primary" heart block. In the present post-mortem series 21 out of 53 cases (40%) were due to bundle branch fibrosis. The pathological basis of primary heart block is therefore bilateral bundle-branch fibrosis; the cause remains unknown, but it is certainly not due to coronary artery disease.

Summary

In a post-mortem study of 53 hearts from patients with chronic atrioventricular block only 8 (15%) were due to coronary artery disease. Bundle-branch fibrosis of unknown aetiology, without major damage to the contractile myocardium, is the commonest cause, being present in 21 cases (40%).

In 14 cases of acute myocardial infarction and A-V block major structural damage to the conduction system was unusual, but, when present, involved the bundle branches.

This work was done during tenure of the William Shepherd Research Fellowship from the Board of Governors of St. George's Hospital. We would like to thank Dr. A. Leatham and Dr. W. B. Robertson for their help in preparing this paper.

REFERENCES

Crawford, T., Dexter, D., and Teare, R. D. (1961). *Lancet*, **1**, 181.
Davies, M. J. (1967). *J. Path. Bact.* In press.
Eusterman, J. H., Achor, R. W. P., Kincaid, O. W., and Brown, A. L., jun. (1962). *Circulation*, **26**, 1288.
Gilchrist, A. R. (1958). *Scot. med. J.*, **3**, 53.
Harris, A., and Bluestone, R. (1966). *Brit. Heart J.*, **28**, 631.
Johansson, B. W. (1966). *Acta med. scand.*, **180**, Suppl. No. 451.
Penton, G. B., Miller, H., and Levine, S. A. (1956). *Circulation*, **13**, 801.
Portal, R. W., Davies, J. G., Leatham, A., and Siddons, A. H. M. (1962). *Lancet*, **2**, 1369.
Zoob, M., and Smith, K. S. (1963). *Brit. med. J.*, **2**, 1149.

Dip-Slide: An Aid to Quantitative Urine Culture in General Practice

DENNIS GUTTMANN,* M.A., M.B., B.CH., B.SC., M.R.C.P.; G. R. E. NAYLOR,† M.A., M.D., M.R.C.P., M.C.PATH.

Brit. med. J., 1967, **3**, 343–345

Since Kass (1956) defined criteria of significant bacteriuria, the use of quantitative assessments of the bacterial population as an aid to the differentiation between infection and contamination of the urine has gained wide acceptance. The pour-plate method is recognized as the standard technique for performing viable counts on urine, but requires trained staff for setting up the cultures. If misleading results are to be avoided, urine specimens must be cultured within an hour or two of collection, or be refrigerated; in general practice it is often difficult to fulfil these requirements. Further, the examination of large numbers of specimens, as at antenatal clinics and in population surveys, makes demands on laboratory services which may become prohibitive if the pour-plate method is employed routinely. A number of simpler cultural methods have been described, such as the filter-paper strip inoculation technique of Leigh and Williams (1964), and the semiquantitative methods of Cattell and Lefford (1963) and of Guttmann and Stokes (1963). Though these are technically less complicated, they are still dependent on the delivery to the laboratory of freshly passed specimens.

Mackey and Sandys (1965, 1966) described a dip-inoculum transport medium in which a metal or plastic spoon carries the culture medium, and which may be inoculated by simply dipping in the specimen, after which it need not reach the laboratory for incubation for 24 or 48 hours. Using standard materials readily available in most laboratories, we have investigated a similar method which we feel has a number of advantages. An ordinary 3- by 1-in. (7.5- by 2.5-cm.) glass microscope slide is coated for a length of about 2 in. (5 cm.) with nutrient agar on one side and with MacConkey's agar on the other. It is held in a small cylindrical aluminium container as supplied in the Public Health Laboratory Service for the collection of faeces specimens. This dip-slide is inoculated by dipping the coated end into the fresh urine specimen. After allowing excess urine to drain for a few seconds, the slide is returned to its container and after replacing the screw cap it is sent to the laboratory, if necessary by post. After overnight incubation the number of colonies which have grown on the slide is counted with a hand lens. The preparation is cheap enough to be discarded after use, and an extensive trial has shown the method to give clinically valuable results. Fig. 1 shows the dip-slide and its aluminium container. Full details of the preparation of the dip-slides are given elsewhere (Naylor and Guttmann, 1967).

Dilutions of broth cultures of Gram-negative rods and Gram-positive cocci isolated from pyogenic infections of the urinary tract were examined by dip-slide inoculation and simultaneous viable bacterial counts: we found a straight-line relationship between the number of colonies on the dip-slide and the number of organisms in the fluid into which it had been dipped; 50 to 100 colonies on the dip-slide correspond to a viable bacterial count of 10,000 per ml. (Naylor and Guttmann, 1967). Fig. 2 shows a series of dip-slides prepared from dilutions of a culture of *Escherichia coli*, and it will be seen that separate colonies readily countable with a hand lens were obtained up to a concentration of 0.6×10^5 organisms per ml. The results of a clinical trial are reported in more detail below.

Methods

From outpatients attending a urinary infection clinic 385 consecutive mid-stream urine specimens were obtained and examined in parallel by the dip-slide, a pour-plate viable count, and the semiquantitative method of Guttmann and Stokes (1963). The last 100 specimens were inoculated on to dip-slides with cycloheximide added to the nutrient agar at a concentration of 100 μg./ml. of medium, as well as on to ordinary dip-slides. Cycloheximide prevents the growth of air-borne mould spores which occasionally were found to contaminate some of the slides during preparation, thus creating difficulties if the dip-slides were stored for some weeks before use. Such a concentration of cycloheximide did not interfere with the growth of bacteria isolated from urine specimens.

Microscopy of the Gram-stained deposit and tests for protein were performed, and white cell excretion rates were estimated by the method of Houghton and Pears (1957), the patients having been instructed to empty the bladder two to three hours before attending the clinic. Preparation of female patients consisted of washing the vulva and perineum with soap and water and drying with a clean towel. Where possible the vaginal orifice was plugged with cotton-wool. A clean catch mid-stream specimen was obtained for bacteriological examination, which was subsequently combined with the remainder of the voided bladder contents for estimation of white cell excretion rates. All specimens were processed within three hours of collection, those which could not be cultured within one hour being refrigerated meanwhile.

---

* Addenbrooke's Hospital, Cambridge.
† Public Health Laboratory Service, Cambridge.

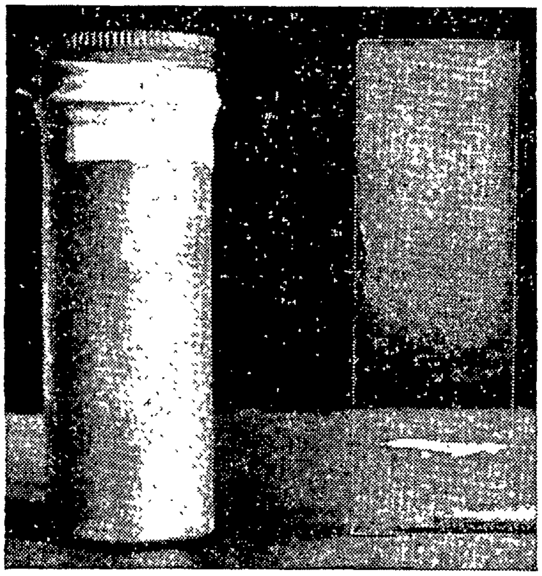


FIG. 1.—The dip-slide.

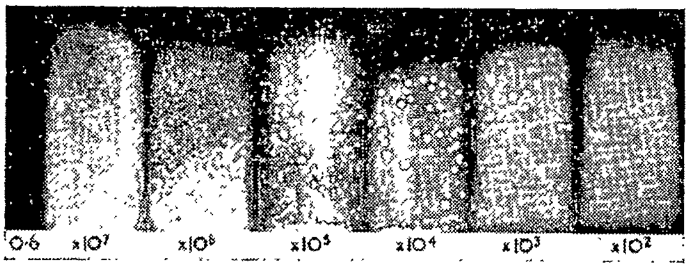


FIG. 2.—Dip-slides inoculated from tenfold serial dilutions of a culture of *E. coli.*

All patients attending the urinary infection clinic had evidence of past or present infection of the urinary tract, and over half the specimens were obtained from patients receiving chemotherapy.

Results

Forty-two specimens were found to contain more than 10^6 organisms per ml., and all these gave a confluent growth on both sides of the dip-slide, except one specimen containing a heavy growth of a coagulase-negative staphylococcus, where no growth was obtained on MacConkey's agar. Fifty-two specimens contained fewer than 100 organisms per ml. and gave no growth on the dip-slide. Culture results on the remaining 291 specimens are shown in Fig. 3; these include 30 specimens containing fewer than 100 organisms per ml., but showing some growth on the dip-slide. The dip-slide colony counts refer to the side of the slide coated with nutrient agar, except where this was overgrown with swarming organisms when the side coated with MacConkey's agar was counted. It will be seen that there is good correlation between the pour-plate counts and the numbers of colonies grown on the dip-slides, the moderate degree of scatter causing no practical difficulty in the interpretation of the results. Essentially similar results were obtained with Gram-negative rods and Gram-positive cocci.

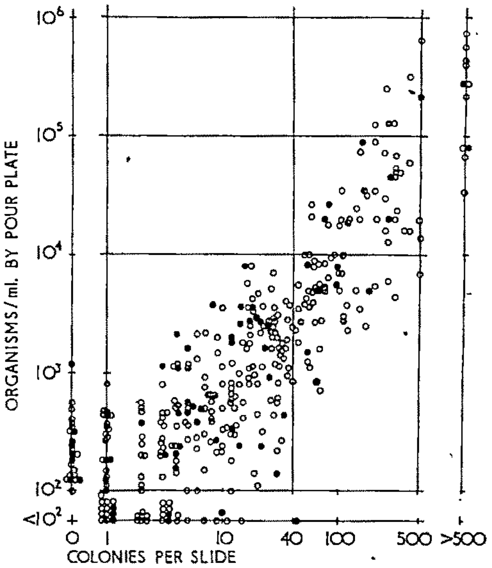


FIG. 3.—Comparison of dip-slide colony counts and viable bacterial counts by the pour-plate method. ○=Ordinary media. ●=Nutrient agar containing cycloheximide 100 μg./ml. (See text.)

In our series of 385 specimens there were 37 which contained between 10^4 and 10^5 organisms per ml., and produced dip-slide counts from 50 to 500 colonies. Six of this group, all from patients receiving chemotherapy, were found by routine methods to give pure cultures of pathogenic organisms, showed protein and increased white cell excretion rates, and were considered to reflect active urinary infection. These could be readily distinguished from heavily contaminated specimens by examination of the dip-slides, the purity or mixed nature of the growth being obvious at this concentration. We believe that there is little danger of missing an active infection of the urine by the dip-slide method even if the viable bacterial count is less than 10^5 organisms per ml. In 4 out of the remaining 31 specimens containing 10^4 to 10^5 organisms per ml. which by routine methods were considered to be heavily contaminated, the dip-slide was wrongly interpreted as indicating true infection; the incidence of false-positive results is therefore acceptably small when the whole series of 385 specimens is considered.

Dip-slide in General Practice

Dip-slides have been used by a number of general practitioners in the Cambridge area, the inoculated slides being sent to the Public Health Laboratory for incubation and reporting. No practical difficulties were experienced and the culture results have been clinically helpful. They have been particularly useful when urine specimens have had to be sent by post, and also when patients attended evening surgeries held after normal laboratory working hours.

A number of patients attending the urinary infection clinic were asked to inoculate dip-slides at home. They were instructed to dip the slide into a mid-stream specimen passed, after perineal toilet, into a basin rinsed with boiling water and allowed to cool, or to wet both sides of the dip-slide in the urine stream while holding the uncoated end in a clothes peg. Preliminary tests showed that the media adhere to the slide firmly enough not to be washed off when the preparation is inoculated in this way. The dip-slide could also be inoculated by pouring urine over both sides if the specimen was collected in a vessel unsuitable for dipping. No difficulty was experienced with excessive contamination of dip-slides inoculated by patients themselves. Home inoculation was found to be of particular value in patients who developed urinary symptoms between visits to the clinic and were unable to attend for a specimen to be collected and examined by routine methods. The response of established infections to chemotherapy could also be followed on an outpatient basis, slides being inoculated on several consecutive days after starting treatment.

Discussion

The dip-slide is based on Mackey and Sandys's idea of a dip-inoculum transport medium. It is made from easily available materials and is cheap. It has two further advantages. Firstly, two media are inoculated simultaneously. This helps considerably in distinguishing between pure cultures of pathogenic organisms and mixed growths due to contamination. Secondly, a larger surface area of medium is available for inoculation. This makes colony counting easier, and the transparency of the preparation is also helpful in this respect. Up to 500 colonies can be easily separated on one side of the dip-slide, the growth becoming confluent only with counts approaching 1,000 colonies. Our clinical trial shows that all specimens containing more than 10^5 organisms per ml. gave dip-slide counts of 200 or more colonies, and specimens with more than 10^4 organisms per ml. produced counts above 40 colonies. Colony counts between 40 and 200 are particularly convenient to read.

We suggest that dip-slide colony counts between 100 and 500 should be regarded as doubtful and an indication for further investigation of the patient. In our series there were 45 specimens in this range, of which eight were considered to be truly infected. It must be remembered that our patients were highly selected, and it is probable that in a random population the incidence of doubtful results would be smaller.

The dip-slide has been in clinical use for over one year. In general practice it was found to overcome difficulties in bacteriological diagnosis which may arise when there is an unavoidable delay between collection of the specimen and its delivery to the laboratory. The ease of inoculation makes it useful in screening clinics where large numbers of specimens have to be processed. With a little experience the majority of dip-slides may be assigned to significantly or non-significantly infected groups by inspection without counting colonies. The quantitative accuracy of the method is greater than that obtained by standard-size loop inoculation methods ; on the other hand, the identification of bacterial species and subculturing are easier than from a pour plate. In our series, which included 60 specimens shown to be infected by conventional methods, the dip-slide yielded no false-negative results, and false-positive results were also not a problem.

We regard the dip-slide as an adjunct to conventional methods of urine examination. It does not obviate the need for microscopy of the deposit, tests for protein, or cultures for the identification of the infecting organism. We do not suggest its introduction for routine use where specimens can be delivered to the laboratory quickly after collection. It may, however, be conveniently used as the only screening method in surveys such as at antenatal clinics. Patients from whom specimens are obtained with dip-slide colony counts in the infected or doubtful range would then be recalled for further investigation by routine methods.

Summary

A dip-inoculum transport medium for the diagnosis of significant bacteriuria is described, consisting of a microscope slide coated with culture media. Laboratory and clinical testing shows the dip-slide to give consistent quantitative results which compare well with pour-plate viable counting.

The dip-slide enables ready differentiation between heavy contamination of urine specimens and genuine infection. In a series of 385 specimens no false-negative results were obtained, and there was an insignificant number of false-positive cultures.

The dip-slide is recommended whenever there is likely to be delay in delivery of urine specimens to the laboratory. It is particularly useful in general practice if specimens have to be sent by post. Owing to the ease of inoculation and reading it is also suited to the routine screening of large numbers of specimens such as at antenatal clinics.

We wish to thank Miss I. J. Barker, Miss V. A. Lane, and Miss S. E. Minns for technical assistance, and the outpatient nursing staff of Addenbrooke's Hospital for their skill in obtaining satisfactory urine specimens. One of us (D. G.) is grateful to Dr. M. H. Gleeson-White for provision of laboratory facilities.

REFERENCES

Cattell, W. R., and Lefford, M. J. (1963). *Brit. med. J.*, **1**, 97.
Guttmann, D., and Stokes, E. J. (1963). Ibid., **1**, 1384.
Houghton, B. J., and Pears, M. A. (1957). Ibid., **1**, 622.
Kass, E. H. (1956). *Trans. Ass. Amer. Phycns*, **69**, 56.
Leigh, D. A., and Williams, J. D. (1964). *J. clin. Path.*, **17**, 498.
Mackey, J. P., and Sandys, G. H. (1965). *Brit. med. J.*, **2**, 1286.
—— —— (1966). Ibid., **1**, 1173.
Naylor, G. R. E., and Guttmann, D. (1967). *J. Hyg. (Camb.)*, **65**. In press.

Sodium Uptake in Peritoneal Dialysis

J. D. SWALES,* M.B., M.R.C.P.

Brit. med. J., 1967, **3**, 345–347

Peritoneal dialysis has come to occupy a prominent place in the treatment of renal disease, and has, indeed, largely replaced haemodialysis in some centres (Cameron, 1966). Pulmonary complications frequently occur, though in many cases they consist of asymptomatic segmental collapse (Berlyne *et al.*, 1966). An occasional, and more often fatal, complication is acute heart failure. In a recent series of 91 patients this complication accounted for two deaths (Stewart *et al.*, 1966).

When dialysis fluid cannot be drained from the peritoneal cavity, fluid overload and heart failure are easily accounted for in terms of the slow absorption of dialysis fluid. However, even where the patient is not in positive fluid balance, heart failure may occur during the course of peritoneal dialysis (see Case Report below). The purpose of this paper is to present data on sodium absorption during 13 consecutive peritoneal dialyses, to suggest that it is the uptake of sodium in hyponatraemic patients which is responsible for the development of heart failure, and to suggest how this potentially fatal complication may be avoided.

Case Report

A 14-year-old schoolboy gave a history of lifelong nocturia. For five years he had had polydipsia and polyuria with recurrent dysuria. In March 1965 he was found to have a blood urea of 450 mg./

---

* Registrar, Medical Professorial Unit, Westminster Hospital, London S.W.1

100 ml., and serum sodium 123, potassium 6.5, and bicarbonate 12 mEq/l. Treatment by continuous bladder drainage and sodium supplements produced a marked improvement and his urea fell to 70 mg./100 ml. He continued as an outpatient, taking 2 g. of sodium chloride and 2 g. of sodium bicarbonate daily. Six months later he was readmitted with a week's history of vomiting. Apart from slight drowsiness there were no abnormal physical signs. His blood pressure was 110/70 mm. Hg. The blood urea was 404 mg./100 ml., serum sodium 125 mEq/l., and serum potassium 4.6 mEq/l. His sodium supplements were stopped, and peritoneal dialysis was started. The dialysis was technically satisfactory in that after eight exchanges he was in a negative fluid balance of 400 ml. However, after 12 hours he became slightly hypertensive (135/95 mm. Hg) and developed an apical gallop rhythm (III sound). At the beginning of the ninth exchange, 22 hours after starting dialysis, he suddenly became acutely dyspnoeic and cyanosed, with fine crepitations over both lung fields. He showed no response to aminophylline, digoxin, and oxygen therapy, and died 20 minutes later. Post-mortem examination showed severe pulmonary oedema with bilaterally shrunken pyelonephritic kidneys containing numerous small cysts.

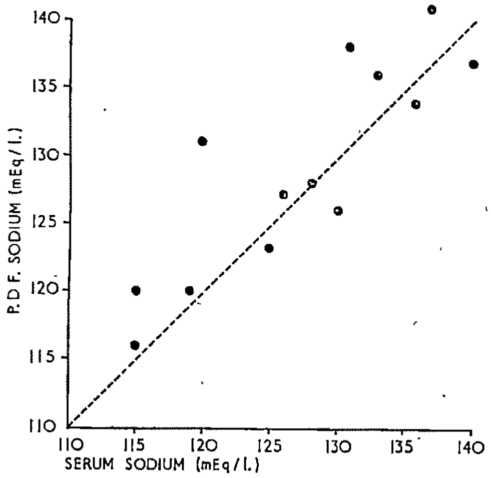


FIG. 1.—Sodium concentration simultaneously measured in serum and peritoneal dialysis fluid at start of peritoneal dialysis.

Comment.—This patient developed a dramatic and fatal pulmonary oedema, though fluid had actually been withdrawn. It could be postulated that significant amounts of sodium were moving along the concentration gradient between the peritoneal dialysis fluid (141 mEq/l.) and his serum (125 mEq/l.), and that this caused the acute pulmonary oedema. No quantitative study has hitherto been made of sodium movements during peritoneal dialysis in relation to the serum sodium concentration. In order to ascertain whether such an uptake of sodium occurs the following study was carried out.

Method

Peritoneal dialysis at this hospital is performed by running in a solution of dextrose (1.36 or 6.36 g./100 ml.) containing the following ions: sodium 141, calcium 3.6, magnesium 1.5, chloride 100.8, bicarbonate (as lactate) 44.6 mEq/l. Generally two such disposable plastic bags are used (Allen and Hanburys). The fluid is warmed to 37° C. and run into the peritoneal cavity through a subumbilical catheter as quickly as possible—usually about 10 minutes. After 45 minutes the fluid is drained out through the same catheter and along a side arm attached to the giving set, which leads to a Winchester bottle beneath the patient's bed. A pressure of −5 mm. of mercury is applied to this bottle by means of a Roberts pump. As much fluid as possible is removed, and then two more bags of fluid are run in. The dialysis in this series continued for 18 to 72 hours. During this period 20 to 35 exchanges were possible.

For this study 13 consecutive dialyses on seven uraemic patients were observed. All the patients were either anuric or severely oliguric and remained so during the period of study. A record was obtained of the type and volume of fluid drained. An aliquot was taken from the dialysis fluid returned from each exchange, and the sodium concentration estimated by means of a flame photometer. Daily serum sodium measurements were also made on the patients.

Results

The serum sodium concentration was low initially in most patients, but generally rose during peritoneal dialysis. The sodium concentration of the peritoneal dialysis fluid which drained from the patient was proportional to the serum sodium concentration, though the dialysis fluid sodium tended to be higher (Fig. 1). This suggests incomplete equilibration between the two fluids.

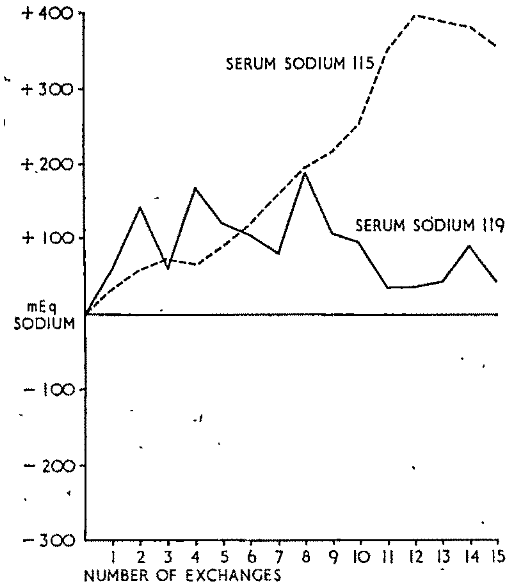


FIG. 2

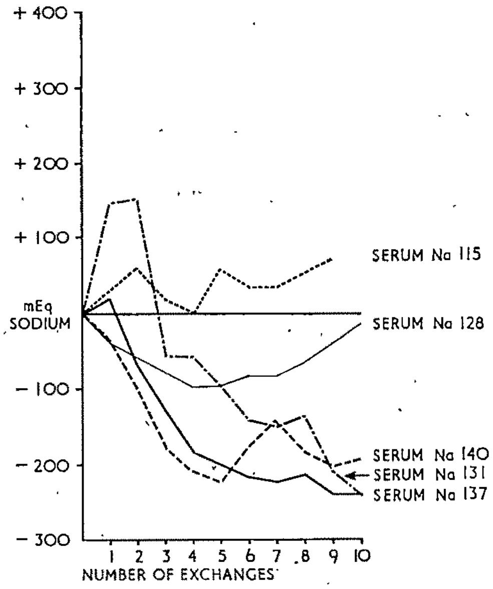


FIG. 3

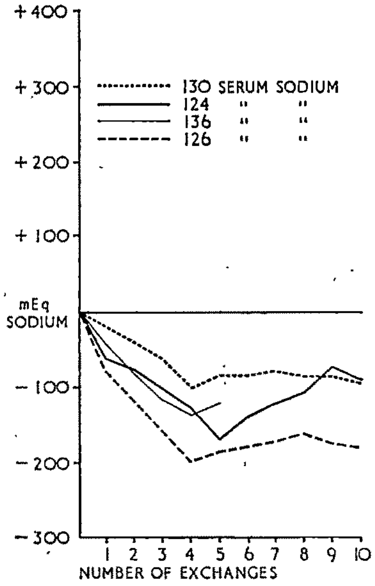


FIG. 4

FIG. 2.—Sodium balance in two patients from whom only small amounts of fluid were removed (0–150 ml. per exchange). FIG. 3.—Sodium balance in five patients from whom 150–300 ml. per exchange was removed. FIG. 4.—Sodium balance in four patients from whom large amounts of fluid were removed (300–450 ml. per exchange).

Four patients developed a positive sodium balance during peritoneal dialysis. In one patient this had reverted to a negative balance by the end of the dialysis. The nature of the sodium balance depended partly on the amount of fluid which was removed (Figs. 2–4) and partly on the initial serum sodium level. Where only a small amount of fluid was removed from a patient with a low serum sodium, a positive sodium balance developed. Two patients are omitted from Figs. 2–4. In one a positive fluid balance occurred because of inadequate drainage, and this was responsible for the sodium uptake of 453 mEq, and in the other fluid was removed more rapidly than in the rest of the series (450 ml. per exchange), with a rapidly developing negative sodium balance in excess of 400 mEq.

Discussion

Urea and electrolytes diffuse along the concentration gradient between fluid within the peritoneal cavity and the serum (Boen, 1961). This process continues until equilibrium is reached after 90 to 120 minutes. During this period the difference in osmolalities determines the volume of fluid absorbed (Shear *et al.*, 1965). The latter workers have shown that subsequently a phase of isotonic absorption occurs when 29.7–39.3 ml. of fluid is absorbed per hour. This latter phase is usually unimportant in peritoneal dialysis, where fluid is not allowed to remain in the peritoneal cavity longer than 45 minutes.

The present study was undertaken to quantify the sodium transfer during the initial period of equilibrium and to determine whether such movement would be physiologically important. The results suggest that significant amounts of sodium are absorbed when a hyponatraemic patient undergoes peritoneal dialysis in which only small amounts of fluid are removed. This may account for the occasional episode of pulmonary oedema during peritoneal dialysis which, as in the case described, may be fatal.

How can this complication be avoided? One answer would be to lower the sodium concentration of the fluid administered. This would necessitate the preparation of several types of dialysis fluid, containing different concentrations of sodium, making the management of peritoneal dialysis a much more complicated operation. Alternatively, one could reproduce the situation seen in the majority of cases in this series, and withdraw large volumes of fluid from the patient by means of the dialysis. The present series shows that this keeps the patient in negative sodium balance.

Hypertonic dialysis fluid may remove greater quantities of urea than isotonic fluid. This is not merely due to the increased amount of fluid withdrawn, but is also partly attributable to the phenomenon known as "solvent drag." When a large volume of fluid passes through a porous membrane, solute tends to move with it, even against a concentration gradient. It has been postulated that solute particles (in this case urea) are entrained in the solvent stream (Henderson, 1966). In order to determine whether sodium could be withdrawn in such a way by using a hypertonic fluid, peritoneal dialysis fluid containing 6.36 g. of glucose per 100 ml. was administered intermittently and the sodium concentration after each such exchange measured. This failed to produce any increase in the sodium concentration of the dialysis fluid removed (see Table).

Effect of Varying Glucose Concentration on Sodium Concentration of Fluid Drained from a Peritoneal Dialysis

Dialysis fluid glucose (g./100 ml.) ..	1·36	1·36	6·36	6·36	1·35
Sodium concentration of effluent (mEq/l.)	125	126	123	122	125

Nevertheless, the present series of cases indicates that if a patient on peritoneal dialysis is kept in a negative fluid balance of several litres there is little danger of excessive sodium absorption.

Summary

In hyponatraemic patients there is a marked gradient between concentration of sodium in the peritoneal dialysis fluid and the serum. In order to establish whether this causes a positive sodium balance the sodium uptake was measured during dialysis. In 4 out of 13 dialyses there was a positive sodium balance, in one case reaching 400 mEq, despite a negative fluid balance in three of these cases. It is suggested that this may be responsible for acute heart failure during dialysis.

REFERENCES

Berlyne, G. M., Lee, H. A., Ralston, A. J., and Woolcock, J. A. (1966). *Lancet*, **2**, 75.
Boen, S. T. (1961). *Medicine (Baltimore)*, **40**, 243.
Cameron, J. S. (1966). *Brit. med. J.*, **2**, 811.
Henderson, L. W. (1966). *J. clin. Invest.*, **45**, 950.
Shear, L., Swartz, C., Shinaberger, J. A., and Barry, K. G. (1965). *New Engl. J. Med.*, **272**, 123.
Stewart, J. H., Tuckwell, L. A., Sinnett, P. F., Edwards, K. D. G., and Whyte, H. M. (1966). *Quart. J. Med.*, **35**, 407.

Thalassaemia and Hydrops Foetalis—Family Studies

DAVID TODD,* M.D., F.R.C.P.ED.; MICHAEL LAI,† B.SC.; CAROLINA A. BRAGA,‡ M.A., M.B., B.S., M.R.C.O.G.

Brit. med. J., 1967, **3**, 347–349

Stillbirth or neonatal death associated with severe hydrops foetalis, hypochromic anaemia, erythroblastosis, and large amounts of haemoglobin Bart's was first described by Lie-Injo and Jo (1960). In subsequent studies Lie-Injo (1962) and Lie-Injo, Lie, Ager, and Lehmann (1962) reported that the parents of such infants showed haematological changes consistent with α-thalassaemia trait, and they thought that the hydropic babies were homozygous for α-thalassaemia. Reports by Diamond, Cotgrove, and Parker (1965) and Pootrakul, Wasi, and Na-Nakorn (1966) lend support to this view.

In Hong Kong haematological studies have been made on the families of seven Chinese babies with severe hydrops foetalis associated with over 75% of haemoglobin Bart's, and, while there was evidence that five were homozygous for α-thalassaemia, in two a possible interaction between α- and β-thalassaemia was suggested. The purpose of this communication is to report these studies.

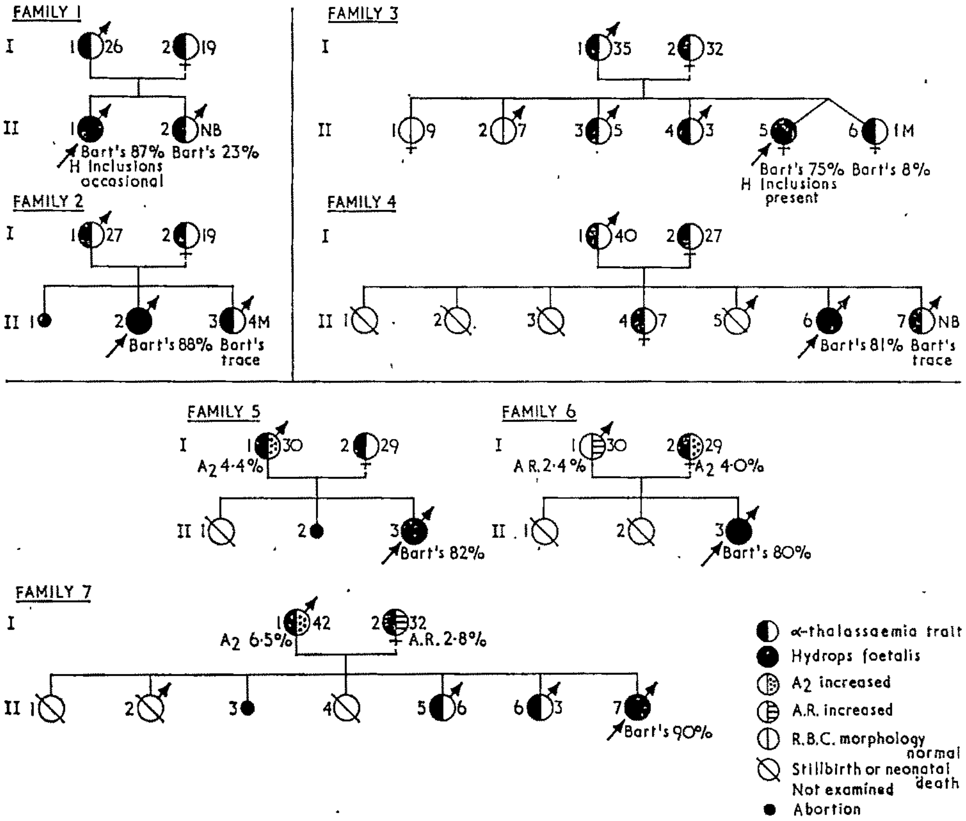
---

* Senior Lecturer, Department of Medicine, University of Hong Kong.
† Demonstrator, Department of Biochemistry, University of Hong Kong.
‡ Senior Lecturer, Department of Obstetrics and Gynaecology, University of Hong Kong

Material and Methods

All the subjects studied were Chinese and comprised seven stillborn babies with severe hydrops foetalis and over 75% haemoglobin Bart's, and their parents and living sibs. In the case of the hydropic babies, whose periods of gestation had varied from 32 to 38 weeks, cord or cardiac blood was examined. Iron deficiency was excluded in the parents of six of the seven families and the living sibs in Family 3 by the finding of normal serum iron levels ; in the remainder the haematological studies were carried out after at least one month of oral iron therapy. The haematological values of the mothers were those obtained after delivery. All parents were Rh-positive.

Standard haematological methods were used throughout. Red cell osmotic fragility was determined by the method described by Flatz, Pik, and Sringam (1965). The direct Coombs test was performed according to Dacie and Lewis (1963). Alkali-resistant haemoglobin was estimated (Singer, Chernoff, and Singer, 1951), and the amounts of haemoglobin A, A_2, and Bart's were determined by starch block electrophoresis at *p*H 8.6 (Kunkel, Ceppellini, Müller-Eberhard, and Wolf, 1957). In 56 control subjects the haemoglobin F levels were invariably less than 2% and the haemoglobin A_2 levels varied from 1.6 to 3.2%. Starch-gel electrophoresis at *p*H 7.0 was carried out according to Huehns, Flynn, Butler, and Shooter (1960) and at *p*H 8.6 according to Smithies (1959). Red cells were incubated with 1% brilliant cresyl blue at 37° C. for 30 minutes to detect haemoglobin H inclusions (Dittman, Haut, Wintrobe, and Cartwright, 1960), and at least 5,000 red cells were examined.



Pedigrees of the families of the seven hydropic babies.

Results

In the seven hydropic babies the necropsy findings were similar to those in the cases reported by Lie-Injo (1962). The haemoglobin levels varied from 3.3 to 10.0 (mean 7.4, S.D. 2.3) g./100 ml., and the blood smears showed markedly hypochromic red cells with anisopoikilocytosis, target formation, polychromasia, and numerous normoblasts. In only two instances (Families 1 and 3) were occasional red cells with haemoglobin H inclusions found. The amount of haemoglobin Bart's varied from 75 to 90% of the total haemoglobin (see Family Trees). The remaining 10 to 25% consisted of haemoglobin which migrated like haemoglobin A on starch block electrophoresis at *p*H 8.6 but was not seen in the position of haemoglobin A on starch-gel electrophoresis at *p*H 7.0. This fraction is being further studied by Dr. E. R. Huehns, of University College Hospital, London, and he has confirmed that the main haemoglobin fraction of the hydropic baby of Family 5 is haemoglobin Bart's. The alkali-resistant haemoglobin levels varied from 35 to 77% (mean 59.7%, S.D. 14.9%), and haemoglobin A_2 was not found in any. The direct Coombs test was negative in all, and three had the same ABO blood group as their mothers.

The haemoglobin levels in the seven fathers varied from 13.0 to 15.2 (mean 13.8, S.D. 0.7) g./100 ml., and in the seven mothers from 8.5 to 12.6 (mean 10.9, S.D. 1.1) g./100 ml. The red cells were hypochromic and showed decreased osmotic fragility in all except the father in Family 6.

The haemoglobin levels in the eight living male sibs varied from 9.8 to 12.5 (mean 11.7, S.D. 0.7) g./100 ml., and in the three living female sibs from 5.4 (a twin) to 13.0 (mean 10.2, S.D. 3.0) g./100 ml. The red cells were hypochromic and showed decreased osmotic fragility in all except two (Family 3, II 1 and 2).

Other details are set out in the accompanying Fig., in which only abnormal values of haemoglobin F and A_2 are shown. Subjects with normal or slightly decreased haemoglobin levels, hypochromic red cells, decreased red cell osmotic fragility, and normal amounts of haemoglobin F and A_2 are thought to be carriers of the α-thalassaemia trait (Weatherall, 1965). In four living sibs, all 4 months or younger, relatively small amounts of haemoglobin Bart's were found. No haemoglobin H inclusions were shown in the red cells of the parents or living sibs.

It will be seen that two parents (Family 6 I 1, Family 7 I 2) had slight but significantly raised levels of alkali-resistant haemoglobin which was thought to be haemoglobin F, as haemoglobin Bart's was not shown on starch-gel electrophoresis at *p*H 7.0. With these two exceptions, haemoglobin F levels were normal in the parents and in the seven living sibs aged 3 years or older, varying from 0.6 to 1.8% (mean 1.1%, S.D. 0.3%). In three parents (Family 5 I 1, Family 6 I 2, and Family 7 I 1) the haemoglobin A_2 levels were above normal, being 4.4, 4.0, and 6.5% respectively, while in the remaining parents and seven living sibs aged 3 years and older haemoglobin A_2 levels were normal, varying from 1.8 to 3.0% (mean 2.4%, S.D. 0.3%).

In Family 3, subjects II 5 and 6 were binovular twins, and subjects II 1 and 2 were haematologically normal. Sibs not studied included three neonatal deaths from unknown cause occurring two to four weeks after birth and one stillborn baby with hydrops foetalis in Family 4; one stillbirth in Family 5; two stillbirths with hydrops foetalis in Family 6; and two stillbirths and one neonatal death from unknown cause in Family 7.

Discussion

In Families 1 to 4 inclusive both parents showed haematological changes compatible with α-thalassaemia trait. Further, the living infants had small amounts of haemoglobin Bart's in addition to a mild thalassaemic blood picture. These findings are similar to those reported by Lie-Injo (1962) and Lie-Injo *et al.* (1962), and are consistent with the hydropic babies being homozygous for an α-thalassaemia gene. The relatively high level of haemoglobin Bart's of 23% in Subject II 2 of Family 1 is of particular interest, but unfortunately he has been lost to follow-up.

The finding in Families 5, 6, and 7 of three parents with high haemoglobin A_2 levels and two with increased haemoglobin F levels indicates the presence of β-thalassaemia trait and has not been previously reported among parents of similar hydropic babies. Since the combination of α-thalassaemia with either high or normal haemoglobin A_2 β-thalassaemia results in a mild thalassaemia only (Weatherall, 1965), it is unlikely that the hydrops foetalis was the result of double heterozygosity for α- and β-thalassaemia. The hydropic babies may have been, like those in Families 1 to 4, homozygous for α-thalassaemia, in which case the parents with the β-thalassaemia trait were by coincidence doubly heterozygous for α- and β-thalassaemia. However, the finding of a β-thalassaemia trait in 5 of 14 parents appears to be more than can be accounted for by chance. Further, the obstetrical histories of the mothers in Families 5–7 appear to be particularly bad, for in 13 pregnancies there were six stillbirths and two abortions in addition to the three hydropic babies (see Fig.). It is not clear what part the β-thalassaemia gene in the father of Family 5 had to play in the production of hydrops foetalis. However, in view of the report by Zuelzer, Robinson, and Booker (1961) that thalassaemia major may result when one parent has a high haemoglobin A_2 β-thalassaemia and the other a normal haemoglobin A_2, high haemoglobin F (4.3%) β-thalassaemia it is possible that the hydropic babies in Families 6 and 7 were the result of interaction between two β-thalassaemia genes and an α-thalassaemia gene, which, in the homozygous state, gives rise to hydrops foetalis. This hypothesis would be supported by the finding among living sibs either of increased levels of haemoglobin A_2 or F similar to those in the parents or of β-thalassaemia major, but unfortunately in the three families concerned out of 13 pregnancies there were only two living children.

The nature of this α-thalassaemia gene is not known, but it would appear to lead to a marked suppression of α-chain synthesis in the homozygous state. It is probably different from the α-thalassaemia gene in Negroes (Weatherall, 1965), as similar hydropic babies have not been reported among that race. It is also probably different from the "mild" α-thalassaemia gene of haemoglobin H disease (Huehns, 1965), which is usually not associated with red cell hypochromia, and, furthermore, haemoglobin H disease and hydropic babies with over 75% haemoglobin Bart's appear to occur in different families. It may be identical with the "severe" α-thalassaemia gene of haemoglobin H disease (Huehns, 1965). So far this severe α-thalassaemia gene has been reported only in Chinese (Lie-Injo, 1962), in Thais (Pootrakul *et al.*, 1966), and in Greek Cypriots (Diamond *et al.*, 1965), in all of whom haemoglobin H disease has also been encountered (Weatherall, 1965).

ADDENDUM.—Since the completion of this paper Kan *et al.* (1967) have reported a case of hydrops foetalis with large amounts of haemoglobin Bart's. The patient's father had an increased level of haemoglobin A_2.

Summary and Conclusions

Haemoglobin studies were carried out on the families of seven Chinese stillborn infants with severe hydrops foetalis and over 75% haemoglobin Bart's. Rh and ABO incompatibility were excluded.

There was evidence that five of the seven cases were the result of the homozygous state for α-thalassaemia. In the remaining two there was the possibility of interaction between an α-thalassaemia gene and a variety of β-thalassaemia major.

We are grateful to Dr. A. C. de Barros Lopes for referring Family 5 to us, and to Dr. John Grant for the serum iron determinations.

REFERENCES

Dacie, J. V., and Lewis, S. M. (1963). *Practical Haematology*, 3rd ed., p. 166. London.
Diamond, M. P., Cotgrove, I., and Parker, A. (1965). *Brit. med. J.*, **2**, 278.
Dittman, W. A., Haut, A., Wintrobe, M. M., and Cartwright, G. E. (1960). *Blood*, **16**, 975.
Flatz, G., Pik, C., and Sringam, S. (1965). *Brit. J. Haemat.*, **11**, 216.
Huehns, E. R. (1965). *Postgrad. med. J.*, **41**, 718.
—— Flynn, F. V., Butler, E. A., and Shooter, E. M. (1960). *Brit. J. Haemat.*, **6**, 388.
Kan, Y. W., Allen, A., and Lowenstein, L. (1967). *New Engl. J. Med.*, **276**, 18.
Kunkel, H. G., Ceppellini, R., Müller-Eberhard, U., and Wolf, J. (1957). *J. clin. Invest.*, **36**, 1615.
Lie-Injo, L. E. (1962). *Blood*, **20**, 581.
—— and Jo, B. H. (1960). *Brit. med. J.*, **2**, 1649.
—— Lie, H. G., Ager, J. A. M., and Lehmann, H. (1962). *Brit. J. Haemat.*, **8**, 1.
Pootrakul, S., Wasi, P., and Na-Nakorn, S. (1966). *Abstracts of Papers, XIth Congress of International Society of Haematology, Sydney*, p. 123.
Singer, K., Chernoff, A. I., and Singer, L. (1951). *Blood*, **6**, 413.
Smithies, O. (1959). *Biochem. J.*, **71**, 585.
Weatherall, D. J. (1965). *The Thalassaemia Syndromes*. Oxford.
Zuelzer, W. W., Robinson, A. R., and Booker, C. R. (1961). *Blood*, **17**, 393.

Preliminary Communications

Virus Antibodies in Subacute Sclerosing Panencephalitis: a Study of 22 Patients*

Brit. med. J., 1967, 3, 350–352

Subacute sclerosing panencephalitis was the term suggested by Greenfield (1950) to cover the subacute inclusion-body encephalitis described by Dawson (1933) and the subacute sclerosing leucoencephalitis of Van Bogaert (1945), as well as mixed forms. This has been accepted to some extent in the English literature (*B.M.J.*, 1965), but the earlier terms are still in use (Ulrich and Kidd, 1966; Dayan *et al.*, 1967). The histological appearances of the condition certainly differ from case to case, but they may also vary during the evolution of the disease; in an example reported by Schiøtt (1959) inclusion bodies were found in brain biopsy material obtained six months from the onset of symptoms, but not in post-mortem material two months later. At present, therefore, the condition cannot be clearly subdivided on histological grounds.

The inclusion bodies suggest that the disease might have a viral origin, but until recently there was no evidence to incriminate any particular virus. However, in 1965 Bouteille *et al.* published electronmicrographs of biopsy material, and the appearances of the inclusions were strikingly similar to those of measles virus grown in dog-kidney-tissue culture (Tawara, 1965). Tellez-Nagel and Harter (1966) and Dayan *et al.* (1967) have published similar pictures from other cases. Connolly *et al.* (1967) have described the presence of measles complement-fixing and haemagglutination-inhibiting antibodies in the serum and C.S.F. of three cases, and have demonstrated fluorescence in post-mortem brain material treated with fluorescein-labelled measles antiserum.

As part of a virological investigation into encephalitis we have examined sera from patients with subacute sclerosing panencephalitis for the presence of viral antibodies. Measles antibody was present in all cases, often in high titre. This report compares the results of serological tests for measles and other viral antibodies in patients and controls.

PATIENTS AND METHODS

We were able to study 22 patients (16 males and 6 females) referred to this department for investigation. One of them was also studied by Connolly *et al.* (1967). Their ages at the onset of neurological symptoms ranged from 5 to 18 years (Table I). Some of them were included in the clinical report of Metz *et al.* (1964); all were observed to suffer from typical repetitive movements, and all had at least two of the following features: convulsions, intellectual deterioration, behavioural disorder, and impaired motor function. The C.S.F. Lange test gave a paretic rise in all but two cases, in one of which it was not performed. All but one had the characteristic E.E.G. changes (Cobb and Hill, 1950). Confirmation of the diagnosis by pathological examination of biopsy or post-mortem material, or both, was obtained in 14 cases, including one with an uncharacteristic E.E.G. and the one in which the Lange test was not done; inclusion bodies were found in eight. Serum was available from all 22 patients, and C.S.F. from nine of them.

Serum was also available from 23 control subjects (13 males and 10 females) of the same age range as the patients (Table I). None suffered from any sort of progressive neurological disease, and they were referred to this department for investigation of childhood infectious diseases, such as gastroenteritis or aseptic meningitis, or for screening for rubella antibodies. None was known to suffer from immunological deficiency.

TABLE I.—*Age and Sex Distribution of 22 Patients and 23 Controls*

		Age in Years													
		5	6	7	8	9	10	11	12	13	14	15	16	17	18
Patients	M	1			1	1	3	3	1	1		2		2	1
	F		2				1	1	1				1		
Controls	M	2	1	1		1	3	2	2			1			
	F		2	1	1		1	2	1	1					1

Before examination sera and C.S.F. specimens were stored at −20° C. for periods of up to six years.

COMPLEMENT-FIXATION TEST FOR MEASLES AND OTHER VIRAL ANTIBODIES

The sera were diluted 1:10 in veronal-buffered saline and inactivated at 56° C. for 30 minutes; two of the patients' specimens proved anticomplementary and required a further 30 minutes' heating. Serial twofold dilutions were then made from 1:10 to 1:2,560. The C.S.F. specimens were not inactivated; they were tested undiluted and in serial twofold dilutions up to 1:32. Antigens and control antisera were kindly provided by the Standards Reference Laboratory at Colindale, except for the herpes antigen, which was made in this department from a strain of herpes simplex cultured in a continuous line of rabbit-kidney cells (RK-13). The test was performed by means of a microtechnique on perspex plates, four units of antigen and two units of complement being used. Fixation was allowed to take place overnight at 4° C., and the following day two volumes of 0.4% sensitized sheep red cells were added. The endpoint of the titration was taken as the highest dilution showing complete or almost complete fixation of complement.

Complement-fixation tests on patients' sera and control sera were performed on different days; a positive antiserum and three of the patients' sera were tested on both occasions, the results agreeing to within one dilution. Serum and C.S.F. pairs were titrated together in five cases and separately in four with identical antiserum results.

HAEMAGGLUTINATION-INHIBITION TEST FOR MEASLES

The sera were diluted 1:2 in normal saline and were then absorbed with 25% kaolin for 20 minutes at room temperature, and with 50% Patas red cells overnight at 4° C. The dilution of the specimens after treatment was taken as 1:4 and serial twofold dilutions were prepared from 1:8 to 1:2,048. Four sera were available only at a dilution of 1:10, at which they had been stored for three weeks; they were absorbed in a similar way and diluted from 1:20 onwards. The C.S.F. specimens were not absorbed; they were serially diluted up to 1:32. Haemagglutinating antigen was prepared in this laboratory from an Edmonston B strain of measles virus kindly supplied by Glaxo Laboratories Limited, and was treated with Tween 80 and ether before use. Eight haemagglutinating doses were used, and the test was carried out by a microtechnique in Takatsy plates. Specimens of serum and C.S.F. were

---

* Supported by a grant from the National Fund for Poliomyelitis Research.

allowed to react with antigen at room temperature for two hours; one volume of 1% Patas cells was then added and the plates were incubated at 37° C. until the cells had settled—that is, for about 45 minutes. The endpoint of the titration was taken as the highest showing complete or almost complete inhibition of agglutination.

All save one of the patients' sera and all the control sera were tested for haemagglutination-inhibiting antibody together on the same day. Five of the serum/C.S.F. pairs were titrated together, and two were done separately; there was insufficient C.S.F. for testing from the remaining two.

RESULTS

The measles complement-fixing and haemagglutination-inhibiting antibody titres in patients and controls are shown in Tables II and III. Where more than one serum was available from a patient the first specimen has been recorded, except for one haemagglutination-inhibition result, where the second specimen has been recorded because the first had been stored at 1:10 dilution; this can cause a fall in titre. The antibody levels in the patients are much higher than in the controls, and the differences are highly significant: grouping the complement-fixing antibody levels into those of 80 and above and those below 80, $\chi^2=30.35$, $P<0.01$; similarly, grouping the haemagglutination-inhibiting antibody levels into those of 64 and above and those less than 64, $\chi^2=9.79$, $P<0.01$. The patients' levels are comparable to those we have found in convalescent measles patients when using the same technique.

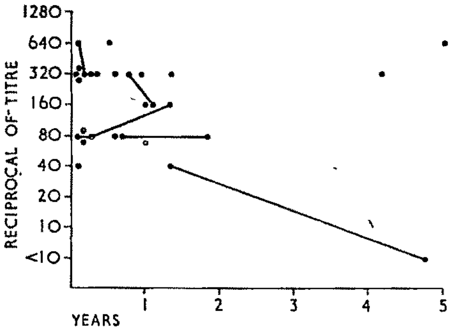


FIG. 1

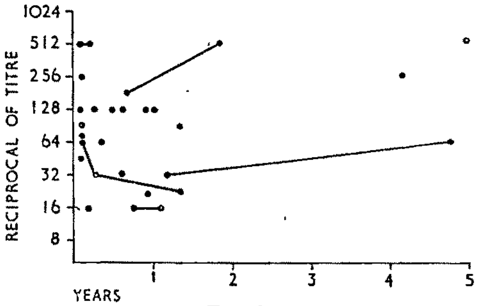


FIG. 2

FIG. 1.—Reciprocal of measles complement-fixing antibody titre related to duration of neurological disease in years in 22 patients. FIG. 2.—Reciprocal of measles haemagglutination-inhibiting antibody titre related to duration of neurological disease in years in 22 patients.

TABLE II.—*Reciprocal of Measles Complement-fixing Antibody Titre in 22 Patients and 23 Controls*

	Reciprocal of Titre							
	<10	10	20	40	80	160	320	640
No. of patients				2	6	1	10	3
„ „ controls	7	5	7	2	2			

TABLE III.—*Reciprocal of Measles Haemagglutination-inhibiting Antibody Titre in 22 Patients and 23 Controls*

	Reciprocal of Titre										
	<8	8	16	24	32	48	64	96	128	256	512
No. of patients			2	1	2	1	3	2	6	2	3
„ „ controls	2	4	7		4		6				

Because patients and controls are not precisely matched for age and sex, the results have been examined for correlation with both these variables for patients and controls, and there is no correlation with either.

Tables IV and V give the antibody levels of patients in whom a neuropathological examination was made, divided into those with inclusion bodies and those without. There is no difference in complement-fixing antibody levels between these groups, and, though haemagglutination-inhibiting antibody levels are higher in the patients with inclusions, the numbers are small and the difference falls short of statistical significance (by Yates's method $\chi^2=3.22$, $0.1>P>0.05$).

TABLE IV.—*Measles Complement-fixing Antibody*

	Reciprocal of Titres				
	40	80	160	320	640
Patients without inclusion bodies	1	2		4	
„ with „ „	1	1	1	3	1

TABLE V.—*Measles Haemagglutination-inhibiting Antibody*

	Reciprocal of Titres					
	16	32	64	128	256	512
Patients without inclusion bodies	1	3	1	1	1	
„ with „ „			1	5	1	1

Figs. 1 and 2 show complement-fixing and haemagglutination-inhibiting antibody titres in relation to the duration of neurological symptoms. No correlation is seen and there is no significant rise in titre in the serial specimens available.

The results of complement-fixation tests against other virus antigens are shown in Table VI. Herpes antibody is present with significantly greater frequency in patients than in controls, but 11 patients had no demonstrable herpes antibody. There is no difference in the incidence or titre of other antibodies.

Measles complement-fixing antibody was demonstrated in the C.S.F. in five out of nine patients tested and haemagglutination-inhibiting antibody in seven out of seven. Herpes complement-fixing antibody could be found in only two out of nine. The serum complement-fixing antibody levels obtained in the simultaneous serum and C.S.F. tests were considerably lower than on several previous estimations, owing to deterioration with storage, so an accurate C.S.F./serum ratio cannot be calculated.

TABLE VI.—*Reciprocal Complement-fixing Antibody Titres to Viral Antigens in 22 Patients and 23 Controls*

		Reciprocal of Titre						
		<10	10	20	40	80	160	320
Mumps S	Patients	18	2	2				
	Controls	19	3	1				
„ V	Patients	13	3	3	1	2		
	Controls	7	4	7	3	1		1
Herpes	Patients	8	5	3	6			
	Controls	19		1	1	1	1	
LCM	Patients	21	1					
	Controls	23						
Flu A	Patients	21	1					
	Controls	22		1				
„ B	Patients	20	1			1		
	Controls	21		1			1	
„ C	Patients	12		9	1			
	Controls	7	4	8	2	2		
Adeno	Patients	12	6	3	1			
	Controls	13	1	7	1			1

DISCUSSION

These investigations have revealed abnormally high titres of both complement-fixing and haemagglutination-inhibiting measles antibodies in the serum of 22 patients with subacute sclerosing panencephalitis. Such titres are usually found only in the convalescent phase of measles, after which complement-fixing antibody declines rapidly and haemagglutination-inhibiting antibody more slowly (Krugman *et al.*, 1965). In one of our patients the neurological illness may have begun with an attack of measles which occurred at the age of 8 months and was complicated by corneal ulceration; her legs became spastic soon afterwards and her subsequent development was retarded, but the full picture of subacute sclerosing panencephalitis was not seen until five years later. However, the remaining 16 patients from whom a history was available had had uncomplicated attacks of measles which preceded their encephalitis by intervals of 3 to 14 years.

Abnormally high titres of measles antibody have also been found in the serum of patients with multiple sclerosis (Adams and Imagawa, 1962; Reed *et al.*, 1964; Clarke *et al.*, 1965), and this has not yet been explained. In subacute sclerosing encephalitis, however, the supporting evidence of electron-microscopy and immunofluorescence justifies the suggestion that measles, or an antigenically related virus, is the cause of the disease. If this is so three possible mechanisms can be considered.

Firstly, measles virus might have entered the central nervous system at the time of the original attack and remained latent there for some years before being reactivated and producing disease. This would be analogous to the generally accepted pathogenesis of varicella-zoster infection in man, and to the deferred encephalitis which can be produced experimentally in rabbits infected with herpes simplex (Good and Campbell, 1948; Schmidt and Rasmussen, 1960). There is a certain amount of evidence that the central nervous system can be involved in natural measles infection. In uncomplicated cases Ojala (1947) found pleocytosis in the C.S.F. in some instances, and Pampiglione (1964) discovered E.E.G. abnormalities in all cases tested. Adams *et al.* (1966) described measles-type inclusions in the brains of patients who had died of acute measles encephalitis. Thus the virus often affects the nervous system in some way, and may gain entry to it in certain circumstances. There is support for the concept of latency in the work of Enders-Ruckle (1965), who reported the isolation of measles virus from lymph nodes and spleen some years after measles infection. At present, however, there is no other recorded example of latent infection with measles or with any other ribonucleic acid virus.

Secondly, the disease may be caused by reinfection with measles in an already immune or partially immune person. It is generally accepted that immunity to measles is long-lasting, but this is based on the fact that second attacks of measles with a rash are exceedingly rare, and the sustained immunity may itself be the result of repeated subclinical infection (Krugman *et al.*, 1965). We have not found any history of exposure to reinfection in our cases.

Thirdly, the disease may be due to a virus related to measles, such as canine distemper virus, which can certainly produce a subacute as well as an acute neurological disease in dogs. At present these two viruses cannot be clearly differentiated on the basis of serum antibodies, immunofluorescence, or electron-microscopy. One of our patients had a pet ferret which died just before his encephalitis began, but we have found no other history of specific contact with animals likely to have been suffering from distemper virus infection.

With any of these mechanisms one would expect the antibody titre to rise in the early stages of the neurological disease, unless latent measles infection had provided a continuing stimulus to antibody production ever since the original attack of measles. We do not know whether these patients' antibody levels were normal in the interval between their original attack and the onset of their encephalitis, and we have not demonstrated a significant rise in titre with progress of the disease. However, in only one case was a specimen of serum obtained in the first month of illness, so that an early rise could have been missed. We have not found any parallel to the case described by Connolly *et al.* (1967) in which the antibody titres rose markedly over a period of 10 months. The mortality rate in this condition is of course high, but in three of our patients the disease has become arrested, and in one there has been a good recovery after about a year's illness. Four years after recovery this patient's complement-fixing antibody level has fallen to an undetectable level, but haemagglutination-inhibiting antibody has not altered significantly.

There is now evidence that measles-like virus particles and virus antigen are present in the brain in this disease, but despite many virological experiments the virus has never been isolated from brain tissue. This situation may be analogous to the experimental work of Rustigian (1962), who described a chronic measles infection in HeLa cells; the infection could be demonstrated by the presence of typical inclusion bodies, specific immunofluorescence, and complement-fixing antigen, but the virus could not be passaged to other tissue cultures.

SUMMARY

Measles complement-fixing and haemagglutination-inhibiting antibodies have been found in the serum of 22 patients with subacute sclerosing panencephalitis in significantly higher titre than in controls. These findings support the results of electron-microscopy and immunofluorescence in suggesting that the disease is due to a measles-like virus. The evidence does not at present enable us to differentiate between a latent measles infection which has become reactivated, a reinfection with measles, and a primary infection with a related agent such as canine distemper virus.

I would like to express my thanks to Dr. J. A. Dudgeon for his advice and encouragement; to Mr. A. I. Fraser and Mr. G. T. Hawkins for their technical work; to the National Fund for Poliomyelitis Research for financial support; and to the Standards Reference Laboratory and Glaxo Laboratories Limited for reagents.

NIGEL J. LEGG, M.B., M.R.C.P.,
Research Fellow, Department of Microbiology, Institute of
Child Health at Great Ormond Street, London W.C.1.

REFERENCES

Adams, J. M., Baird, C., and Filloy, L. (1966). *J. Amer. med. Ass.*, **195**, 290.
—— and Imagawa, D. T. (1962). *Proc. Soc. exp. Biol. (N.Y.)*, **111**, 562.
Bouteille, M., Fontaine, C., Vedrenne, C., and Delarue, J. (1965). *Rev. neurol.*, **113**, 454.
Brit. med. J., 1965, **2**, 252.
Clarke, J. K., Dane, D. S., and Dick, G. W. A. (1965). *Brain*, **88**, 953.
Cobb, W., and Hill, D. (1950). Ibid., **73**, 392.
Connolly, J. H., Allen, I. V., Hurwitz, L. J., and Millar, J. H. D. (1967). *Lancet*, **1**, 542.
Dawson, J. R. (1933). *Amer. J. Path.*, **9**, 7.
Dayan, A. D., Gostling, J. V. T., Greaves, J. L., Stevens, D. W., and Woodhouse, M. A. (1967). *Lancet*, **1**, 980.
Enders-Ruckle, G. (1965). *Arch. ges. Virusforsch.*, **16**, 182.
Good, R. A., and Campbell, B. (1948). *Proc. Soc. exp. Biol. (N.Y.)*, **68**, 82.
Greenfield, J. G. (1950). *Brain*, **73**, 141.
Krugman, S., Giles, J. P., Friedman, H., and Stone, S. (1965). *J. Pediat.*, **66**, 471.
Metz, H., Gregoriou, M., and Sandifer, P. (1964). *Arch. Dis. Childh.*, **39**, 554.
Ojala, A. (1947). *Ann. Med. intern. Fenn.*, **36**, 321.
Pampiglione, G. (1964). *Brit. med. J.*, **2**, 1296.
Reed, D., Sever, J., Kurtzke, J., and Kurland, L. (1964). *Arch. Neurol. (Chic.)*, **10**, 402.
Rustigian, R. (1962). *Virology*, **16**, 101.
Schiøtt, C. R. (1961). *Proceedings of a 1959 Symposium on Electro-encephalography and Biochemistry of Encephalitides*, edited by L. Van Bogaert, J. Radermecker, J. Hozay, and A. Lowenthal. Amsterdam.
Schmidt, J. R., and Rasmussen, A. F. (1960). *J. infect. Dis.*, **106**, 154.
Tawara, J. (1965). *Virology*, **25**, 322.
Tellez-Nagel, I., and Harter, D. H. (1966). *Science*, **154**, 899.
Ulrich, J., and Kidd, M. (1966). *Acta neuropath. (Berl.)*, **6**, 359.
Van Bogaert, L. (1945). *J. Neurol. Neurosurg. Psychiat.*, **8**, 101.

Medical Memoranda

Diffuse Systemic Sclerosis with Abnormal Liver and Gall Bladder

Brit. med. J., 1967, 3, 353–354

A case of diffuse systemic sclerosis is described in which the gall bladder was involved in the sclerotic process, an occurrence not previously noted.

CASE HISTORY

A woman aged 51 was seen at St. Thomas's Hospital by Dr. H. J. Wallace in 1963 with a five-year history of generalized pruritus. One year previously she had suffered an impacted fracture of the neck of the right humerus with separation of the greater tuberosity. This healed satisfactorily, but despite physiotherapy the arm lost much of its usefulness because of the rapid development of tightness of the skin of that arm and hand. She had had Raynaud's phenomenon in both hands and feet. On examination advanced scleroderma of the right forearm and hand and widespread guttate scleroderma, mainly of the upper arms and shoulders, were present, along with a generalized increase of pigmentation. There were many telangiectases of face, lips, buccal mucosa, tongue, and both hands—important physical signs of diffuse systemic sclerosis (Johnston *et al.*, 1965).

She had had infectious hepatitis at age 17, being jaundiced for two weeks. Stasis eczema of the leg had occurred at age 35 after an operation for varicose veins. Later she had developed contact eczema due to hypersensitivity to an antihistamine cream. She did not drink alcohol and had had no drugs known to cause liver damage.

Haemoglobin was 82% and E.S.R. (Westergren) 105 mg. in one hour. No L.E. cells were seen in the peripheral blood. Serum antinuclear factor was negative. Serum protein electrophoresis showed raised alpha-2, beta, and gammaglobulins. Serum creatine was 1 mg./100 ml. The blood urea and creatinine clearance were normal. The formiminoglutamic acid test was slightly positive. Fatty-acid excretion in a five-day stool save averaged 6.7 g./24 hours. E.C.G. and chest *x*-ray picture were normal. A supine barium swallow and meal showed normal oesophageal peristalsis and no oesophageal varices, but a hiatus hernia was present with free gastro-oesophageal reflux.

In October 1964 she was admitted to Kingston Hospital with shortness of breath and anginal pain on exertion. She had had melaena for the previous week and had recently had heartburn associated with regurgitation of bitter fluid. On examination she was very pale, with a raised jugular venous pressure, sacral oedema, and bilateral basal crepitations. The liver was enlarged and firm.

Her haemoglobin was 33% and M.C.H.C. 24%. The red cells showed extreme hypochromia. The E.S.R. was 149 mm. in one hour. Sternal marrow showed normoblastic hyperplasia and no free iron could be demonstrated. No L.E. cells were seen in the peripheral blood. Serum calcium was 9.8 and phosphate 4.2 mg./100 ml. The serum vitamin B_{12} was 600 μμg./ml. Liver-function tests showed bilirubin conjugated and total 0.75 mg./100 ml., thymol turbidity 6.0 units, serum cholesterol 270 mg./100 ml., alkaline phosphatase 95 units, aspartate transaminase 68 units, alanine transaminase 57 units, and total serum proteins 8 g./100 ml. (albumin 4 g., globulin 4 g.). Electrophoresis showed increased gammaglobulin. Prothrombin index was 100%. Electrophoresis of the alkaline phosphate enzyme suggested an origin from liver rather than bone. The histidine loading test was figlu-positive. Four specimens of stool were positive for occult blood, and two separate three-day collections of stool showed an average fatty-acid excretion of 3 and 4.8 g./day respectively. Barium-meal examination showed no dilatation or delay in the oesophagus, but free oesophageal reflux and a sliding hiatus hernia were present. No oesophageal varices were seen. The stomach, duodenum, and small bowel were normal.

A diagnosis of bleeding from the hiatus hernia was made and oral iron and folic acid were given. Six weeks later the haemoglobin was 75%.

In view of the abnormal liver-function tests a cholecystogram was taken; this showed poor concentration of the contrast medium in spite of a double dose. Good contraction of the gall bladder occurred after a fatty meal. No opaque calculi were seen, but some small non-opaque stones were suspected in the fundus. Aspiration liver biopsy: serial histological sections showed diffuse infiltration of the portal tract by moderate numbers of mixed inflammatory cells; to a small extent this exudate involved the adjacent parenchyma, which was otherwise normal. Because of the possibility of extrahepatic biliary obstruction laparotomy was performed by Mr. W. J. D. Bradfield. The liver was very nodular and the spleen enlarged. The gall bladder was yellowish but contained no calculi. The common bile duct was normal and a cholangiogram via the cystic duct was normal. Cholecystectomy and liver biopsy were performed. The gall bladder was 9 cm. long and its wall was thickened and oedematous. Microscopy showed an intact mucous membrane, but there was a considerable degree of fibrosis of the serosa without obliterative endarteritis, suggesting that the fibrosis was more likely to be part of a diffuse systemic sclerosis than to be due to chronic cholecystitis. The liver biopsy revealed the histological appearances of an early but uniform fibrosis, most pronounced in the portal tracts but also spreading out into the parenchymal tissue (Figs. 1 and 2).

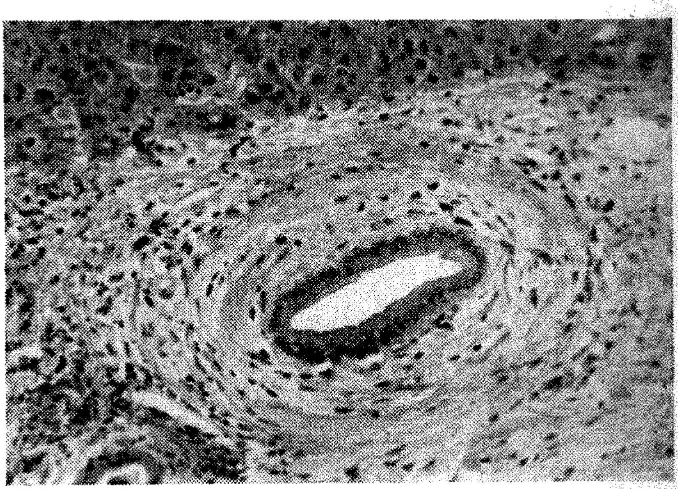


FIG. 1.—Liver, showing fibrosis round bile ductule and moderate chronic inflammatory changes. (H. and E. ×80.)

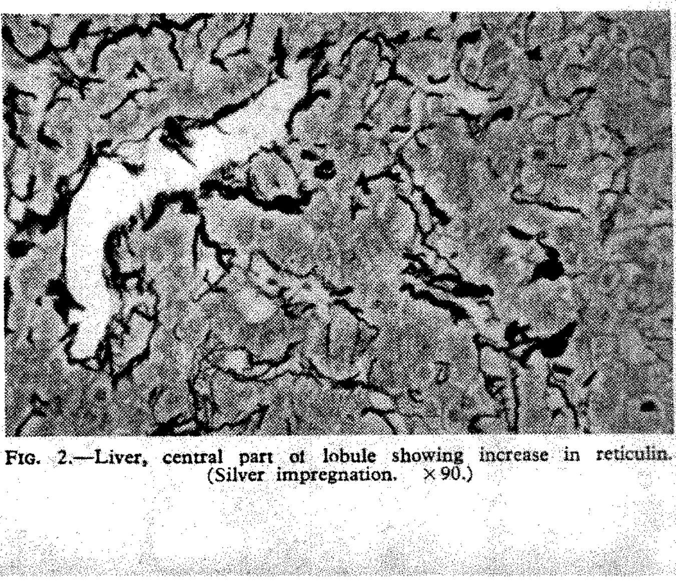


FIG. 2.—Liver, central part of lobule showing increase in reticulin. (Silver impregnation. ×90.)

The patient made a good recovery from the laparotomy. However, during the next year her spleen became intermittently palpable and she was slightly jaundiced. Liver-function tests on 8 October 1965 resulted as follows: bilirubin conjugated 1.3 mg./100 ml., total 1.5 mg., thymol turbidity 4.0 units, serum cholesterol 335 mg./100 ml., alkaline phosphatase 110 units, aspartate transaminase 88 units, alanine transaminase 96 units, total serum proteins 7.3 g./100 ml. (albumin 3.8 g., globulin 3.5 g.). Electrophoresis showed increased gammaglobulin.

DISCUSSION

The two unusual features in this patient were the rapid progression of the scleroderma of the arm after fracture of the humerus and the involvement of the liver and gall bladder. The only other reference we have found to trauma apparently influencing scleroderma is made by Zarafonetis (1964). In that case scleroderma of the left arm developed after a cut on the hand.

In view of the histological appearances there is little doubt that the abnormal gall bladder in the present case was due to involvement by the sclerotic process. Such involvement has not to our knowledge been previously described, though acute arteritis and periarteritis in the gall bladder were mentioned in one case by Leinwand *et al.* (1954). The liver involvement in the present case seems also to be related to the scleroderma, but it is impossible totally to exclude its being a sequel of the previous hepatitis. The histological features, however, are atypical for this, and the involvement of the gall bladder further diminishes this possibility.

Some previous accounts of liver abnormalities in scleroderma were summarized by Tuffanelli and Winkelmann (1961) and by Bartholomew *et al.* (1964), and in the latter series of 727 cases of scleroderma a "severe non-specific cirrhosis of unknown aetiology" was present in four. Other references include three examples of "focal necrosis" and one of portal cirrhosis (Piper and Helwig, 1955) and one of chronic biliary cirrhosis (Goetz, 1945), but histological details are insufficient to compare these with the present case. The histological changes in the case described by Batsakis and Johnson (1960), however, are very similar to those in the case we describe. But in two cases reported by Beigelman *et al.* (1953) the changes affected the centre of the hepatic lobule and were dissimilar.

Calvert *et al.* (1958) reported two cases of systemic scleroderma and hepatic fibrosis which bled from oesophageal varices. Treacy (1960) recorded hepatic failure as the cause of death in one patient. Though involvement of the hollow viscera in some degree is probable in most cases (Haubrich, 1965), liver involvement in scleroderma is undoubtedly rare. No cases were seen among 150 patients investigated by Leinwand *et al.* (1954), and none was discovered in the review of the literature by Goldgraber and Kirsner (1957). In addition, it is not mentioned in standard textbooks on liver disease (Kleckner, 1960; Popper and Shaffner, 1961; Sherlock, 1963; Schwartz, 1964) or in books on connective-tissue disorders (Richardson, 1963) or on skin pathology (Allen, 1954; Lever, 1961). It is therefore essential that detailed histology should be reported in all future cases, so that an attempt may be made to establish finally whether such involvement is aetiologically related, and, if so, what is the characteristic macroscopic and microscopical pattern.

Similarly, a catalogue of liver-function tests in future cases might reveal a diagnostic spectrum. The present case showed a striking pattern with a grossly raised serum alkaline phosphatase, a moderate rise in serum transaminases, and very slight rises in the thymol turbidity and bilirubin. It is known that scleroderma alone does not produce abnormal liver-function findings, though the serum gammaglobulin is often increased (Stáva, 1958).

Our thanks are due to Dr. H. J. Wallace for advice, to Dr. M. E. A. Powell for much help with the pathology, and to Mrs. Eileen Walsh for secretarial assistance.

P. W. MONCKTON COPEMAN, M.B., M.R.C.P.,
Senior Registrar, Skin Department, Westminster Hospital, London S.W.1.

W. E. MEDD, M.D., M.R.C.P.,
Physician, Kingston Hospital Group, Kingston-upon-Thames, Surrey.

REFERENCES

Allen, A. C. (1954). *The Skin: a Clinicopathologic Treatise.* St. Louis.
Bartholomew, L. G., Cain, J. C., Winkelmann, R. K., and Baggenstoss, A. H. (1964). *Amer. J. dig. Dis.*, **9**, 43.
Batsakis, J. G., and Johnson, H. A. (1960). *Arch. Path.*, **69**, 633.
Beigelman, P. M., Goldner, F., and Bayles, T. B. (1953). *New Engl. J. Med.*, **249**, 45.
Calvert, R. J., Barling, B., Sopher, M., and Feiwel, M. (1958). *Brit. med. J.*, **1**, 22.
Goetz, R. H. (1945). *Clin. Proc.*, **4**, 337.
Goldgraber, M. B., and Kirsner, J. B. (1957). *Arch. Pathol.*, **64**, 255.
Haubrich, W. S. (1965). In *Gastroenterology*, vol. 3, 2nd ed., edited by H. L. Bockus. London.
Johnston, E. N. M., Summerly, R., and Birnstingl, M. (1965). *Brit. med. J.*, **1**, 962
Kleckner, M. S. (1960). *Cirrhosis of the Liver.* Springfield, Illinois.
Leinwand, I., Duryee, A. W., and Richter, M. N. (1954). *Ann. intern. Med.*, **41**, 1003.
Lever, W. F. (1961). *Histopathology of the Skin*, 3rd ed. London.
Piper, W. N., and Helwig, E. B. (1955). *Arch. Derm. Syph. (Chic.)*, **72**, 535.
Popper, H., and Schaffner, F. (1961). *Progress in Liver Diseases.* New York and London.
Richardson, J. S. (1963). *Connective Tissue Disorders.* Oxford.
Schwartz, S. I. (1964). *Surgical Diseases of the Liver.* London.
Sherlock, S. (1963). *Diseases of the Liver and Biliary System*, 3rd ed. Oxford.
Stáva, Z. (1958). *Dermatologica (Basel)*, **117**, 147.
Treacy, W. L. (1960). Quoted by Bartholomew *et al.* (1964).
Tuffanelli, D. L., and Winkelmann, R. K. (1961). *Arch. Derm.*, **84**, 359.
Zarafonetis, C. J. D. (1964). *Amer. J. med. Sci.*, **248**, 550.

Current Practice

ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Sodium Chloride and Renal Calculi

Q.—*What is the rationale of giving sodium chloride regularly to prevent the formation of renal calculi in those prone to them?*

A.—The solubility of calcium phosphate and calcium oxalate is a function not so much of the concentrations of their constituent ions in the medium (be it urine or simple electrolyte solution) but of the activities of these ions. The activity coefficient of an ion is inversely related to ion strength, and the higher the concentration of, for instance, sodium chloride in urine the lower will be the activity coefficients of the calcium, phosphate, and oxalate ions and the higher the solubility of the stone or precipitate. In practice, the effect of urinary ion strength on stone solubility is of little significance at ion strengths over 0.15 but may be of some practical importance at ion strengths below this value.

Relying on this consideration, Udall[1] has shown that urinary calculi in lambs can be controlled by force-feeding of sodium chloride. Modlin[2] has also emphasized the effect of sodium on apatite solubility, and suggested that stone formation is rare when the sodium/calcium ratio in the urine is high. However, the high sodium/calcium ratios in non-stone-forming populations to which he draws attention are as much due to a low urinary calcium as to high urinary sodium.

It would be premature to advocate the treatment of renal stone disease with sodium chloride feeding at the present time.

REFERENCES

[1] Udall, R. H., *Amer. J. vet. Res.*, 1962, 23, 1241.
[2] Modlin, M., *Ann. roy. Coll. Surg., Engl.*, 1967, 40, 155.

Sialagogues in Sjögren's Syndrome

Q.—*What satisfactory sialagogues, apart from pilocarpine, are available for a patient with Sjögren's syndrome?*

A.—Sjögren's syndrome is a particularly distressing affliction, for its treatment is so unsatisfactory. Methylcellulose artificial tears help to overcome symptoms due to keratoconjunctivitis sicca. Sulphacetamide eye-drops and ointment minimize bacterial complications, including corneal ulceration. Because of their bland alkalinity, these eye-drops are also soothing. Sealing of the puncta by cautery helps to conserve what little moisture is present.

Since Sjögren's syndrome is commonly in women aged between 40 and 50, oestrogens might be helpful. The association is strengthened by the fact that hydroxyproline excretion is greatly increased in those suffering from the syndrome, and this biochemical abnormality can be corrected by oestrogens. Since Sjögren's syndrome is regarded as an autoimmune phenomenon similar to systemic lupus erythematosus and to primary biliary cirrhosis, immunosuppressive drug regimens are sometimes used. Local and oral corticosteroids have been given and even azathioprine considered, but relapses follow cessation of treatment and the danger of corneal ulceration is always present with such regimens. Because of the similarity to lupus erythematosus, chloroquine has been tried and found more effective than a placebo in a double-blind trial.

Patients with Sjögren's syndrome are often depressed. The affliction may be sufficient to account for this, but there could also be an element of endogenous depression for which nortriptyline or imipramine is indicated. Contact lenses may give relief. Every patient has his own favourite prescription for overcoming dryness of the mouth. Polo mints seem to be favoured as much as anything.

Liquid Paraffin as Carcinogen

Q.—*Is there any evidence that the regular use of liquid paraffin or preparations such as petrolagar may cause carcinoma in the gastro-intestinal tract?*

A.—Medicinal liquid paraffin is a highly purified product. Nevertheless, Druckrey and his colleagues[1] thought that purification may not entirely remove all the carcinogens shown to be present in crude mineral oils.[2] Boyd and Doll[3] found an appreciable excess among patients with gastrointestinal cancer of a history of the use of liquid paraffin. There was no excess in the use of laxatives of other types nor in the overall use of purgatives among such patients as compared with patients suffering from diseases other than of the gastrointestinal tract. For various reasons, these authors did not feel that this evidence indicated that liquid paraffin is more than very weakly carcinogenic.

REFERENCES

[1] Druckrey, H., Schmähl, D., and Preussmann, R., *Arzneimittel-Forsch.*, 1959, 9, 600.
[2] Shubik, P., and Saffiotti, U., *Acta Un. int. Cancr.*, 1955, 11, 707.
[3] Boyd, J. T., and Doll, R., *Brit. J. Cancer*, 1954, 8, 231.

Reaction to Triple Antigen

Q.—*What dosage of adrenaline is recommended for the emergency treatment of collapse after injection of triple antigen in infants aged 3-to 12 months? Is an injection of a corticosteroid a better treatment in this situation?*

A.—Most pertussis vaccines produce a slight rise in temperature and an associated mild degree of irritability within one to eight hours of injection. These reactions are particularly common and more severe after quadruple vaccines (D.T.P./Polio) and pertussis vaccines prepared from organisms grown in liquid media.[1]

Collapse is one of the rarer and more alarming of the reported reactions. It has a sudden onset one to four hours after immunization and lasts from one-half to one hour, but recovery is usually complete within 24 hours. Its main features are marked pallor, cold skin, hypotension, and general physical collapse. It is not an anaphylactic reaction nor is it due to any other immunological phenomenon.

Since the reaction resembles shock induced by injected endotoxin from Gram-negative bacteria it is inadvisable to treat it with adrenaline. Corticosteroids are more likely to be effective and less likely to aggravate the condition. When, therefore, the condition gives rise to immediate concern the administration of corticosteroids should be considered.

REFERENCE

[1] Haire, M., Dane, D. S., and Dick, G., *Med. Offr*, 1967, 117, 55.

Glycosuria after Myocardial Infarction

Q.—*What is the explanation for a period of glycosuria that frequently seems to come after a myocardial infarction?*

A.—Glycosuria after a cardiac infarction is due to a raised blood sugar, which in turn may be caused by a number of factors such as an excess adrenaline producing glycogenolysis, considerable mental and physical stress increasing adrenal cortical activity and gluconeogenesis, and a decreased capacity of the liver to handle carbohydrate, due to a fall in hepatic blood flow. There is also evidence that many people who have cardiac infarcts are latent or potential diabetics. The stress during an acute infarct then precipitates carbohydrate intolerance for a short period, and it is analogous to the principle of the steroid-loaded test for prediabetes.

Preventing Scarring in Chicken-pox

Q.—*What is the best treatment in a case of chicken-pox to minimize the risk of subsequent scarring when the pustules have healed?*

A.—The chicken-pox lesion is situated in the middle and deeper layers of the epidermis. Except in very severe cases, there is very little inflammatory change in the corium, so that when the scab separates a normal re-epithelized surface is left behind. The risk of scarring is therefore very slight in uncomplicated chicken-pox. Deeper penetration may occur if the lesions become secondarily infected. The pus should be cultured and the appropriate antibiotic or other drug given by mouth. Local applications do more harm than good.

Book Reviews

Cerebrospinal Fluid

Physiology of the Cerebrospinal Fluid. By Hugh Davson, D.Sc.(Lond.). (Pp. 445+vii; illustrated. 84s.) London: J. & A. Churchill. 1967.

Dr. Hugh Davson's previous volume *The Physiology of the Ocular and Cerebrospinal Fluids*, published ten years ago, is well known to both neurologists and ophthalmologists. As he points out in his preface to his new book, there have been many papers in recent years on experimental studies of the formation and circulation of cerebrospinal fluid, and he therefore wisely decided that a new volume devoted exclusively to the cerebrospinal fluid was necessary. In this work he studies in turn morphological aspects of the fluid, its chemical composition and secretory nature, and the blood–spinal-fluid and blood–brain barriers. He has also devoted space to considerations of the extracellular space of the brain and cord, as well as to acid–base balance, the control of respiration, and the influence of these and other factors on cerebrospinal-fluid pressure. The book is carefully and logically arranged. The illustrations are in general of outstanding quality and consist in part of excellent graphs and line drawings, but in addition there are many half-tone illustrations of radiographs, photomicrographs, and electronmicrographs which add considerably to the value of the work.

In parts the text is so technical and highly concentrated that the book does not always make easy reading, but nevertheless it is one that repays careful study, as it is a mine of information, and it is difficult to imagine that anything of importance concerned with the cerebrospinal fluid has been omitted. Though its title suggests that it is a study of the physiology of the fluid, there are substantial sections devoted to pathophysiology and to the changes which occur in disease. There is also a full bibliography and a comprehensive index, so that the work is an excellent source of reference. Without question this book will become the standard work on the cerebrospinal fluid. The author is to be congratulated on the orderly format and scope of this scholarly monograph, and the publisher on the standard of production.

JOHN N. WALTON.

Mind and Brain

The Memory System of the Brain. By J. Z. Young. (Pp. 128+vi; illustrated. 28s.) London: Oxford University Press. 1967.

This short book comprises the Hitchcock lectures delivered by Professor Young at the University of California in 1964, and presents a readable and penetrating account of the way this distinguished biologist views the neural basis of memory at this moment in the history of its investigation. Based in essence on his well-known work on the Neapolitan octopus, it affords a splendid justification for the years of patient study the author has devoted to this unprepossessing cephalopod. The octopus was chosen for the experimental analysis of memory because of the simplicity of its sensory equipment and its motor repertory, but Professor Young transcends so limited a brief. His lectures go some way towards bridging the critical gap between neurology and psychology. They range widely over the more general implications of his experimental studies, and abound in original and arresting speculations.

To select from the author's many felicitous ideas a few which indicate the flavour of the book is not easy, but the reviewer was intrigued by his concept of evolutionary survival through the arrangement by which the body machine, discarded on the death of the individual, is perennially rebuilt from the "code of instructions" handed on, with amendments, at each reproductive cycle. In human memory also a complex neural organization, and a relatively long life that affords scope for extensive learning experience, are reinforced by man's development of information stores outside himself that endow him in this connexion with what the author aptly describes as a "multiparental inheritance."

Throughout the book Professor Young employs the ideology and the language of computer science to describe the working of the brain in recording, storing, and recalling discrete items of memory, but he goes far beyond the cruder analogies so often drawn in this connexion, and even at our present early and fragmentary stage of knowledge in this field he maintains a firmly biological orientation.

This illuminating and thoroughly enjoyable study emphasizes the fatuity—if indeed it requires emphasis—of the artificial division between structure and function that is perpetuated in the continued existence of independent departments of anatomy and physiology in medical schools and universities. It also furnishes comforting evidence that there are neurophysiologists of distinction who devote their genius to studying the behaviour of the whole organism and not merely of the isolated cell. To paraphrase its author, the content of a book furnishes more interesting material for study than the chemical composition of printer's ink.

HENRY MILLER.

Clinician and Bacteriologist

The Clinical Practice of Bacteriology. By Kevin Anderson, M.D.(Lond.), M.R.A.C.P., M.C.P.A., M.C.Path. (Pp. 243+x; illustrated. 42s.) Oxford: Blackwell. 1966.

This short well-written book is intended to bring the clinician and clinical bacteriologist closer together. Improved appreciation of one another's work and problems should result in better use of the laboratory to the ultimate benefit of clinician and bacteriologist, and, most of all, the patient. These important sentiments will be endorsed by many; but beyond advertising them I am not sure how the book will further them.

My greatest difficulty has been in identifying the audience Dr. Anderson had in mind. It was evidently not clinical bacteriologists. Apart from the fact that 100% sales to them would hardly make a best seller, the bacteriology is largely elementary. Evidently it was not clinicians either. The accounts of infectious diseases are largely those of the textbooks. If we safely assume that the book is intended for the student of clinical bacteriology (in the widest sense), it suffers from being written at a number of levels. Although most of it is elementary, it assumes some existing knowledge of bacteriology and medicine and there are references to more complicated matters of which some are mystifyingly brief.

The main difficulty for the student is that the book is in no sense a textbook. It is not comprehensive and the choice of material is arbitrary. For example, under the heading "non-bacterial meningitis" there appears only an account of meningeal infiltration in Hodgkin's disease and leukaemia. There is a table showing all the concentrations of antibacterial agents to be incorporated in media used for testing the sensitivity of *Myco. tuberculosis*, but beyond a mention there is no account of atypical mycobacteria. The references are few, often old, and usually support some relatively minor matter. It is, in a word, a highly personal book and is enlivened by personal case histories. Accepted as such, it makes interesting and enjoyable reading. Whether this is sufficient recommendation to ensure its reaching a wide enough audience to secure the author's admirable objective remains to be seen.

F. O'GRADY.

X-ray of the Abdomen

Radiographic Examination in Blunt Abdominal Trauma. By James J. McCort, M.D. (Pp. 252+viii; illustrated. £3 13s. 6d.) London: W. B. Saunders. 1966.

Dr. McCort, Professor of Radiology in Stanford University Medical School, has gathered together in one volume many and diverse *x*-ray signs of injury to the abdomen and its contents, signs that it would be difficult to run to earth in the many standard textbooks of diagnostic radiology. This book has therefore a particular value to those clinicians and radiologists who are engaged in the running of casualty departments.

The first 50 pages are devoted to the appearances in the plain *x*-ray film of the normal and injured abdomen. Mention is made of the pioneer work of Frimann-Dahl in the *x*-ray study of the abdominal wall in health and disease. This section is probably the most important, since every abdominal casualty should have at least a plain film taken of the abdomen, and much can be learnt from it—haemorrhage, rupture of a solid or perforation of a hollow viscus, or mere injury to the abdominal wall.

A short section outlines special *x*-ray procedures—barium and Gastrografin alimentary studies, pneumoperitoneography, abdominal arteriography, and urography.

The rest of the book is devoted to a detailed study of the *x*-ray signs of injury to the various abdominal organs; the spleen (it is the commonest), liver, gastrointestinal tract, pancreas, kidney, and bladder. It contains a wealth of information in a commendably concise form and is warmly recommended to those who are engaged in this work.

S. COCHRANE SHANKS.

Range and Concepts of Epidemiology

Clinical Epidemiology. Revised edition. By John R. Paul. (Pp. 305+xix; illustrated. 56s.) London: University of Chicago Press. 1966.

This book is a volume in the series "The Scientist's Library: Biology and Medicine." The purpose of this series is to provide information not only for the expert but also for workers in various fields of biology and medicine on developments which have occurred in recent years in subjects which lie outside their own specialty. The book is not a textbook in the usually accepted sense, but rather a review of the range and concepts of epidemiology. These have been discussed in three sections: principles, definitions, and history; methods and uses; and sample diseases. Problems in public health, social, preventive, and industrial medicine are used as examples of the epidemiological approach, but no attempt has been made to introduce any statistical or mathematical methods of analysing data.

The first edition of this book was mainly confined to the epidemiology of infectious diseases, but this edition includes non-infectious diseases such as coronary artery diseases and cancer. Influenza, except for a brief note on outbreaks among Eskimos, has not been discussed, and this is rather surprising in view of the vast amount of work which has been done both in America and Britain. Each chapter is followed by a bibliography; the number of papers to which the reader is referred varies from three to 50, but some of the references occur at the end of more than one chapter. As might be expected in an American book, most of the papers referred to were published in America—for example, slightly over three-quarters of the 49 references following the chapter on infectious serum hepatitis were American publications, and many good British and Continental investigations are not mentioned.

The conditions under which investigations are carried out in the United States differ in some respects from those in England. The methods of population sampling used in the American inquiries is not applicable to Britain, since we do not have "census tracts." The use of questionaries is perhaps easier in America, where the population has been conditioned to form-filling. The difficulty of defining a perinatal death rate is purely an internal affair, since every state determines what should be considered a foetal death. In England a stillbirth must be of 28 weeks gestation, while in the United States the general rule is that foetal deaths over 20 weeks are registered as stillbirths, but this period varies between states, and in some states all products of conception must be registered, even miscarriages at eight weeks.

In a revised edition it seems strange that a typographical error should occur twice: Newcastle upon Tyne is referred to as New Castle-upon-Tyne. The index to the book is not complete and it appears to be a matter of chance whether the name of an author quoted in the text appears in the index.

The questions that a new book poses are: Is there a place for another book on this subject, and, if so, has the author fulfilled this need? With this book the author has succeeded in his main aim of presenting for the general reader a broad and interesting description of the concepts of epidemiology and the range of subjects that have been studied and the problems involved. Not only the amateur but investigators and teachers of epidemiology will find this book interesting and profitable.

W. J. MARTIN.

Edinburgh School

The Principles and Practice of Medicine. 8th edition. By Sir Stanley Davidson, B.A.Cantab., M.D., F.R.C.P.Ed., F.R.C.P. Lond., M.D.Oslo, LL.D., F.R.S.Ed. (Pp. 1342+ix; illustrated. 40s.) Edinburgh and London: E. & S. Livingstone. 1966.

It is a measure of the popularity of this textbook that since the first edition in 1952 a new edition has been called for every two years. It represents the distillation of medicine as it is taught and thought by the Edinburgh school under the inspiration of Sir Stanley Davidson. Clearly, therefore, it fills a need felt not only in this country but in all the large number of countries where it is sold. It would be a tremendous achievement even to be able to cover the whole field of medicine in such a relatively small space and still retain the impression of literature as opposed to a tabulation of so-called facts. There is no doubt that for quick reference to the major points in the important diseases this book is excellent. It achieves this by taking the reader at a brisk trot through the major manifestations of disease mounted on short pithy sentences. It is to be hoped that a major reason for its popularity is not the lack of any controversial matter, nor any consideration of the weight of evidence for one view or the other, but a nasty suspicion remains that this may be so. If so, then the teachers of the students who follow this as their bible have much work to do, for while the Practice may be clear the Principles are not.

W. S. PEART.

Botulism

Botulism 1966. Symposium, Moscow, 1966. Edited by M. Ingram, M.A., Ph.D., and T. A. Roberts, B.Pharm., Ph.D. (Pp. 531+xii; illustrated. £6 6s.) London: Chapman & Hall. 1967.

Attendance at this symposium was limited to those "actively working" on its subject, and participants numbered only 55. This must have ensured well-informed discussions, but they are not reported. The papers are evidently in condensed form, but adequately illustrated, and include numerous tables and extensive reference lists. Twenty-four are by workers in the United States, 10 from the United Kingdom, 8 from the Soviet Union, 4 from Canada, and 1 or 2 each from six other countries. They deal first with the distribution of *Clostridium botulinum* in nature, particularly type E, which is almost always responsible when the food causing botulism is imperfectly preserved fish. It is reassuring to read in a paper from the Torry Research Station, Aberdeen, that though this organism is common in dredgings from the sea bottom off Norway it is apparently non-existent on our side of the North Sea. A further and longer series of papers deals with conditions affecting survival of the spores, their growth, and toxin production in foodstuffs. The toxins themselves, their chemistry, antigenicity, and pathological effects, botulism in animals, and laboratory methods, particularly for the isolation of *Cl. botulinum*, are the main subjects of the remaining papers. Included in the last-named are two papers, both by workers in England, on the fluorescent antibody technique for the recognition of the organism.

Botulism is a terrifying disease, and the toxins causing it are of course by far the most powerful poisons known. It strikes brutally in unexpected places, as at Loch Maree in 1923. There is little of the romance or horror of botulism in these rather dry pages. Indeed human outbreaks are mentioned only in the first and last papers. One records that all outbreaks in the Soviet Union since 1959 have been due to home-canned or home-pickled foods (fish, ham, or vegetables). The other reports an incident in Canada, fortunately controlled by recalling all tins of a product which had been under-processed owing to a misunderstanding, no allowance having been made for heat penetration according to the volume of the can contents.

Some interesting points emerge: it seems, for instance, that smoked salmon is an inimical medium for the growth of *Cl. botulinum* because the smoke contains phenols and, surprisingly, formaldehyde. Another author presents evidence that in the human disease toxin continues to be formed in the bowel as well as absorbed from it, and he therefore advocates administration of antitoxin by duodenal tube and high enema as well as intramuscularly. It may be news to most people that large numbers of ducks and gulls die of the disease.

Everyone directly interested in this subject must naturally possess this book. It is evidently because such people are few that the price is high, particularly for a volume reproduced by photolithography from typescript.

L. P. GARROD.

Rod and Serpent

The Rod and Serpent of Asklepios. Symbol of Medicine. By J. Schouten. (Pp. 260 +ix; illustrated. 65s.) London: Elsevier. 1967.

The snake-entwined staff, an example of which adorns the cover of the *B.M.J.*, is today universally recognized as the symbol of medicine and healing. But why the staff, and what is the significance of the snake? Dr. Schouten, a Dutch historian of art, gives the full and absorbing story in this beautifully produced and scholarly book.

The god of healing of the ancient Greeks was Asklepios, also known to the Romans as Aesculapius, who was depicted holding a staff around which a snake was coiled. Both are thought to have represented healing, and this heathen symbolism, having survived the Christian Middle Ages, came to be used with increasing commonness to signify medicine and pharmacy, especially in herbals and pharmacopoeias, examples of which Dr. Schouten lists and illustrates. It was more popular in the Northern Reformation countries than in the parts of Europe where the Catholic patron saints of medicine, Cosmas and Damian, predominated.

Since the sixteenth century the staff encircled by two snakes, the Caduceus of Hermes-Mercury, has at times replaced the Asklepian symbol as the emblem of medicine, though it was not used as such in antiquity. It has the same allegorical significance of healing, one of the best-known uses being in the insignia of the U.S. Army Medical Department.

This is an important work which illustrates the contribution which can be made by the non-medical scholar to the history of medicine. No one without Dr. Schouten's knowledge of art history and of the background influences of mythology, religion, and allegory could have tackled this complex topic, and his book will become the standard reference work on it. Perhaps not many doctors will care to follow Dr. Schouten through all his carefully annotated data, but on the other hand anyone who wonders why his profession is symbolized by the rod-and-serpent will wish to consult this book, even if only to read the summary and to admire the excellent illustrations.

EDWIN CLARKE.

Books Received

Review is not precluded by notice here of books recently received.

The Young Offender. By Dr. D. J. West. (Pp. 333. 35s.) London: Gerald Duckworth. 1967.

Student Health Services in Great Britain and Northern Ireland. By Professor Alex Mair. (Pp. 236+xii. 42s.) Oxford: Pergamon. 1967.

Atlas of Stereotaxic Anatomy of the Telencephalon. Anatomo-Radiological Studies. By J. Talairach and G. Szikla. (Pp. 326+xix; illustrated. 260 F.) Paris: Masson. 1967.

Parkinson's Disease. By Leslie Oliver, M.B., B.S., F.R.C.S., F.A.C.S. (Pp. 69; illustrated. 21s.) London: William Heinemann. 1967.

Insulin-Kohlenhydratstoffwechsel und Nervale Regulation. Verhandlungen der Deutschen Gesellschaft für Experimentelle Medizin. Vol. 15. Edited by Professor K. Lohmann. Pp. 247; illustrated. £1 17s. 10d.) Jena: Volk und Gesundheit. 1966.

Current Concepts in Ophthalmology. By Bernard Becker, M.D., and Robert C. Drews, M.D. (Pp. 265+x; illustrated. £6 10s.) London: Henry Kimpton. 1967.

Pediatric X-ray Diagnosis. 5th edition. By John Caffey, A.B., M.D. (Pp. 1192+xxiv; illustrated. £15.) London: Lloyd-Luke. 1967.

Essentials of Healthier Living. 3rd edition. By Justus J. Schifferes, Ph.D. (Pp. 450+xvii; illustrated. 60s.) London: John Wiley. 1967.

Medical Cytogenetics. By Mihaly Bartalos, M.D., and Theodore A. Baramki, M.B., B.Ch. (Pp. 419+xxiii; illustrated. £5.) Edinburgh and London: E. & S. Livingstone. 1967.

Cheadle Royal Hospital. A Bicentenary History. By Nesta Roberts. (Pp. 189+x; illustrated. 30s.) Altrincham, Cheshire: John Sherratt. 1967.

Nouveau Traité de Technique Chirurgicale. Vol. 9. Paroi Abdominale. Sutures Digestives. Laparotomies. By Philippe Détrie. (Pp. 473; illustrated. 115 F.) Paris: Masson. 1967.

Nouveau Traité de Technique Chirurgicale. Vol. 13. Système Porte. Rate. By Lucien Leger and Jean Patel. (Pp. 332; illustrated. No price given.) Paris: Masson. 1967.

Intravenous Abdominal Aortography and Placentography. By Melvyn H. Schreiber, M.D., and Fred J. Wolma, M.D., F.A.C.S. (Pp. 57+ix; illustrated. $8.75.) Springfield, Illinois: Charles C. Thomas. 1967.

Brain Mechanisms Underlying Speech and Language Edited by Frederic L. Darley. (Pp. 261+x; illustrated. $7.75.) New York and London: Grune & Stratton. 1967.

Pharmakopsychiatrie und Psychopathologie. Edited by Professor H. Kranz and Dr. K. Heinrich. (Pp. 203. DM. 26.) Stuttgart: Georg Thieme. 1967.

Geburtshilfliche Operationen. Edited by Heinrich Martius and Gerhard Martius. (Pp. 206 +xvi; illustrated. DM. 19.80.) Stuttgart: Georg Thieme. 1967.

Strahlentherapie. Eine Einführung. By Professor Eberhard Scherer. (Pp. 222+vi; illustrated. DM. 9.) Stuttgart: Georg Thieme. 1967.

Underwater Physiology. By C. J. Lambertsen. (Pp. 497+xx; illustrated. £6 15s.) Edinburgh and London: E. & S. Livingstone. 1967.

Medicine. Essentials for Practitioners and Students. 9th edition. By G. E. Beaumont, M.A., D.M.(Oxon.), F.R.C.P., D.P.H.(Lond.). (Pp. 854+xvii; illustrated. 60s.) London: J. & A. Churchill. 1967.

The Neuroses. By Henry P. Laughlin. (Pp. 1076+xii. £8 18s. 6d.) London: Butterworth. 1967.

Cardiac Pacemakers. By Harold Siddons, M.Ch., F.R.C.S., and Edgar Sowton, M.D., M.R.C.P. (Pp. 331+xvi; illustrated. $16.75.) Springfield, Illinois. Charles C. Thomas. 1967.

Cancer of the Head and Neck. Edited by John Conley, M.D. (Pp. 650+xi; illustrated. £10 15s.) London: Butterworth. 1967.

Electrocardiography in the Diagnosis of Congenital Heart Disease. By George E. Burch, M.D., and Nicholas P. De Pasquale, M.D. (Pp. 755; illustrated. £9 15s.) London: Henry Kimpton. 1967.

Age and Function. By Alastair Heron and Sheila Chown. (Pp. 182+x; illustrated. 45s.) London: J. & A. Churchill. 1967.

L'Hypertension Artérielle et son Traitement. By. D. Fritel and P. Meyer. (Pp. 243; illustrated. 38 F.) Paris: Librairie Maloine. 1967.

An Introduction to Diagnostic Neurology. A Course of Instruction for Students. Vol. 1. 2nd edition. By Stewart Renfrew. (Pp. 194 +x; illustrated. 12s. 6d.) Edinburgh and London: E. & S. Livingstone. 1967.

An Introduction to Diagnostic Neurology. A Course of Instruction for Students. Vol. 2. 2nd edition. By Stewart Renfrew. (Pp. 224 +vii; illustrated. 12s. 6d.) Edinburgh and London: E. & S. Livingstone. 1967.

The Subculture of Violence. Towards an Integrated Theory in Criminology. By Marvin E. Wolfgang and Franco Ferracuti. (Pp. 387 +xxiii. 63s. Paper 30s.) London: Tavistock. 1967.

Medical Terminology. A Programmed Text. 2nd edition. By Genevieve Love Smith and Phyllis E. Davis. (Pp. 289+xvii; illustrated. 45s.) London: John Wiley. 1967.

Classification for Medical Literature. 5th edition. By Eileen R. Cunningham. Revised and enlarged by Eleanor G. Steinke and Mary Louise Gladish. (Pp. 267+xix. $6.00.) Nashville, Tennessee: Vanderbilt University Press. 1967.

The Anxiety Makers. Some Curious Preoccupations of the Medical Profession. By Alex Comfort. (Pp. 208; illustrated. 30s.) London: Thomas Nelson. 1967.

Transplantation von Organen und Geweben. Edited by Dr. K. E. Seiffert and Dr. R. Geissendörfer. (Pp. 240+vii; illustrated. DM. 58.) Stuttgart: Georg Thieme. 1967.

Leptospiren und Leptospirosen. Part 1. Edited by Professor Johannes Kathe and Dr. Hanspeter Mochmann. (Pp. 482+xx; illustrated. 87s. 10d.) Jena: Gustav Fischer. 1967.

X-rays and Radium in the Treatment of Diseases of the Skin. 5th edition. By Anthony C. Cipollaro, M.D., and Paul M. Crossland, M.D. (Pp. 830; illusltrated. £10 14s.) London: Henry Kimpton. 1967.

The Intensive Therapy Unit and the Nurse. By Eric K. Gardner, F.R.C.S., F.F.A.R.C.S., and Brenda Shelton, S.R.N., S.C.M., B.T.A. Illustrated by Audrey Besterman. (Pp. 162; illustrated. 22s. 6d.) London: Faber & Faber. 1967.

Die Pocken. Erreger. Epidemiologie und Klinisches Bild. By Professor A. Herrlich. (Pp. 360+xvi; illustrated. DM. 89.) Stuttgart: Georg Thieme. 1967.

Middle Articles

Pathology in Britain in the First Half of the Twentieth Century, with a Glance Forward*

C. H. BROWNING,† M.D., F.C.PATH., F.R.S.

Brit. med. J., 1967, 3, 359–362

I appreciate greatly the opportunity to commemorate my friend E. H. Kettle. Not only was he a distinguished pathologist, too early taken from us, but his wide culture, shining humanity, and rich sense of humour inspired deep affection and respect in all who had the good fortune to know him. We were contemporaries and our active lives in pathology began with this century. In Britain it was an exciting period, since only recently had the subject ceased to be a mere servant of the clinicians. The pioneers of the change were the generation immediately our seniors. Thus beginners like Kettle and myself found circumstances that were new. The current roll of our Pathological Society shows that under 3% were pathologists in 1924, therefore I shall try to picture affairs during the first half of the century, so that you may appreciate how the present state has evolved. Training, practice, teaching, and research will be touched on. If I draw largely on personal experiences, that is because they are the most vivid. But my conditions were not unusual, except perhaps that the men who influenced me were of quite phenomenal calibre. In the light of what I have learned I shall offer some opinions which may be shared but are not borrowed.

Scope and Status of Pathology—How it Became a Career

Pathologists had come to belong practically to two classes, hospital and academic. A good physician's interest in his patient after death was to find out whether the postmortem findings had been correctly predicted. In a word, the hospital pathologist was his ancillary. This routine verification of well-known facts was essential for teaching the natural history of disease, but not much to the benefit of future victims. Of course, there were the occasional curiosities. Surgeons, however, thanks to Lister, now dared to inspect deep lesions during life and supply fresh human tissues for examination. Thus, reporting on operation specimens was a considerable duty. A hospital pathologist's appointment, unlike the clinicians', did not promise lucrative private practice, there being small demand. A few university professorships of pathology existed ; but the chance of reaching such a position was remote. These academic pathologists in their departments were isolated from patients in hospital, where at that time the obvious problems lay.

In Glasgow Joseph Coats, besides engaging in clinical work, had been pathologist to a large general hospital and teacher of pathology for about 25 years. Finally he became full-time professor, and soon effected a revolution by securing at the Western Infirmary an Institute where teaching and hospital work were carried on jointly. On its inauguration in 1896 he stated: "Our circumstances here are, I think I may say, unique, and I think I may add that they are in a sense ideal. . . . There is thus combined under one roof and under one superintendence both the Infirmary and the University Pathological Departments. . . . My pathological friends tell me that such a conjunction of interest is a happy ideal which is nowhere else realized" (see Browning, 1952). Glasgow's example, however, was only tardily followed elsewhere.

Running a combined department was relatively simple at the beginning. Apart from teaching, the chief occupation was with the hospital's morbid anatomy and histology (including blood examinations). Histological methods were similar to today's, but fewer and simpler—present histochemical methods are an example of the change. The preservation of natural colours in naked-eye museum preparations had begun, but the treasures on the shelves were in spirit. I remember concluding that time could be spent better than by visiting there. Chemical pathology was represented chiefly by simple side-room tests. Medical microbiology and parasitology consisted mainly of examining pus for organisms, throat swabs for diphtheria bacilli, sputum and urine for tubercle bacilli, intestinal contents for the typhoid bacillus, dysenteric amoebae, or worms, and blood for malarial parasites or microfilariae. Serology consisted of a micro form of Widal test. Animals were occasionally inoculated for detection of tuberculosis, also for plague which visited Glasgow at that time. Blood cultures were rarely asked for. Research in pathology was generally taken to mean the description of unusual cases ; the experimental method was reintroduced to us in 1899 by Coats's successor, Robert Muir, with his investigation on leucocytosis. The most striking later advances have been the wider understanding of chemical pathology, the growth of bacteriology (including immunology and virology) stimulated especially by the war of 1914–18, haematology, and genetics. Increased interest in the living patient and the active development of the experimental approach have been of vital importance. It is scarcely possible to exaggerate the debt of human pathology to the scientific study of protracted model diseases induced in animals. Various names are given to different aspects of this discipline ; but since all centre on altered function and structure, they are pathology.

After Coats's innovation there arose the problem of training a body of young pathologists for future needs. Pathology had always attracted keen men ; for a few years they acted as junior teachers or hospital pathologists, but then shifted to the clinical side. Earlier still there were the famous physicians and surgeons whose names live in the diseases they identified. One of the later examples was a young surgeon, John Bland-Sutton, who made outstanding contributions on the pathology of the ovaries and Fallopian tubes. When a clinical panjandrum asked where such things were seen, the reply was, "In the public mortuary." A friend who apparently did not relish necropsies had provided this opportunity. The tradition of pathologist–

---

* Based on the Kettle Memorial Lecture given before the College of Pathlogists on 7 February 1967.

† Professor Emeritus of Bacteriology, University of Glasgow.

physician lingered and "when I was a pathologist" was a familiar expression in London. There were some who could afford to continue their hobby of pathology through possessing private resources—for example, "marrying a nursing-home" or practising vaccine therapy when that became fashionable. Others again were just infatuated with pathology and felt that things must eventually turn out all right; possibly national temperament explained this faith, for at the first meeting of the Pathological Society William Osler remarked that the language of the Society was Scots.

Coats at the opening of his Institute said: "I cannot think of a better way of advancing the scientific position of our school and at the same time conferring great benefits on the community than by some man who is able, conferring a moderate endowment on those who may devote themselves to research." He did not live to see this hope realized, but a Coats memorial scholarship was established in 1899. Growing appreciation of the value of medical research led to foundations and grants by private and public bodies. Personally, I must thank chiefly the Carnegie Trust, the M.R.C., and I.C.I. for support. Various circumstances have increased the demand for pathologists until the number now far exceeds the most sanguine hopes of 1900. Dible's (1957) history of the Pathological Society tells of the devoted men who won recognition for their subject as an independent scientific discipline. A similar magnification of the pathologist's status has occurred in other spheres, and all these changes have accelerated (see Ledingham, 1925). No longer kennelled in the dead-house, the pathologist is now important clinically and in general social esteem. Let us hope that he will not be forced to go abroad in order to find conditions congenial for research, nor be frustrated officially in his effort to serve individual patients.

Training

As a student starting with a term of morbid histology, both the subject and my teachers, Robert Muir and A. R. Ferguson, greatly attracted me and, being encouraged, I haunted their department. At the time a local epidemic of smallpox broke out and Ferguson was studying the behaviour of the leucocytes and the histopathology of the skin. My interest was aroused and, anxious to do some work, I asked Professor Muir for a subject; he proposed the development of the granular leucocytes in the human foetus. When the results came into print I had graduated in medicine and, the Coats scholarship being open, I applied. There was no other candidate, and after a practical examination I became the first holder; the tenure was a year. Professor Muir asked me to take part in his work on haemolytic sera. He interpreted the scholar's duties in a most enlightened way by arranging that only part of the time was spent on research, thus leaving the rest at disposal for me to become familiar with the round of the Institute. I also attended a postgraduate laboratory course in medical bacteriology. My only "menial" duty was, in the first few months, to wash blood suspensions by turning a hand centrifuge until a small electric one was built. I read widely round the various subjects of the daily work and tutored several students—an admirable exercise for a future instructor.

Gaining a Carnegie fellowship and, on Muir's recommendation, accepted by Ehrlich as a voluntary worker, I went to Frankfurt late in 1905 and stayed till the autumn of 1907. At first I worked on haemolysis under the kindly eye of Hans Sachs; but soon Roehl, engaged on the biological side of trypanosomiasis chemotherapy, left and I replaced him. This was the greatest good luck, because during a year and a half I came into the centre of Ehrlich's chief interest. The Georg-Speyer-Haus for experimental chemotherapy was soon opened with both chemical and biological departments; so I made contact with the chemists. A landmark of that time was the arrival of Miss R. Gulbransen in the biological department. Afterwards, in 1916, I was able to invite her with support of the M.R.C. to share in research on the aminoacridine antiseptics; she came at once to Britain from her native Norway to further this work. Thus began a fortunate collaboration, which lasted some 20 years.

The personalities of both Ehrlich and Muir fascinated me. Muir was rather uncommunicative as a rule, from preoccupation mainly, and his intentions had to be divined; on formal occasions, however, he was magnificently clear. Ehrlich, never at rest, talked with telling vivacity and wit, yet nothing was unpremeditated. Both were highly concentrated men and did not relish interruptions. I recall vividly their occasional reactions. The laboratory which Muir used for haemolytic experiments was shared by a budding clinician doing a small bit of bacteriology. No doubt he hailed meetings with an influential figure like the professor as a useful opportunity to ripen acquaintanceship; so he made small talk. This was tolerated for a time, until one day on opening the door Muir saw the man and immediately, raising his arm prophet-wise, said emphatically, "X, I am busy this morning." Once on going to Ehrlich's room I found him arranging matters with a senior member of the institute; concluding, he said that they would continue next forenoon. The other replied that he was sorry, but he had a piano lesson at that time. Ehrlich courteously changed the hour and they parted; then eyeing me sternly he said, "You must have only one wife." I can think of no greater exhilaration for a young pathologist than the period with Ehrlich, though eventually, I fear, one would have burnt up in his fire, just as he consumed himself. With Muir I spent over 25 years; his fine critical mind, unbreakable integrity, generosity in allowing pupils to follow their own bent, and high appreciation of life both mental and material made a lasting imprint (Ehrlich, see Muir 1915-6; Browning, 1954, 1955; Muir, see Cappell, 1961).

These first four graduate years—including six months as house-physician—were a sort of informal apprenticeship quite free from the burden of impending examinations or other routine. They were the most memorable and valuable part of my scientific education. Nowadays, I fancy, it will be almost impossible to reach a senior position without an extra degree in science; however, I doubt whether such training is superior to my less formal course. But if the extra degree is necessary meanwhile, I should recommend the bare minimum of written examinations. These may serve in the words of Robbie Burns as the fear of hell that holds the wretch in order; but I am sure that such trials ultimately sap independence of mind. For the beginner, time spent in research, especially jointly with an experienced investigator, is invaluable and enjoyable. It shows how difficulties arise and the ways in which they are tackled. Sound initiative, usually a slowly maturing faculty, is fostered. There is a dilemma—how much to read? The immense cargo of knowledge piling up everywhere today may eventually hinder advance; repeatedly I have met sharp young people who decided from reading that what can be has been done, so why further effort. It appeals to me as a most enlightened provision of this College that Membership may be gained by published original work. I hope this approach will be freely encouraged.

Practice and Teaching

I was offered a university assistantship by Professor Muir soon after my return from Frankfurt. Personal selection of staff worked well in his hands to judge by the performance of the long line of his young people. At first I shared the general teaching and hospital work, later becoming responsible successively for bacteriology and clinical pathology. In 1911-12 the professor's official medical staff consisted of three, with several part-time demonstrators for the practical classes. When I was appointed first director of the Bland-Sutton Institute at the Middlesex Hospital duties were similar, except that I secured

Ernest Kennaway to undertake chemical pathology. In time the irresolvable uncertainties of histopathology disillusioned me; it is an essential subordinate, but can be a deceitful master and may lead its devotees into devious courses—for example, fixing all of a specimen where tuberculosis might be suspected.

On returning to Glasgow in 1919 to the new chair of bacteriology, I fortunately was housed in the Pathological Institute. At Muir's suggestion pathology and bacteriology lectures were closely dovetailed. For instance, as soon as the other aspects of pyogenic diseases were dealt with, their bacteriology was taken up. I am convinced that such integration is the best way of dealing with the pathology of infections for medical students. They require a basic understanding of the science without the detail suited to specialists. I quote as the highest compliment words of Sir Robert Muir (1950): "Many teachers of the present day would benefit if they knew both what bacteriology was and how much Browning thought it necessary to teach the ordinary medical student. If they cut their courses accordingly, I think it would be of great importance in the medical curriculum." As to the form of teaching, since knowledge is best acquired through as many sensory paths as possible, specimens and lantern demonstrations accompanied each lecture. However, tutorials and demonstrations should familiarize students with the main points of a subject before they attend formal lectures by a senior teacher; these can then be a perspective with emphasis on outstanding features. Unfortunately the order is usually reversed and one has to talk systematically to an audience both ignorant of the vocabulary and incapable of taking useful notes. Practical courses in pathology should contribute to training in manual dexterity. Medical men require skill in using their hands; and opportunities to acquire this are indispensable. The teaching which was mutually most rewarding took place in small practical classes and discussions with graduates engaged in research. When a junior turned his results into words for publication an important duty was to ensure that he made himself intelligible. I always found lucid, accurate expression on paper difficult; and few others seem less hampered. I chose knowledgeable young people to read my own MSS. When they queried any point, an acceptable alteration was devised. Obviously, if the reader had difficulty in grasping what was intended, the writer had failed and it was best to try again. Often I have asked the author of an unintelligible jumble, "Tell me what you wish to say," and at once he would give a brief and clear statement. However, I do not suggest composition by direct dictation. It is essential to write a draft, read it, make changes, rearrange words, paragraphs, etc., and then get a typed copy, which will show up further imperfections. I have known half a dozen redrafts to be required.

Examining never gave me satisfaction. Excellence in written papers is certainly no guarantee that a candidate will be good at his profession, but only means that he has a faculty commonly associated with general capacity. I have greater confidence in "practicals" and "vivas," which represent conditions much more akin to situations in real life. However, there are many young people who prefer written tests. This, I fancy, depends much on two factors—one is the elasticity of the inexperienced mind, which can accommodate a whole science for several days and disgorge chunks on demand; the other is shyness, which recoils from a possibly unsympathetic human confrontation. Not all examiners possess the tact of Kettle—once when about to interview a Scottish student, he asked, "Who are you?" and the answer was "Fine, thank you"; whereupon Kettle paused, looked at his list again and said, "Very good; now what is your name?" If there were sufficient teachers I would accept their opinion that a candidate should pass. In case of an adverse judgement an independent examination would be available as a sort of court of criminal appeal. I entirely agree with a statement of Robert Muir that good performance in examinations serves chiefly to bring to the notice of their seniors students who lack financial backing.

Research

While in the inanimate world spectacular triumphs of accomplishment abound—for example, in engineering—it is humiliating that we still signally fail to cope with more than a few of the biological derangements which afflict man and other animals. Research, actively pursued, is imperative. A medically trained pathologist who does not feel that adventure in his domain is a large part of the salt of life has surely mistaken his vocation. But the way has been difficult. As we saw, this century found the pathology departments of universities and hospitals mainly separate. Hospital authorities generally viewed research in pathology, particularly of the experimental kind, as at best a luxury. There is now much improvement, but even yet facilities for research could be more accessible; all who show aptitude (which is not yet measurable by the usual examinations) should possess the opportunities. The idea of separating research sheep from routine goats, with no common field, is frustrating. To be convinced of this one has only to watch the personality of an individual who, in addition to answering the calls of others, is also making progress with an investigation, preferably of his own choice. There is, too, the mass benefit conferred on his fellows. Of course, this implies no criticism of fine research institutions—for example, the Lister, a private organization, or the National Institute. As to "team-work," this can be highly effective only when it is a free association of individuals possessing various mental or physical skills, who jointly face an intricate problem.

Valuable results could be obtained even recently with moderate material outlays apart from the essential element of time. But now expenses grow ever greater; where are the means to be got? Calls in the name of specified diseases used to be very successful. But benefactors cannot be guaranteed any sure return; the only promises are past successes. Another important consideration is that investigation may be hampered by too precise terms of a gift. Cancer, coronary thrombosis, poliomyelitis are all dreaded and appealing words. But the best prospects of ameliorating such maladies and of general progress in the mastery of disease probably lie in research under less restricted designations—for example, growth, degeneration, viruses. As Ehrlich aptly put it, research is like a voyage in a balloon; one never knows in advance what the scenery will be on landing, but it is essential to be prepared to appreciate its features. It is clear that the number of people able to play Maecenas has of late drastically diminished. Their successors are committees, boards, or trusts, all multiple impersonalities whose judgements will be governed by presumed responsibility to others, compromise, and so on. Collectively they are likely to lack the faculty of making the bold wise decision open to one person disposing of his own. In any case, nobody but the researcher himself should decide what road he will follow, and he must be trusted. That does not mean that his judgements will always be right. Nevertheless, at least a proportion of research should be financed privately. If there are no longer large givers, there might well be many moderate ones responsive to appeals honestly advanced.

How does the investigator get his ideas—probably in various ways, sometimes unknown to himself. Certain minds seize fruitful analogies which are unguessed by most. For Medicine, particularly, a classic instance is Lister's inspiration that the agents of sepsis in wounds, like those of Pasteur's fermentation and putrefaction, must be micro-organisms. On the whole, however, there is not much explicit information as to why experimenters have acted as they did. In my experience, which conforms with general belief, new concrete facts are usually discovered by the scientific exploration of observations made under novel conditions. Such conditions may arise spontaneously or be produced experimentally; they need not be created on the basis of a theory. It must be added, however, that extraneous circumstances often play a large part in determining the importance attributed to any particular discovery.

Prospects

Extension of the field has been phenomenal and yet so many unsolved problems remain that one cannot but be hopeful of further progress. Most encouraging is the knowledge of what Nature unassisted occasionally brings about. It is foolish to guess what will be the next discoveries; there have been too many fatuous prophecies. After all, *Penicillium notatum* was wafted on to the culture of one who had spent much effort to demonstrate the impossibility of effecting locally what penicillin afterwards accomplished systemically. Again, to promulgate that cancer is an inevitable genetic vice seems a gambler's throw when metastases may develop after 20 years of latency following surgical removal of a primary; and still more astonishing is spontaneous regression of malignant tumours in man. Pathology is a science and art dependent on tools provided by chemistry and physics. It is now obvious that physical pathology will be actively fostered like its chemical twin. On one thing, however, I feel sure—so long as we remain human beings we shall never fathom the whole intricacy of disease processes. But we can expect to multiply powers of modifying these processes at decisive points, so as to prevent, compensate for, or even reverse derangements which interfere with healthy functioning.

I would pose several questions with another bearing. Even recently, medical pathologists were competent technicians, free to advance their subject by new methods and observations. Is this to be suppressed by administrative demands or replaced by computers? Again, what about the respective responsibilities of those medically qualified and the others who lack this background? Can the latter be reliable advisers in many problems concerning patients? On medical education in general my only comment is strong approval of the view that a nominally "all-in" qualification is an anachronism. It should be replaced by a primary qualification requiring a less detailed but broader pupillary curriculum, and this would be followed in a proportion of cases by preparation for a special qualification. Further, it is only common sense that a candidate's primary qualification should normally be gained at about age 25 and thereafter he be entitled to earn as well as learn. Means must be found, however, to prevent the cruel waste involved in rejecting candidates at the later stages of primary training.

To end, I recognize that pathology has now reached a diversity and a complexity which prevent more pathologists of my sort from emerging. The conditions of Membership of the College are clear evidence for this. At the same time I cannot but regret that an existence so varied and enjoyable should become impossible.

REFERENCES

Browning, C. H. (1952). *Fortuna Domus*, p. 249. Univ. Glasgow.
—— (1954). *Brit. med. J.*, **1**, 664.
—— (1955). *Nature (Lond.)*, **175**, 570, 616.
Cappell, D. F. (1961). *J. Path. Bact.*, **81**, 261.
Dible, J. H. (1957). Ibid., **73**, Suppl. pp. 1-35.
Ledingham, J. C. G. (1925). *Brit. med. J.*, **2**, 554.
Muir, R. (1915-16). *J. Path. Bact.*, **20**, 350.
—— (1950). *Lancet*, **1**, 936.

CONFERENCES AND MEETINGS

Disorders of Protein Metabolism: Conference at R.C.P. London

[FROM A SPECIAL CORRESPONDENT]

A conference on recent advances in plasma-protein disturbances and proteinuria was held at the Royal College of Physicians of London on 7 and 8 July.

Professor SHEILA SHERLOCK (Royal Free Hospital, London) was chairman of the first session, at which Dr. T. FREEMAN (National Institute for Medical Research, London) outlined the functions of certain plasma proteins. He pointed out that Laurell electrophoresis had now made possible both the quantitative and qualitative assessment of plasma-protein fractions, and that nearly 50 different types, several of them still unnamed, had been demonstrated, though the functions of most of them were not yet understood. Dr. Freeman divided the plasma proteins of known function into two categories—"suicidal" proteins, which were broken down in performing their task, and biophilic proteins, which were used repeatedly. Chain reactions employing suicidal proteins might be a safety device resembling a combination lock, the proteins being destroyed because their actions, in some cases at least, were potentially dangerous. Complement and the formation of fibrin from fibrinogen were examples of this.

Though albumin comprised the largest fraction of the plasma proteins and had been studied most, its function was still poorly understood. In the past albumin had been thought of as a reserve pool of amino-acids, but at least two other functions were more likely possibilities. Firstly, albumin provided a non-specific transport mechanism for many substances, including bile acids, metals, drugs, and excesses of vitamins and hormones. Secondly, in common with the other plasma proteins, albumin maintained the colloid osmotic pressure of the blood. Nevertheless, high albumin levels were not essential for the latter because patients with the rare condition of analbuminaemia generally remained remarkably well. Dr. Freeman went on to describe the functions of two other plasma proteins which were better understood. The substance transferrin bound iron atoms and carried them to the reticulocytes, and it also appeared to have some antibacterial action. Haptoglobins of several types combined with haemoglobin, and probably acted as scavengers. He thought that it was likely that all plasma proteins had specific functions, and that new techniques would lead to great advances during the next ten years.

Liver Disease

Discussing the influence of liver disease on plasma-protein levels, Dr. V. M. ROSENOER (Royal Free Hospital) divided the plasma proteins into two main groups—the immunoglobulins, synthesized extrahepatically, and the remainder, synthesized wholly or mainly in the liver. A high proportion of patients with liver conditions had increased immunoglobulin levels, but these were not disease-specific and therefore had no use in differential diagnosis, neither did their presence imply the existence of an autoimmune process in the liver. Similarly, the fall in blood levels of plasma proteins formed in the liver had been found to bear no direct relation to individual hepatic diseases. Nevertheless, it had been possible to develop methods for the direct study of plasma-protein synthesis rates in the liver by the use of radioactive tracers. Surprisingly, these studies had produced no evidence of a feedback mechanism by which the serum albumin concentration could influence the rate of albumin synthesis.

Dr. Rosenoer concluded by emphasizing the importance of an adequate supply of amino-acids for protein synthesis, and suggested that protein intake should not be unduly restricted in patients with liver disease; nor, on the other hand, was it useful to give excessive quantities of protein. Normal dietary levels were usually best.

Dr. G. NEALE (Royal Postgraduate Medical School, London) instanced some diseases associated with hypoproteinaemia, pointing out that low levels of albumin and other plasma proteins were caused either by reduced production (in liver diseases and malnutrition of the kwashiorkor type), by increased catabolism in acute illness, or by direct loss from the body. The last took place through the skin after burns, from the kidneys in the nephrotic syndrome, and from the gut in protein-losing enteropathy. Protein loss from the gut occurred at various levels: from the stomach in carcinoma and hypertrophic gastritis; from the small bowel in regional ileitis, idiopathic steatorrhoea, tropical sprue, and after irradiation; and from the colon in carcinoma and ulcerative colitis.

Dr. Neale emphasized that severe hypoproteinaemia could produce a clinical picture closely resembling kwashiorkor, the effects of inadequate dietary intake being mimicked by malabsorption or maldigestion. Thus two clinical types of hypoproteinaemia could be distinguished: firstly protein loss causing caloric undernutrition, and secondly inadequate adsorption leading to the kwashiorkor type. Intravenous albumin had proved valuable in treatment of the latter. In the subsequent discussion Dr. Neale said that corticosteroids were not often successful in the treatment of patients with protein-losing enteropathy.

Impaired Immunity

The first part of the afternoon session, under the chairmanship of Professor C. E. DENT, F.R.S. (University College Hospital, London), was devoted to hypogammaglobulinaemia. Dr. J. R. DAVIS (Institute of Child Health, London) described the normal course of immunoglobulin levels during intra-uterine life and in the newborn. Maternal gammaglobulin-G crossed the placenta in late pregnancy, giving protection to the baby after birth until the latter's own gammaglobulin-G production took over. In premature babies, on the other hand, maternal gammaglobulin-G levels fell before the infant's own production was sufficient to give protection against infection. Thus premature babies often lacked immunity at about the time of their discharge from hospital, just when they were first exposed to infection. Dr. Davis suggested that this situation predisposed to overwhelming infection and cot death, and he proposed a large-scale trial of the administration of gammaglobulin to premature babies.

Turning to hypogammaglobulinaemia in children, Dr. J. F. SOOTHILL (Institute of Child Health) said that antibody deficiency was only one aspect of impaired immunity. Both antibody and cellular immunity could be either qualitatively or quantitatively deficient or both. Hypogammaglobulinaemia in children was a quantitative antibody deficiency, commoner in boys, which could be a temporary, self-correcting phase; a familial tendency; the result of congenital rubella; or due to some unknown cause. Children with hypogammaglobulinaemia were particularly susceptible to coccal infections, whereas those with a deficiency in cellular immunity had an impaired resistance to virus infections. Several measures could be employed in the management of children deficient in antibodies. Chemotherapy for individual attacks (or prophylactically), gammaglobulin injections, and immunization were all useful, though live virus vaccines were potentially dangerous in these children and best avoided. *Pneumocystis carinii* infections, the commonest cause of death among boys with hypogammaglobulinaemia, could now be successfully treated with pentamidine.

Dr. K. M. CITRON (Brompton Hospital, London) described hypogammaglobulinaemia in adults, classifying this as either primary or secondary, the latter having several possible causes, including the toxic effect of drugs and neoplasia. The sex incidence of the primary type was about equal among adult patients, who often had histories of multiple infection. Though the adult form always had its onset in adult life, there was some evidence of a familial pattern, and it might be precipitated by the influence of exogenous factors on genetically predisposed individuals. Cellular immunity was normally intact.

Paraproteins and Malignancy

The second part of the afternoon session was devoted to paraproteins, and Dr. J. R. HOBBS (Royal Postgraduate Medical School) described the clinical aspects of paraprotein production. In contrast to the wide range of antibodies produced in response to antigens, paraproteins were almost always of a single immunoglobulin type in each affected person, and were derived from abnormal cell clones. These were associated with malignant conditions—myelomatosis, lymphoma, and leukaemia—in about three-quarters of those affected, but appeared to run a benign course or resolve spontaneously in the remaining quarter. Though the abnormal immunoglobulins (paraproteins) of myelomatosis were of several types, two paraproteins were found in the same patient in about 2% of cases. All the abnormal immunoglobulins were immunologically deficient, and the excretion of large quantities of their light chains in some patients with myelomatosis could be detected as Bence Jones protein in the urine.

Concluding, Dr. Hobbs emphasized the progressive increase of abnormal immunoglobulin levels in all malignant paraproteinaemias, and he deduced from the rate of progression that a single abnormal cell might take 40 years to proliferate to the point at which a paraproteinaemia became clinically apparent. Patients known to have paraproteins in their blood should be retested annually in case the condition was progressive.

Discussing the treatment of the paraproteinaemias, Dr. D. A. G. GALTON (Chester Beatty Research Institute, London) gave some provisional results of a Medical Research Council trial which had shown that melphalan and cyclophosphamide were about equally effective in the treatment of myelomatosis. The response to treatment had been found to be very slow in some patients, and it was important to persist even if the initial response seemed disappointing. Nevertheless, the possible improvement obtainable by chemotherapy had to be carefully weighed against the toxic effects of the agents at prevent available.

The first day's proceedings concluded with the Lilly Lecture on "Antibodies without Antigenic Stimulation," in which Professor J. G. WALDENSTRÖM (University of Lund, Sweden) surveyed the field of paraprotein disease with special reference to myelomatosis.

Lipoprotein Disorders

Lipoprotein disorders were the subject of the paper by Dr. JUNE K. LLOYD (Institute of Child Health) given at the final session of the conference, with Dr. J. C. HAWKSLEY (University College Hospital) in the chair. After outlining methods for identification of lipoproteins by paper electrophoresis and ultracentrifuge separation, Dr. Lloyd described the primary disorders of lipoprotein metabolism due to genetic defects. Lipoproteins were deficient in a-betalipoproteinaemia and Tangier disease (alphalipoprotein deficiency), both conditions being inherited as autosomal recessives. The first of these was characterized by acanthocytosis of the red blood cells, steatorrhoea, pigmentary retinopathy, and ataxic neuropathy, while patients with Tangier disease had cholesterol deposits visible in the tonsils and causing lymph-node enlargement and hepatosplenomegaly.

By contrast, lipoprotein levels were raised in the other inherited conditions described by Dr. Lloyd. Elevation of triglyceride, also inherited as an autosomal recessive, was fat-induced in essential hypertriglyceridaemia (idiopathic hyperlipaemia) and brought on by carbohydrates in the carbohydrate-induced hypertriglyceridaemias. These conditions were treated by restriction of fats and carbohydrates respectively, and medium-chain triglycerides could usefully be added to the low-fat diets. Familial hypercholesterolaemia (hyperbetalipoproteinaemia) was an autosomal dominant condition seen in both homozygous and heterozygous forms, of which the latter was more common. Very high blood-cholesterol levels, especially in the homozygous form, were associated with coronary artery disease having its onset in childhood, adolescence, or early adult life. Satisfactory management was difficult—again particularly so in homozygous patients—but polyunsaturated-fat (such as corn oil) diets and cholesterol-lowering drugs had been found to produce some reduction in blood-cholesterol levels.

Massive Proteinuria

The conference concluded with two papers devoted to proteinuria, in the first of which Dr. J. D. BLAINEY (United Birmingham Hospitals) described a study of massive proteinuria, defined as loss of more than 10 g. of protein per 24-hour period in adults. This loss took place from the glomeruli, and oedema and low serum-albumin levels were found consistently in such patients, who suffered from nephritis of various types (but not from pyelonephritis, which seldom caused massive proteinuria). A total of 430 patients had been subjected to detailed investigation, including renal biopsy and protein studies on the serum and urine. Treatment consisted of continuous corticosteroid therapy in minimal effective dosage; a high-protein, high-calorie diet; and prophylactic oral penicillin. In addition, a salt-free diet was given while patients had oedema, and hypotensive drugs were used if the diastolic pressure exceeded 100 mm. Hg.

In the final paper, Dr. H. S. PLATT (University College Hospital) discussed the causes of tubular proteinuria, which produced much smaller losses of proteins of lower molecular weight than those found in the massive glomerular proteinuria of the nephrotic syndrome. Tubular proteinuria could be due to any one of a number of causes, including chronic cadmium poisoning, the Fanconi syndrome, and galactosaemia. It was also found mixed with glomerular proteinuria in Wilson's disease, phenacetin nephropathy, chronic pyelonephritis, and other conditions.

Centenary Annual Meeting of Canadian Medical Association

[FROM A SPECIAL CORRESPONDENT]

The Canadian Medical Association celebrated its centenary by holding the 1967 Annual Meeting in Quebec City, the place of its founding in the year of Canadian Confederation, and in Montreal. As part of this meeting scientific sessions were held at the Château Frontenac Hotel, in Quebec. A report of some of these sessions is given below.

Triple-X Female

Dr. MURRAY BARR (London, Ontario) opened the scientific meeting with a discussion on the trisomy of chromosomes, with particular reference to that of the X chromosome. Dr. Barr—who during the course of the meeting was presented with the F. N. G. Starr Award by the Canadian Medical Association, as recognition of his contributions to the field of genetics—outlined the various genetic abnormalities that at present were identified with chromosomal non-disjunction. The latter was an error of mitosis, in which two similar chromosomes (instead of the usual one) were contributed to the daughter cell during germ cell maturation. This might occur with any of the 22 pairs of autosomes or with the sex chromosome.

Dr. Barr reminded his audience that each chromosome contained hundreds of genes, the number varying with the length of the chromosome. The deoxyribonucleic-acid-containing genes elaborated ribonucleic acid, both of a specific nature for each gene locus, and the ribonucleic acid in turn guided the production of specific cytoplasmic enzymes. When trisomy existed, each gene locus was present three times instead of twice, and consequently enzymes under control of the trisomic chromosome would theoretically be produced at 50% above their normal values. Enzymatic imbalances occurred and interfered with normal embryonic development. Dr. Barr observed that the longer the chromosome the greater the expected damage would be, and the details of the abnormalities produced would vary depending on which chromosome was trisomic.

When chromosomes were arranged as a conventional karyotype, the 44 autosomes could be divided into seven groups, A to G, on the basis of morphological similarity. Trisomy of autosomes in all seven groups was found in spontaneously aborted foetuses, while numerical chromosome abnormalities accounted for at least 20% of embryonic loss. Trisomy of autosomes was usually lethal during the first trimester, and with rare exceptions only three types of autosomal trisomy allowed the foetus to proceed to live birth—namely, trisomy 15, trisomy 18, and trisomy 21 (which caused mongolism or Langdon Down's syndrome).

Dr. Barr pointed out that, though the X chromosome was large, X chromosome trisomy did not result in death or in the production of serious physical defects as would be expected. The X chromosomes were about the same length as autosome 6, with a large number of gene loci, only a few of which were concerned directly with sex differentiation. Trisomy of the X chromosome did not interfere more drastically with the normal development of various systems and organs because of the phenomenon of X chromosome heteropyknosis—where one of the chromosomes of the female was tightly coiled, compact, and adherent to the inner surface of the nuclear membrane. This chromosome was relatively genetically inactive and ensured that there was not a great predominance of active genetic material from the female. Moreover, the X chromosome of paternal origin could take this inactive heteropyknotic role also, and the form of the X chromosome, paternal or maternal, was decided at the moment when the embryo underwent implantation.

This ability to form inactive X chromosomes gave the subject a protective mechanism not afforded in cases of autosomal trisomy, and gave a reasonable basis for explaining the lesser degrees of malformation found in triple-X trisomy. Dr. Barr presented accounts of six patients with X trisomy and noted that, though a clear clinical syndrome had not been established, certain features might be found in some cases—including club foot, subluxation of the elbow, flexion deformities of the fingers and other skeletal abnormalities, webbed fingers, hydrocephalus, spastic quadriplegia, optic atrophy, cataract, and corneal opacities. Nevertheless, triple X females were usually physically normal, but they ran a greater risk than average of some sort of defect, with no consistent pattern.

Concluding, Dr. Barr suggested that the incidence of X trisomy was 1 in 850 female babies, and noted that until mass chromosome analyses were done on all newborns chromosome abnormalities of this type would go undetected, lacking as they did a well-defined clinical picture.

Calcium Homoeostasis

Discussing the regulation of body calcium, Dr. D. H. COPP (Vancouver) emphasized that, though the body of a 60-kg. man contained over 1 kg. of calcium, less than 0.1% of this was extracellular and involved in important functions such as muscular contraction, neuromuscular excitability, membrane permeability, and enzyme activity.

Using sequential high calcium and low calcium perfusions of the parathyroid gland, Dr. Copp and his associates had observed a very rapid fall in plasma calcium during the high calcium perfusions, and the expected rise with low calcium perfusions—this presumably due to endogenous parathyroid hormone. Following the final perfusion, the test animals had had the thyroid and parathyroid glands removed. Instead of the expected fall in plasma calcium a marked and sustained rise had occurred, and it was suggested that the fall in calcium during high calcium perfusions was not due to suppressed parathyroid hormone production but to a humoral agent which actively lowered blood calcium. Hence they had concluded that a previously unrecognized hormone was involved. This was now accepted as calcitonin or thyrocalcitonin, derived from the " light cells " or " C " cells, which made up 2–4% of the mammalian thyroid.

Calcitonin was a straight-chain polypeptide, as was parathyroid hormone, but it was about one-half the size and lacked three amino-acids found in parathyroid hormone: isoleucine, trytophane, and cysteine. It was antigenic, with definite species differences, and was effective in man in doses of less than 0.1 mg.

Calcitonin had been found to be effective after nephrectomy and total evisceration, so that its action was not through either kidney or intestine. It was also effective in the parathyroidectomized animal, so that it was more than an inhibitor of parathyroid action. Experimental evidence suggested that, while parathyroid hormone increased osteolysis, calcitonin inhibited normal osteolysis, the osteolytic effect of parathyroid hormone, and also the osteolysis induced by vitamin A. Active remodelling of bone, stimulated by parathyroid hormone, was inhibited by calcitonin, with a reduction in the number of osteoclasts.

The control of serum calcium levels had two facets: firstly a fine control mechanism, and secondly a relatively crude control, which operated in the thyroparathyroidectomized animal. The former was the parathyroid-hormone–calcitonin system, in which each hormone could act independently of the other, and where the hormone output was controlled by the concentration of calcium ions in the blood. The latter depended on such factors as the labile calcium store in bone, the availability of calcium from the gut (favoured by the presence of vitamin D), the excretion of calcium, and the effect of calcium and phosphate in blood on the deposition of new bone mineral.

Dr. Copp emphasized that the clinical value of calcitonin had not been established. The great hope was that it might have a beneficial effect in cases of osteoporosis, but, discouragingly, calcitonin had been found to act much more effectively in the young animal in inhibiting osteolysis.

Gastrointestinal Polyps

Reviewing current concepts about polyps of the gastrointestinal tract, Dr. WALTER MACKENZIE (University of Alberta, Edmonton) decried the tendency for the terms polyp and adenoma to be used interchangeably, and stated that this lack of precision, which was particularly noticeable in recent articles, had led to improper treatment.

In the diagnosis of benign tumour of the oesophagus, Dr. MacKenzie stressed the importance of careful *x*-ray examination, which revealed a smooth filling defect with normal mucosa overlying the tumour mass. He felt that gastric polyps were precarcinogenic, and he referred to a 12-year study of 20 patients with multiple gastric polyps, when three had developed proved malignancy. The use of gastroscopy had been invaluable in diagnosis, and could give an early indication of malignancy. Partial gastrectomy was the treatment of choice for multiple polyps, since this avoided the increased mortality and morbidity associated with total gastrectomy, and also the serious nutritional problems associated with the latter procedure.

The use of transillumination of the bowel in a dark-adapted operating-room was a useful procedure in visualizing small bowel tumours. The radiological examination of the small bowel was, Dr. MacKenzie stated, only as effective as the degree of awareness of the clinician and the degree of care taken by the radiologist.

In the colon a papillary or villous adenoma was potentially more dangerous than an adenomatous polyp, with an associated malignancy rate of 30–40 per cent. The relation of the adenomatous polyp to carcinoma remained one of the most controversial areas in the field of general surgery, though Dr. MacKenzie felt strongly that a significant positive correlation existed, pointing out that the frequency of carcinoma rose proportionately with the presence of multiple polyps. He supported the view that polyps might be the " flags " which signalled a carcinogenic stimulus. In congenital multiple polyposis of the colon possibly the carcinoma might be merely a manifestation of the large number of polyps and their potential to become malignant.

In the case of rectal polyps, it was generally agreed that removal of those within reach of the sigmoidoscope was indicated and was relatively simple. For those above this level he recommended colotomy and polypectomy for those which were clinically benign, and resection of the involved portion of the bowel for those which were not. He felt that the incidence of existing malignancy was greater with increased polyp size, but could see little justification for attempting to establish a so-called " critical " polyp size.

Industrial Rehabilitation

Mr. LAWRENCE PLEWES (Dunstable, Great Britain) outlined the services in the field of industrial rehabilitation available in England under the Disabled Persons Act. He pointed out that both the Ministry of Health and the Ministry of Labour were actively involved in this area, their activities being co-ordinated by a National Advisory Committee, composed of doctors, trade unionists, employers, and officials from both Ministries. At the local level there was the Disablement Advisory Committee with a similar composition, concentrating its efforts on local employment situations and individual disability problems.

Mr. Plewes felt strongly that traditional occupational therapy should be confined to diversional schemes for bed-ridden patients, and had no place in a modern rehabilitation service. All forms of passive physical therapy —such as heat, massage, diathermy, and ultrasonics—should be and had been replaced by exercises and machines and games. This change from the passive to the active form of therapy had not been easy, since it was difficult to persuade a patient, in a push-button age, that the best results would follow his own muscle contractions.

The usual pattern at a district general hospital was for limited rehabilitation services to cope with urgent short-stay patients. Regional centres with accommodation for in-patients catered for the more serious and long-term problems. The rehabilitation centre, such as the one at Luton, used a factory milieu to both mobilize and evaluate the recovery of the patient. Simple machines, which employed a conditioned reflex on the part of the operator, were generally used, and enabled the patient to do useful work, avoiding the boredom of simple exercise, and in addition fostering a feeling of accomplishment. Noise was purposefully present in a moderate degree, allowing for a gradual adjustment back to a noisy environment while the patient was under sedation. This was important in post head-injury cases, where sudden exposure to noise could be intolerable. Dr. Plewes stressed that this industrial method was used no matter what type of employment the patient had previously held, and it had been found effective.

In those patients who were unable to return to normal employment sheltered workshop accommodation should be available. Once a patient had progressed to a point satisfactory from the medical aspect, he could be either returned to his normal occupation or referred to the industrial rehabilitation unit. At the latter the disabled person was evaluated by a highly skilled staff, and was then given a trial at several different appropriate occupations or sent to a private industrial concern for highly specialized rehabilitation courses. In all cases rehabilitation was on industrial lines. The pace was graded, and vocational assessment was a continuing feature. If further training was necessary the patient was sent to a Government training centre or technical college.

Dr. Plewes felt that the involvement of trade unionists in these programmes was most important for their success. He estimated that a community of 230,000 should have an industrial rehabilitation centre for 50 persons at the hospital, another 50 places in local industry, and a sheltered workshop for 50 disabled persons, plus an additional 100 places for the mentally disabled, to meet adequately the demand for service.

Growth Hormone Deficiencies in Childhood

Professor DOUGLAS HUBBLE (Birmingham, Great Britain) delivered the Tisdall Lecture (established in memory of Dr. Frederick Tisdall, a great Canadian paediatrician and nutritionist), on defective growth in childhood. Detailing his experience with a group of twenty-one cases of growth hormon deficiency, he classified this into idiopathic, genetic, and secondary. Thirteen of his cases fell into the first category, and included perinatal injury. Two cases were classified as genetic, which would be either autosomal recessive or non-sexed linked. Under secondary causes Professor Hubble included cases of craniopharyngioma, chromophobe adenomas, healed tubercular meningitis, and trauma.

Only seven cases were isolated growth hormone deficiencies ; eleven cases also had thyroid-stimulating-hormone deficiency, as shown by low serum protein-bound iodine levels. Professor Hubble felt that in some cases there was some failure of the thyroid gland dependent on the growth hormone deficiency, though attempts to verify this hypothesis had been unsuccessful. Corticotrophin deficiency occurred in four of his patients. The clinical picture of patients with growth hormone deficiency was apparent immaturity, normal intelligence, truncal obesity, retarded skeletal maturation, marked growth retardation, and, in many cases, episodes of spontaneous hypoglycaemia. All the patients over 15 years of age had shown retardation of puberty.

A combination of the radioimmunoassay and the intravenous insulin-tolerance test had been used for diagnosis, in conjunction with the human growth hormone nitrogen-retention test. Although these involved considerable technical difficulties, these tests had enabled the diagnosis of growth hormone deficiency to be made with precision, and for it to be excluded in other cases.

In children with growth hormone deficiency the treatment was with growth hormone derived from human pituitaries, since preparations of animal growth hormone gave no response. The dosage varied from 6 mg. weekly to 18 mg. weekly, and produced a greatly accelerated velocity of growth in the first year of treatment. This initial spurt was called the " catch-up " period. Normal growth rates could be achieved by prolonged therapy, but the " catch-up " growth period by no means allowed the leeway which had occurred in the early years to be made up. Most of the 40 cm. of rapid growth in the first three years of life was irrecoverable. If hypothyroidism was present, thyroxine should be given concurrently, for the two hormones appeared to act synergistically, though thyroxine could not replace growth hormone.

RESEARCH IN PROGRESS

M.R.C. Annual Report

At the end of March 1967 the Medical Research Council's own establishments consisted of the National Institute for Medical Research and 77 research units, including four overseas. The Council's report,[1] which was published on 27 July, states that individual members of the Council's external scientific staff continued to be attached to other institutions, and that the Council supported 46 research groups.

At a total of £11,885,000 the Parliamentary grants-in-aid represented an increase, at constant prices, of 13.4% over the previous year, and the report points out that in the past few years there has been a rate of increase of between 10 and 13%. In the same period the increase in the recurrent costs of the Council's own establishments has been about 6%, at constant prices, owing, the report says, to new building projects, "sophistication" in staffing and equipment, and an increased number of new investigations.

The Council also received £1,016,039 from other sources, enabling it to spend a total of £12,800,000 during the period. Nevertheless, the report points out that, because of existing commitments, only £900,000 of this was "freely deployable" within the year, and it comments that this latter sum is of particular significance in forward planning if the Council is to encourage new lines of research.

Expenditure on research grants now accounts for over 17% of the Council's total budget, compared with 10% or less up to five years ago; in the year 1966–7 a total of £2,210,000 was spent in this way. The report also states that the Council provided 24 travelling fellowships, 224 scholarships for training and further education, and 157 awards for intercalated courses.

Revised Charter

The report also records the fact that the revised Charter of the M.R.C. received the Queen's assent on 26 October 1966. The M.R.C.'s first Charter was granted in 1920, and, though the new Charter does not alter the constitutional position, it will enable the number of members to be raised from 12 to a maximum of 16. All members of the M.R.C. are now appointed by the Secretary of State for Education and Science, the Chairman and Deputy Chairman after consultation with the Council and the scientific members with the Council and the President of the Royal Society.

Discussing the M.R.C.'s policy on computers, the report says that the Council's Computer Advisory Committee has advised the M.R.C. that its computer unit in London, which was established at the beginning of this year, will be able to serve the needs of all staff locally and some of them elsewhere. The Council's policy is that as much work as possible should be done on large computers providing a general service, and that smaller machines should be provided for local use only if there are special indications.

Record Linkage

With regard to a proposed national system of record linkage, the report says that the Council's Committee on General Epidemiology believes that this could be created on existing practices. The basis of the suggested scheme would be birth, marriage, and death records, together with selected data of long-term interest from hospital inpatient records. Besides enabling long-term studies on, for example, people exposed to occupational hazards, such a scheme would aid studies in genetics, of screening programmes, and of the delayed toxic effects of drugs. Though the Council recognizes that, besides requiring changes in the law and administrative procedures, the project would be costly to introduce, it believes that "the advantages of such a scheme are so manifold as to outweigh the difficulties of its implementation."

Work is in progress on Phase I and Phase II of the New Clinical Research Centre at Northwich Park, which will include, respectively, part of the Research Institute and some hospital beds, and the main operating theatre block and the maternity department (see *B.M.J.*, 1966, **1**, 535).

It is planned to have a multidisciplinary approach at the Centre, with interchange of workers between the various scientific fields, and it is hoped that roughly half the scientific staff will be clinical and half non-clinical workers.

Medical Education

The Council's evidence and advice to the Royal Commission on Medical Education are also mentioned in the report. These include, firstly, the suggestion that universities should be encouraged to make their entry requirements as broad as possible, and in particular that mathematics should be an alternative to one of the subjects required for entry to the preclinical course. Secondly, the Council recommended that both the duration and the context of the preclinical course should be as flexible as possible, and that the range of intercalated courses should be widened to include biological and paraclinical studies other than the traditional subjects. Thirdly, since the length of the present clinical course might lessen the prospects of an individual's success in original work, consideration should be given to introducing a short clinical course, designed to introduce him to the problems and opportunities rather than towards training for practice. Finally, the Council proposed that optional subjects concerned with research methods might be introduced into courses designed for training specialists.

New Committees

Besides mentioning that six committees have been disbanded, the report also records that the following new ones have been established or reconstituted (names of chairmen in parentheses): *Research in Industrial and Applied Psychology* (Professor Sir Austin Bradford Hill, F.R.S.); *Dental* (Professor B. Cohen); and *Non-ionizing Radiations* (Professor A. R. Currie). Three new working parties have also been set up: on *Anti-human Lymphocyte Serum* (Professor M. F. A. Woodruff); on *The Use of Anti-D Gamma Globulin for the Prevention of Iso-immunization of Rh-negative Women During Pregnancy* (Professor P. L. Mollison); and on the *Treatment of Myocardial Infarction* (Professor W. Melville Arnott).

As well as summaries of the work of the Council's own research establishments and of other projects supported by it, the report contains a series of articles on selected aspects of medical research. The subjects of the latter are: studies on the human Y chromosome; ageing; the control of protein synthesis in living cells; experimental studies on viral carcinogenesis; progress towards the control of leprosy; some problems in the control of virus vaccines; pulmonary hypersensitivity disease due to organic dusts; recent research on thrombosis; some aspects of the organization of visual pathways; and some observations on the age of reaching puberty.

---

[1] *Medical Research Council Annual Report April 1966–March 1967.* London, H.M. Stationery Office, price 26s. 6d. 1967.

Correspondence

Letters to the Editor should not exceed 500 words.

Snakebite Poisoning

SIR,—A newspaper recently reported[1] that a man was bitten by a snake which he subsequently brought to hospital. The report alleges that doctors could not identify the snake and were thus unable to decide if antivenom should be given. The snake was therefore taken to a zoo, while back at the hospital "... doctors were waiting for the vital identification."

Distinction of poisonous from non-poisonous snakes is often difficult, but is *not* important for the clinician—his function should be to diagnose whether poisoning has or has not occurred, and, if so, of what severity. In Britain the only naturally occurring poisonous snake is a viper, and thus there is no need to distinguish between viper-bite poisoning and envenoming from elapid bites (a problem in some tropical countries). The assumption that poisonous snake bite is the same as snakebite poisoning is wrong; it has greatly confused the medical treatment of snakebite. In at least half the victims bitten by poisonous snakes no venom is injected; this half can be immediately recognized in hospitals because there is no swelling (local swelling starts within minutes of an adder bite if venom has been injected). Antivenom should not be given to such patients.

It is my belief and practice that antivenom should be given only to the minority of snakebite victims (about one-quarter) showing clinical evidence of *systemic* envenoming as well as local effects of poisoning. In systemic viper-bite poisoning, the common early signs are vomiting and blood-stained spit (the victim should cough hard to produce this spit). An hour or so later blood becomes non-clotting. More details on the medical treatment of snakebite have been recorded previously in your columns.[2]—I am, etc.,

H. ALISTAIR REID.

School of Tropical Medicine,
Liverpool.

REFERENCES

[1] *Daily Express*, 21 July (Liverpool Edn.), p. 1.
[2] Reid, H. A., *Brit. med. J.*, 1963, 1, 1675.

Undesirable Effects of Marijuana

SIR,—The use of marijuana (cannabis), usually in the form of cigarettes, is widespread. Its undesirable effects, alone or combined with other drugs, are not fully known. Accounts of four young men referred to me over the past six months may therefore be of interest.

(1) An undergraduate of 19 smoked "reefers" at parties about a dozen times without ill effects. He relaxed and was able to appreciate music, companionship, and conversation more keenly. He then smoked "an extra large one and something exploded inside him." He felt intense anxiety and a frightening sense of unreality. That night he was given a hypnotic. Four months later, in spite of psychiatric treatment, he still experiences severe anxiety and unreality, and has frightening hypnagogic hallucinations.

There are no psychotic features. He is an obsessional young man, trying to resolve neurotic problems of adolescence. The effect of the drug has been to precipitate an acute anxiety state.

(2) An art student of 19 experimented with lysergic acid diethylamide (L.S.D.) over a period of several months without obvious ill effect. At a party he took 100 mg. L.S.D. by mouth and smoked two "reefers." He felt "depersonalized, about to disintegrate, and go mad." He became extremely anxious. He was treated with trifluoperazine 2 mg. three times a day and chlordiazepoxide 10 mg. three times a day for a fortnight, and symptoms subsided. A week later he again smoked a "reefer." Anxiety immediately returned and he experienced fleeting visual hallucinations. These subsided slowly with treatment over several weeks.

After full recovery he was resolved not to smoke marijuana again.

(3) A man of 24 was admitted to hospital, having drilled a hole into, but not through, his skull. He had done this with a dental foot-drill, under the influence of marijuana. He gave a clear account of himself. After obtaining an honours degree in law he drifted in and out of several jobs. On coming down from Cambridge he came under the influence of a group of people who believe that, after a suitable period of preparation with L.S.D. and marijuana, trepanning of the skull, by releasing cerebral pressure, will enable an individual to conquer time.

Although he showed no overt psychotic signs, other than what amounted to a delusional belief in this idea, his history suggested schizophrenia simplex. He refused psychiatric treatment.

(4) This patient, aged 24, began to smoke marijuana after leaving art school, without apparent ill effect. Two years ago he became involved with the same group of people mentioned in Case 3. Under their influence he took L.S.D and marijuana. At the beginning of this year he became frightened and felt that he had been chosen as a guinea-pig for a trepanning experiment. Psychotic symptoms developed and spread. He was treated by psychoanalytic methods for several months without relief of psychotic symptoms. During this time he continued to smoke marijuana in spite of the fact that this seemed to increase the intensity of his symptoms. Eventually he was admitted to a nursing-home and treated with phenothiazine drugs.

He appeared to be an "inadequate personality," the psychotic state having been brought about by L.S.D. and marijuana.—I am, etc.,

PETER DALLY.

Department of Psychological Medicine,
Westminster Hospital,
London S.W.1.

Disturbed Geriatric Patients

SIR,—Dr. R. C. Greenberg's resolution at the Annual Representative Meeting (*Supplement*, 22 July, p. 91) deploring the lack of facilities for the care of disturbed geriatric patients did not in my view go far enough. There is, I think, an urgent need for the medical and other requirements of the aged to be rationalized. At the present time the services provided by the local authorities are usually subdivided into two parts—one ruled by the medical officer of health dealing with the domiciliary services, health visiting, home nursing, chiropody, etc., the other by the chief welfare officer and his separate staffs running the local authority welfare homes.

From the point of view of the family doctor, and in an emergency the medical officer of health, difficulties arise in assessing whether an old person requires a bed in an old people's home, a geriatric hospital, or a mental hospital. The beds in each are controlled by different people and more often than not the liaison between these people is less than it might be. Not only are patients sometimes sent to unsuitable accommodation in the first place, but transfers from one type of bed to another are far from the simple administrative manœuvres that one would expect them to be.

Somehow, and as a matter of urgency, the facilities available for the old people must be integrated, or at least co-ordinated, if the best uses of the available resources are to be made. The suggestion that a senior doctor, from either the hospital or the local authority service, should be responsible for this co-ordination is long overdue.—I am, etc.,

H. M. DAVIES,
Assistant County Medical Officer.

Newton Abbot,
Devon.

Hetacillin and Ampicillin

SIR,—A recent article entitled "Laboratory and Pharmacological Studies in Man with Hetacillin and Ampicillin" (24 June, p. 804) presents data obtained by Beecham researchers utilizing ampicillin (Beecham) and hetacillin (Bristol). The hetacillin used in these studies was partly prepared by Beecham and partly acquired in the market.

The absorption and excretion results cited in this paper are at variance with those reported by independent investigators in this country.[1 2] Indeed, the variation in the data obtained by the Beecham investigators themselves (Study A vs. B and C vs. D) might have prompted their enlisting the aid of independent observers, particularly when, surprisingly enough, their ampicillin levels are much higher and their hetacillin levels much lower than those found by independent investigators.[1 2]

The authors conclude by stating "that hetacillin would be expected to possess inferior therapeutic efficacy compared with ampicillin." To date, in well-conducted clinical trials on file with the Food and Drug Administration, over 3,000 patients have been treated, with results which refute this statement. Infections caused by both Gram-positive and Gram-negative micro-organisms have responded to hetacillin in the same or lower dosages than those recommended for ampicillin. Details of these clinical studies will appear in print shortly.—I am, etc.,

R. E. WEISSGERBER,
Vice President—Scientific Director,
Bristol Laboratories International
Corporation.

New York.

REFERENCES

[1] Bunn, P. A., Milicich, S., and Lunn, J. S., *Antimicrobial Agents and Chemotherapy, 1965*, 1966, p. 947.

[2] Kirby, W. M. M., and Kind, A. C., *Proc. N.Y. Acad. Sci.*, 1967, in press.

Treatment of Mendelson's Syndrome

SIR,—I read with interest the report of a case of Mendelson's syndrome treated with tracheostomy and hydrocortisone (17 June, p. 745). This article indicates yet once again the considerable dangers associated with obstetric general anaesthesia. Pulmonary complications secondary to aspiration of gastric contents before, during, and after obstetric anaesthesia remain an important cause of morbidity and mortality.[1] However, these are largely preventable and treatable. The initial improvement in the patient described by Dr. R. M. Nicholl and his colleagues following intravenous hydrocortisone and oxygen under pressure illustrates the basis of the treatment in Mendelson's syndrome.[2 3] The endotracheal tube was removed prematurely before the pulmonary oedema had been alleviated, and as a result respiratory distress and hypoxia persisted.

Endotracheal intubation (preferably nasal) should have been performed again and continuous intermittent positive pressure ventilation with warmed humidified gases and tracheobronchial toilet instituted. This is an excellent method of reducing dead space in the short-term case. With controlled or assisted ventilation, the pulmonary symptoms and hypoxia exhibited by this patient would have been remarkably improved within hours. The decision to perform a tracheostomy could then have been delayed in the expectation of a rapid improvement in the patient's condition. The drugs used during anaesthesia were not described and could have had a bearing on the management of the case. Arterial blood-gas studies should have been performed (if equipment was available) to determine the oxygen tension and the acid-base status of the patient.

The prevention and treatment of Mendelson's syndrome should be along the following lines:

(1) Recognition that all obstetric patients in labour who are to have general anaesthesia must be regarded as having a full stomach irrespective of the last oral intake of food or drink.[4 5]

(2) Prior to anaesthesia, oral premedication with antacids will reduce the gastric acidity, and therefore the incidence of Mendelson's syndrome will be diminished.[4 6]

(3) Should pulmonary aspiration occur, clearance of the airways is essential. Endotracheal intubation (preferably nasal) should be performed followed by deep suction if respiratory distress ensues.[2 3] Tracheal-bronchial lavage is not advised as dissemination of the acid occurs.[7]

(4) Intermittent positive pressure ventilation with 100% oxygen should be instituted[2 3] and premature removal of the endotracheal tube should be avoided.

(5) Generous hydrocortisone administration, both intravenously and intramuscularly, should be given.[5 8 9]

(6) Bronchodilator drugs may be used to alleviate bronchospasm.[3 5]

(7) Antibiotic coverage is essential in any case of pulmonary aspiration.[10]

(8) Determination of the *p*H of the gastric contents is necessary to estimate the severity of the pulmonary complications. When the *p*H of the aspirated fluid is 2.5 or under, Mendelson's syndrome is likely to occur.[4] The *p*H of the aspirated fluid suctioned from the trachea will give a falsely high value as the bronchial mucosa attempts to neutralize the acid rapidly, by the outpouring of oedema fluid.

Vomiting and regurgitation of stomach contents in the obstetric patient should be regarded as preventable. If pulmonary complications do occur as a result of either of these incidents, rapid and vigorous treatment must be instituted.—I am, etc.,

GORDON TAYLOR.

Stanford University
School of Medicine,
Palo Alto,
California, U.S.A.

REFERENCES

[1] Phillips, O. C., and Hulka, J. F., *Anesthesiology*, 1965, 26, 435.

[2] McCormick, P. W., Hay, R. G., and Griffin, R W., *Lancet*, 1966, 1, 1127.

[3] Thomas, I. D., and Pfanner, D. W., *Med. J. Aust.*, 1963, 1, 134.

[4] Taylor, G., and Pryse-Davies, J., *Lancet*, 1966, 1, 288.

[5] Marx, G. F., *J. Amer. med. Ass.*, 1967, 201, 51.

[6] Mendelson, C. L., *Amer. J. Obstet. Gynec.*, 1946, 52 191.

[7] Bannister, W. K., Satillaro, A. J., and Otis, R. D., *Anesthesiology*, 1961, 22, 440.

[8] Hausmann, W., and Lunt, R. L., *J. Obstet. Gynaec. Brit. Emp.*, 1955, 62, 509.

[9] Marshall, B. M., and Gordon, R. A., *Canad. Anaesth. Soc. J.*, 1958, 5, 438.

[10] Hamelberg, W., and Bosomworth, P. P., *Anesth. Analg. Curr. Res.*, 1964, 43, 669.

What is Psychosomatic Disease?

SIR,—The article by Dr. F. Feldman and others (1 July, p. 14) and your leading article (1 July, p. 1) both raise the general question of the use of the term "psychosomatic disease." If it is merely thought that one factor among many in the aetiology of a disease is sometimes emotional disturbance, it seems a plain misuse of words to describe the disease simply as psychosomatic. This term can be justified only if a disease is invariably —in the words of your leading article—"an illness in which the organic lesions are the consequence of emotional disturbances."

Dermatitis artefacta can properly be called psychosomatic. So, in a special sense, can alcoholic cirrhosis of the liver and even obesity. But none of the diseases which are often alleged to be "psychosomatic," such as colitis, asthma, and duodenal ulcer, warrant that description. Attacks of asthma can surely be precipitated by respiratory infections, by non-specific irritants such as smog, by allergens, or by emotional upsets. The only possible justification, therefore, for claiming that asthma is psychosomatic is that the defect in the bronchioles in asthmatic individuals is itself caused by emotional disturbance. This view can be reached only by faith, not by observation and reason. No doubt in some subjects of duodenal ulcer there is a relationship between the emotional state and the attacks. But attacks often have no discoverable cause. Feldman and others have done a valuable service by revealing the unsatisfactory nature of many of the papers which have purported to demonstrate that ulcerative colitis is psychosomatic.

Even if it were true that psychological factors are all-important in ulcerative colitis this would not justify the belief of the "some physicians" of your leading article who "regard psychotherapy as the mainstay of treatment." The only reason for reaching that conclusion is the existence of objective evidence that psychotherapy is beneficial. Deducing that a remedy must be effective because it follows from a theory of aetiology is one of the great errors made by our profession over the centuries. Trephining the skull (to release the demon), bleeding, starving, purging, eradicating septic foci, and pleating the stomach were all thus justified. —I am, etc.,

Farnham, Surrey. JOHN W. TODD.

Fulminating Ulcerative Colitis

SIR,—Your leading article (22 July, p. 188) rightly draws attention to the importance of an early resort to surgery in fulminating ulcerative colitis. The often lethal complication of colonic perforation is the most important reason for the striking difference in mortality figures when results of emergency surgery and planned surgery in ulcerative colitis are compared. To say, therefore, that surgery is "kept in reserve for failed medical treatment or when there is perforation . . ." is capable of misinterpretation; we need to recognize the pre-perforation state and operate at this earlier time.

The risk of perforation determines not only the timing of surgery but also the type of operation done. The danger in only raising an ileostomy (because the patient is gravely ill) is that the disease is left in situ and perforation can still occur. The best operation, even in the seriously ill patient, is one that removes the colon; the standard subtotal colectomy with ileostomy is the procedure of choice, therefore, even under these conditions. This policy is well borne out by the excellent paper by Professor J. C. Goligher and his colleagues in the same issue (p. 193). —I am, etc.,

T. A. BOXALL.

St. Bartholomew's Hospital,
London E.C.1.

Abdominal Decompression and Foetal Blood Gases

SIR,—In foetuses at increased hazard of death during labour foetal heart rate monitoring and foetal blood collection are used routinely in our hospital. The value and safety of these procedures have been established.[1-3] In many of the foetuses studied where clinical evidence of foetal distress (meconium in the liquor or abnormal foetal heart rate) was present both the subsequent foetal heart rate record and the foetal blood measurements were normal. This routine use of foetal diagnostic methods in the presence of clinical foetal distress presented us with the opportunity of testing the hypothesis that abdominal decompression improves oxygenation of the foetus.[4]

An Emerson Birtheez abdominal decompression suit was used applying a negative pressure of 70–110 mm. Hg. The first five patients were decompressed using the intermittent technique of 15 seconds on, 15 seconds off, for 10 to 35 minutes; the next nine had continuous decompression maintained for 10 to 20 minutes.

Thirteen patients were in the first stage of labour and one was at full dilatation; foetal heart rate was monitored in nine[5] and intra-amniotic pressure in five. All had clinical evidence of foetal distress. Foetal scalp capillary blood[2] was collected before and during abdominal decompression, and in seven of the 14 patients a further specimen was taken five to 45 minutes after stopping decompression. Foetal blood *p*H, Pco_2, and Po_2 were measured in an I.L. 113 Sl ultramicro electrode assembly. (Table I.)

Abdominal decompression did not significantly alter Po_2, *p*H, or Pco_2 (see Table II).

The mean Po_3 change was smaller than the 99% confidence limits of the Po_2 measurements, ±1.2 mm. Hg.[6] Resting amniotic pressure fell during decompression by a mean of 14 mm. Hg (7, 12, 13, 14, and 25 mm. Hg). The foetal heart rate pattern did not change during the experiments—this included two cases with slowing of 20 to 30 beats/min. during contractions. Labour pain was diminished, but several patients complained of discomfort when decompression above 70 mm. Hg was attempted.

Case No. 3 deserves special comment because of the presence of foetal acidosis and hypercapnia. The mother's capillary blood *p*H was normal at 7.43. Abdominal decompression for 35 minutes did not result in any improvement in foetal *p*H, Po_2, or Pco_2. Foetal heart rate recorded after the decompression was normal. The baby was delivered by vacuum extraction and had an Apgar score of six at two minutes. The cord was twice around the neck at delivery. This was the probable cause of the foetal acidosis, and acidosis due to cord compression may not respond to decompression. On the other hand, placental insufficiency due to pre-eclampsia may respond to repeated decompression, as Blecher's results[7] suggest.

This study was stopped after 14 investigations were completed, as it was clear that abdominal decompression produced no increase in foetal scalp blood Po_2. Even if a very large series showed a small but significant increase of foetal blood Po_2 one would not know whether decompression increased general foetal oxygenation or merely improved venous drainage from the scalp. Venous return from the scalp may be improved during decompression by slight elevation of the foetal head and by increasing the venous-pressure difference between the foetal great veins and scalp veins. If such a change occurred it could raise the scalp-capillary blood Po_2 several mm. Hg.

Heyns often uses higher pressures for decompression than those used in the present study (60–150 mm. Hg compared with 60–110 mm. Hg). Also the design of his decompression suit is different from that of the Emerson unit. Apart from these limitations of the present investigations, no evidence was found that during one period of abdominal decompression foetal oxygenation was improved. Of course, the effect of repeated abdominal decompression during the last two months of pregnancy might be different. A reliable way of increasing foetal blood Po_2 is for the mother to breathe 100% oxygen by the CIG polymask or anaesthetic face mask.[6]—We are, etc.,

TABLE I

No.		Po_2	Hb o_2%	*p*H	Pco_2	Base Deficit	
(1)	Baseline	26	57%	7·30	53	−0·7	
	Decompression 20′	13	<20%	7·27	66	−4·7	
	Decompression 23′	21	36%	7·20	59	3·3	
	Off 30′	20	38%	7·27	56	0	
(2)	Baseline	28	63%	7·29	52	1·4	
	Decompression 10′	33	71%	7·30	45	3·2	
	Off 15′	33	73%	7·32	42	3·8	
(3)	Baseline	22	36%	7·17	57	5·7	Acidotic
	Decompression 35′	22	36%	7·17	66	5·4	
(4)	Baseline	21	41%	7·25	38	7·8	
	Decompression 30′	23	47%	7·27	39	6·7	
(5)	Baseline	24	57%	7·35	41	0·5	
	Decompression 20′	26	61%	7·33	41	1·0	
(6)	Baseline	26	58%	7·30	38	5·3	
	Decompression 15′	24	55%	7·30	40	4·3	
(7)	Baseline	26	57%	7·29	47·5	2·7	
	Decompression 15′	32	75%	7·37	37·5	1·9	
(8)	Baseline	20	39%	7·27	50	1·7	
	Decompression 15′	24	46%	7·23	61	2·3	
(9)	Baseline	15	22%	7·26	52·5	1·6	
	Decompression 10′	18	32%	7·29	51	0·0	
(10)	Baseline	26	53%	7·26	46	6·4	
	Decompression 17′	24	51%	7·28	42	5·9	
	Off 5′	23	48%	7·28	42	4·7	
(11)	Baseline	29	63%	7·29	34	7·3	
	Decompression 15′	35	72%	7·26	39	8·6	
	Off 45′	29	63%	7·29	38	5·3	
(12)	Baseline	33	75%	7·35	39	3·0	
	Decompression 20′	31	70%	7·35	43	0·8	
	Off 15′	31	73%	7·36	41	1·1	
(13)	Baseline	26	52%	7·27	—	—	
	Decompression 12′	26	54%	7·26	—	—	
	Off 8′	20	35%	7·25	—	—	
(14)	Baseline	26	58%	7·31	43	2·7	
	Decompression 15′	32	68%	7·32	54	−1·3	
	Off 15′	30	70%	7·37	39	1·2	

TABLE II

	n	Mean Values				
		Po_2	Hb o_2%	*p*H	Pco_2	Base Deficit
Control	21	25·4	54	7·29	44·5	1·9
Experiment	15	25·6	53	7·28	46·6	2·1

J. W. NEWMAN.
E. C. WOOD.

The Queen Victoria
Memorial Hospital,
Melbourne, Australia.

REFERENCES

[1] Wood, C., Ferguson, R., Leeton, J., Newman, W., and Walker, A., *Amer. J. Obstet. Gynec.*, 1967, **98**, 62.
[2] Saling, E., *Arch. Gynäk.*, 1962, **197**, 108.
[3] Hon, E. H., in *Proceedings of the Vth World Congress of Obstetrics and Gynaecology* (to be held September 1967), Sydney.
[4] Heyns, O. S., *Abdominal Decompression*, 1963. Johannesburg.
[5] Hon, E. H., *Conn. Med.*, 1960, **24**, 289.
[6] Newman, J. W., McKinnon, L., Phillips, L., Paterson, P., and Wood, C., *Amer. J. Obstet. Gynec.*, in press.
[7] Blecher, J. A., *S. Afr. med. J.*, 1965, **39**, 960.

Lyell's Toxic Epidermal Necrolysis

SIR,—The aetiology of toxic epidermal necrolysis (Lyell's disease, scalded-skin syndrome) is unknown but several agents have been implicated. In adults there often is a close association with drug ingestion, whereas in children bacterial infection seems to be relevant. Dr. J. Jefferson (24 June, p. 802) has demonstrated a high incidence of *Staphylococcus aureus*, especially phage type 71, among his 31 cases occurring in infants and children, and has suggested that the primary skin lesion could be caused by a toxin elaborated by this organism. Other authors also have observed this association.[1] Furthermore, Ritter's disease of neonates, which closely resembles Lyell's disease, has yielded a high incidence of the staphylococcus of phage types 3B/71[2] or 55/71.[3] The relationship of these Group 2 bacteria to the lesions of Lyell's disease was recently the subject of a short editorial.[4]

With such observations in mind I have reviewed the clinical records of four typical cases of histologically confirmed Lyell's disease. Cases 1 and 2, which proved fatal, have been previously reported.[5] Subsequently Cases 3 and 4 have been successfully treated at the Royal Perth Hospital.

All were elderly females. There was no instance of a clearly defined relationship between ingestion of drugs and the onset of the skin syndrome. Shortly after admission Case 1 manifested a urinary infection from which *Staphylococcus aureus* was cultured in significant numbers. At necropsy in Case 2 a lung abscess caused by *Staphylococcus aureus* was revealed. Histologically the wall of this abscess was undergoing organization and therefore was probably developing at the time of onset of the skin disease some 10 days previously. The skin lesions, which in both the above patients had been treated before admission to this hospital, were sterile. Sections of skin taken at necropsy, however, showed numerous organisms, including clumped Gram-positive cocci. In the third and fourth patients, who recovered after five and nine weeks respectively, skin swabs taken on admission grew abundant *Staphylococcus aureus.*

Further studies concerning grouping and phage-typing of these organisms were not undertaken. Nevertheless, the incidence of the suggested pathogen in all four patients may be of some significance. It points to a possible common denominator in the disease of infants, children, and adults and suggests that the presence of *Staphylococcus aureus* should be sought, in future, when the diagnosis of toxic epidermal necrolysis is made.—I am, etc.,

KEITH B. SHILKIN.

Department of Pathology,
Royal Perth Hospital,
Perth, Western Australia.

REFERENCES

[1] Lowney, E. D., Baublis, J. V., Kreye, G. M., Harrell, E. R., and McKenzie, A. R., *Arch. Derm.*, 1967, 95, 359.
[2] Rycheck, R. R., Taylor, P. M., and Gezon, H. M., *New Engl. J. Med.*, 1963, 269, 332.
[3] Benson, P. F., Rankin, G. L. S., and Rippey, J. J., *Lancet*, 1962, 1, 999.
[4] *J. Amer. med. Ass.*, 1967, 200, 547.
[5] Shilkin, K. B., and Muston, W. B., *Aust. J. Derm.*, 1966, 8, 219.

Warning of Massive Pulmonary Embolism

SIR,—The paper by Dr. M. A. Barraclough and Mr. M. V. Braimbridge (28 January, p. 217) of a successful surgical removal of a massive embolism in a nurse, and the subsequent letter by Dr. J. S. Short (20 May, p. 510), underline several important points. I heartily endorse Dr. Short's statement that an early diagnosis at the time of the usual "warning embolus" is not difficult, but often wanting. Pulmonary embolism, with or without infarction, is a common and potentially fatal disease. In addition to the commonly recognized associations, such as bed rest, obesity, and pregnancy, it can occur in apparently healthy young adults.[1, 2]

There are many excellent papers, leading articles,[3] and letters[4] on the subject, but patients undoubtedly still die because of misdiagnosis and failure to institute immediate anticoagulant therapy. Surgical removal of massive pulmonary emboli, thrombectomy, and partial vena cava obliteration should now be possible in most major general hospitals.[5, 6] Many of these patients need never reach the operating-theatre if a correct early diagnosis had been made in the patient with faintness, syncope, transient cerebral ischaemia ("vasospasm"), "unexplained" dyspnoea, "pleurisy," and "recurrent or unresolved" pneumonia. Such patients need not have any definite signs in arms, legs, or elsewhere.

The current controversy about the relation of venous thrombosis and oral contraceptives may, perhaps, help to raise the general index of suspicion.—I am, etc.,

W. G. SMITH.

Sir Charles Gairdner Hospital,
Shenton Park 6008,
Western Australia.

REFERENCES

[1] Fleming, H. A., and Bailey, S. M., *Brit. med. J.*, 1966, 1, 1322.
[2] Loehry, C. A., ibid., 1966, 1, 1327.
[3] Ibid., 1966, 1, 1129.
[4] Marquis, R. M., ibid., 1966, 1, 1480.
[5] Ibid., 1966, 1, 183.
[6] Stansel, H. C., Hume, M., and Glenn, W. W. L., *New Engl. J. Med.*, 1967, 276, 717.

"Swallowed" Endotracheal Tube

SIR,—In the medical memorandum by Mr. J. A. S. Dickson and Mr. G. C. Fraser (24 June, p. 811) "Swallowed Endotracheal Tube," and in the subsequent correspondence, one most important point has not been sufficiently emphasized. All the babies recovered despite the iatrogenic efforts to prevent resuscitation. This must mean that these neonates were not really in need of intermittent positive pressure respiration via an endotracheal tube, except possibly the case reported by Mr. M. G. Prinn (15 July, p. 176).

Your correspondents insist on the need for training of junior obstetric staff in endotracheal intubation. To me this seems to be putting the cart before the horse. These junior staff should first of all be taught the difference between the neonate who merely requires what might be called primitive but time-honoured methods of resuscitation plus a good deal of patience, and the infant in need of all the most sophisticated techniques available. In the latter case the young doctor should be able to call on specialized experienced help.

If junior medical staff are taught sophisticated techniques without also being given considerable practical tuition in selection of the correct type of case on which to use these techniques, then serious, possibly tragic, accidents will occur. This is an aphorism by no means confined to obstetric anaesthesia.

The nub of the problem lies in the last words of Dr. R. A. Binning's letter (8 July, p. 111) ". . . a neonate which is *really* in need of intubation"—the italics are mine.—I am, etc.,

Royal Hospital,
Chesterfield.

H. E. POOLER.

SIR,—I find myself in complete agreement with Dr. J. V. I. Young (22 July, p. 242) in his contention that the routine use of endotracheal intubation in the presence of neonatal asphyxia is wrong. The indiscriminate passage of an endotracheal tube, I believe, comes under the heading of "meddlesome midwifery."

In the absence of obstruction due to mucus, meconium, etc., the passage of an endotracheal tube, owing to its cross-section acting as a foreign body in the lumen of the trachea, actually impairs the airway instead of improving it. It would be interesting to know the result of a long-term follow-up done to show whether the damage done to the delicate mucous membrane of a baby's vocal cords persists into adult life.

Intubation in the presence of neonatal asphyxia should be performed only when the child fails to respond to oxygen given by face-mask and gentle pressure on the rebreathing bag.—I am, etc.,

London W.1.

MASSEY DAWKINS.

Intrauterine Contraceptive Devices

SIR,—Over 35,000 intrauterine devices have now been inserted at the 170 clinics of the Family Planning Association so far approved for this purpose. Usually the device has been a Lippes loop, but some Birnberg bows and Saf-T-Coils have been fitted.

Analysing a large international series, Tietze[1] reports that the Lippes loop escaped through the uterine wall in about 0.04% of cases—usually without any apparent harm to the patient. We have not yet heard of the uterus being perforated during or after insertion of an I.U.D. in one of our clinics, but this has almost certainly happened from time to time. We should be grateful if gynaecologists would let us know of any such cases that have come to their notice—or may do so in the future.—We are, etc.,

HILARY HILL,
Medical Secretary.

SARA R. ABELS,
Assistant Medical Secretary.

Family Planning Association,
London W.1.

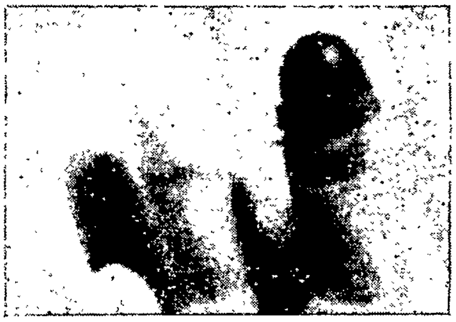
REFERENCE

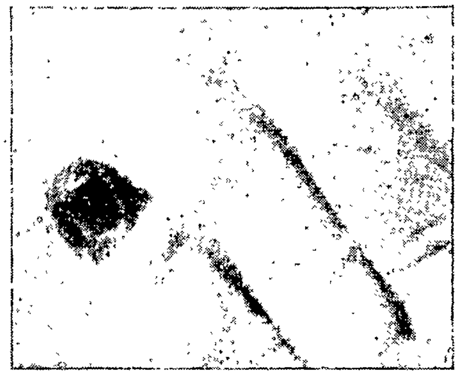
[1] Tietze, C., *Amer. J. Obstet. Gynec.*, 1966, 96, 1043.

Hazard from Nylon

SIR,—The following case report illustrates the danger of using nylon fibre in babies' clothing.

A 7-day-old infant had mittens of knitted nylon fibre "wool." Some hours after these had been put on by her mother they were removed to reveal that a piece of nylon fibre from the inside of the mitten had formed a tight constricting band round the tip of the middle finger just distal to the terminal interphalangeal joint. The tip of the finger (see photographs) was black and obviously ischaemic.





A similar band had formed round the middle finger of the other hand, but fortunately had not produced ischaemia.

My thanks are due to Mr. R. L. Lewis, Consultant Surgeon, Haverfordwest, for his help and advice with the case.

—I am, etc.,

Haverfordwest,
Pembrokeshire.

G. G. NOOTT.

Nalidixic Acid and Intracranial Hypertension

SIR,—Following the report of Drs. L. O. Boréus and B. Sundström (17 June, p. 744), I should like to record another case of intracranial hypertension in a child during treatment with nalidixic acid.

A male infant, born with ectopia vesicae and epispadias, was admitted to hospital at 9 weeks of age for corrective surgery. At 7 months of age, eight weeks after his discharge from hospital, the infant was given nalidixic acid 250 mg. four times a day for a presumed urinary infection, as he seemed to have colic and had made a poor weight gain. Three days later the infant began to vomit his feeds and became irritable. The following day he continued to vomit, cried incessantly, and was noticed to have a bulging fontanelle. On admission to hospital the infant was considerably underweight, being only 11 lb. 3 oz. (5.1 kg.). The anterior fontanelle was tense and bulging, the scalp veins were prominent, but there was no neck stiffness and Kernig's sign was negative. The head circumference was 16½ in. (42.1 cm.) and the chest circumference was 16 in. (40.9 cm.). Although irritable and crying, the infant was afebrile and alert, there was no infection of the ears, nose, or throat, and the fundi and all other systems were normal except for the surgical procedures previously undertaken for the congenital abnormalities. In view of the raised intracranial pressure a subdural tap was performed and C.S.F. was obtained. It contained 1,600 R.B.C., 14 W.B.C., 4 polymorphonuclear leucocytes, 10 lymphocytes, glucose 50 mg., protein 30 mg., and was sterile on culture. Nalidixic acid therapy was immediately discontinued. Additional investigations showed a white blood count of 11,500 with 42% polymorphonuclear leucocytes and 58% lymphocytes, blood urea 41 mg./100 ml., serum sodium 148, chlorides 109, and potassium 4.9 mEq/l. A blood culture was sterile and the urine contained numerous pus cells and *Escherichia coli*. *X*-ray of skull showed slight separation of the sutures.

Following the "subdural" tapping the fontanelle was less tense, the baby became less irritable, and the vomiting ceased. Within four days the tension was normal and the infant had returned to a happy and contented state. Ampicillin 125 mg. six-hourly was given during this period for the urinary infection, but as the organism proved to be resistant to this drug nitrofurantoin 15 mg. six-hourly was substituted.

Seven days later, when the infant was feeding well and beginning to gain weight, a further course of nalidixic acid in the same dose, 250 mg. six-hourly, was given and within 48 hours there was definite increase in tension and bulging of the anterior fontanelle with prominence of the scalp veins. The following day the infant was irritable, and in view of the obviously raised pressure the drug was withdrawn; three days later the fontanelle tension had returned to normal. At this time his urine still contained *E. coli*, now insensitive to nitrofurantoin but sensitive to ampicillin, so this was substituted in dosage of 125 mg. six-hourly. During the next six weeks the infant fed well and gained 3½ lb. (1.6 kg.) in weight. He was therefore discharged home on a maintenance dosage of ampicillin 125 mg. 12-hourly and has remained well on follow-up.

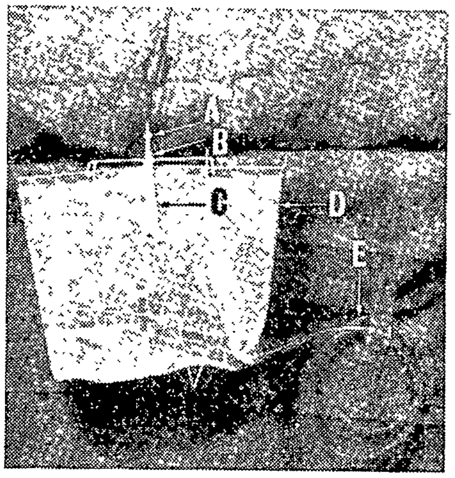
In the present case the dosage of nalidixic acid prescribed for the infant was twice the recommended one of 100 mg. per kg. body weight per day, and this was used in the second course to see if the condition could be reproduced. As headache and vomiting have been reported as side-effects of nalidixic acid therapy, the possibility of raised intracranial pressure should be considered if such symptoms are severe or prolonged. In view of the increasing use of nalidixic acid in infancy and childhood, this complication, especially if larger than normal dosage is used, should be appreciated, as a bulging fontanelle in the infant has serious implications and presents a difficult problem in differential diagnosis.—I am, etc.,

O. D. FISHER.

St. Bartholomew's Hospital,
Rochester, Kent.

Disposable Drainage Bag for Peritoneal Dialysis

SIR,—Drainage of the peritoneal cavity during dialysis poses the same problems in asepsis as closed drainage of the bladder, and standard urine collection bags are sometimes used for the purpose. The emptying of these bags every hour provides a useful opportunity to confirm that each cycle has drained adequately and to check fluid balance, but it involves at least 24 disconnexions of the drainage circuit per dialysis, with the inevitable risk of introducing infection. We have therefore adapted the Aldon urine collecting bag[1] to provide unbroken closed drainage while retaining the advantage of an hourly check on drainage and fluid balance.



The bag shown in the accompanying Figure is supplied sterile by Aldington Laboratories, Aldington Frith, Mersham, Ashford, Kent, at a price that makes it readily disposable. It incorporates the following features:

(A) Female Luer connector which accepts the Dialaflex peritoneal dialysis set (Allen and Hanburys) as illustrated.

(B) Short connecting tube. When this is cut aseptically below the Luer connector it will accept the Plexitron R 61 L peritoneal dialysis set (Baxter Laboratories).

(C) Non-return valve consisting of a length of soft plastic tubing. This is very effective in preventing reflux of fluid during emptying of the bag, but small air bubbles occasionally slip past it. It is therefore advisable to clamp the drainage arm of the peritoneal dialysis set just above the bag during emptying operations as an additional safeguard. Kinking of the plastic tube—which is easily seen and corrected without disconnexion of the bag—has obstructed drainage on one or two occasions.

(D) Bag of capacity about 3.2 l.—sufficient for a single drainage cycle even during dehydration with hypertonic fluids.

(E) Four foot (1.2 m.) drainage tube for emptying bag. This is closed by a spigot which can be discarded and replaced by a haemostat on the tube if preferred.

The bag is made of strong plastic which withstands repeated distension and emptying—in over 100 dialyses we have not encountered a "burst." It does not have the volume graduations found on urine collecting bags, since these graduations are not sufficiently accurate for fluid balance during peritoneal dialysis and they become more inaccurate after the bag has been refilled several times. The volume can be measured accurately in a 4 l. polypropylene measuring cylinder. If it is essential to avoid spilling peritoneal fluid (e.g., if the patient has hepatitis) the long drainage tube (E) can be connected to a stoppered 20 l. jerrycan mounted on a patient-weighing scale.—We are, etc.,

G. DOUGLAS.
D. N. S. KERR.
M. R. PEARSON.

Department of Medicine,
Royal Victoria Infirmary,
Newcastle upon Tyne.

REFERENCE

[1] Gonzales, E. B., *Brit. med. J.*, 1966, 1, 24

Fenfluramine

SIR,—I was very interested to read the account in "Today's Drugs" of our product fenfluramine (Ponderax) (15 July, p. 159). I would, however, like to bring to your attention two points on dosage and cost.

We recommend an adult dose of two tablets a day. In refractory obesity[1] the dosage employed was four tablets a day, and this higher dosage explained why there was a higher incidence of side-effects than normal. We regard this flexibility of dosage as being very important in the management of obesity.

As from 1 May 1967 the basic N.H.S. cost of 100 tablets was 35s., and there is of course considerable saving on packs of 500 and 1,000 tablets.—I am, etc.,

A. BOIS,
Managing Director.

Selpharm Laboratories Ltd.,
London W.1.

REFERENCE

[1] Munro, J. F., Seaton, D. A., and Duncan, L. J. P., *Brit. med. J.*, 1966, 2, 264.

Screening for Cervical Cancer

SIR,—In your leading article (24 June, p. 782) it was suggested that the results of routine cervical screening have been disappointing, on the basis of a report that the incidence of invasive carcinoma of the cervix has remained virtually unchanged,[1] in spite of the detection of large numbers of pre-invasive lesions. But it has been the general experience that many unsuspected cases of early invasive carcinoma, as well as carcinoma-in-situ, are brought to light by a screening programme, so the incidence of invasive carcinoma may be expected to remain virtually unchanged, or even to rise at first.

In the comprehensive survey in British Columbia[2] the incidence of invasive carcinoma per 100,000 females was 3.4 and 3.5 in those who had had previous cervical smears, and 32.3 and 24.1 in those who had not been included in the screening programme. These impressive differences occurred 13 and 14 years after the initiation of the mass screening programme.

There have been several references recently[3-6] to the fact that no major reduction in mortality from carcinoma of the cervix has been shown to result from a screening programme. But a reduction in mortality caused by the elimination of carcinoma-in-situ from a population would not become evident for approximately 20 years after the introduction of a mass screening programme (allowing 10–15 years for carcinoma-in-situ to progress to invasive carcinoma, and another 10 years or so before this resulted in death). As few screening programmes started much before 1950, these data cannot yet be available. As mentioned in your leading article, figures from Montreal, where screening was started in a small way in 1945, show a considerable increase in five-year survival rates in carcinoma of the cervix, and this is attributed directly to cytology screening.

Though many questions concerning cervical cytology are so far unanswered, or unanswerable, it is to be hoped that efforts to continue the screening of all adult women should not be prejudiced.—I am, etc.,

NORA SPENS.

Department of Clinical
Pathology,
Southampton General Hospital,
Southampton.

REFERENCES

[1] Green, G. H., *J. Obstet. Gynaec. Brit. Cwlth*, 1965, 72, 13.
[2] Bryans, F. E., Boyes, D. A., and Fidler, H. K., *Amer. J. Obstet. Gynec.*, 1964, 88, 898.
[3] Franks, L. M., *Brit. med. J.*, 1967, 1, 498.
[4] Boyd, J. T., Gibbs, D. F., Labrum, A. H., and Philps, F. R., Ibid., 1967, 2, 785.
[5] Knox, E. G., *Int. med. Trib.*, 1966, 1, No. 26, p. 9.
[6] Cochrane, A. L., ibid., 1967, 2, No. 18, p. 1.

Coroners' Jurisdiction

SIR,—In his letter (24 June, p. 845) Dr. Ivor M. Jones claims that my letter (3 June, p. 642) was "seriously misleading," and then proceeds to give an account of the facts which is a masterly example of *suppressio veri*. I maintain that "Deaths in the Community" was produced in 1963 by the Forensic Subcommittee, before the Brodrick Committee was set up in 1964. It was received by the Central Consultants and Specialists Committee, but not accepted. It may also be true that the General Medical Services Committee also never considered it in detail.

The answers to the questionary sent to the Association by the Brodrick Committee were given by the Forensic Subcommittee without consultation with the C.C. and S. Committee and also, I believe, with the G.M.S. Committee. Neither these answers nor the evidence to be given to the Brodrick Committee were ever published and were not known to the large majority of consultants and general practitioners.

The Forensic Subcommittee consists of three pathologists, three police surgeons, three general practitioners, and the Secretary of the Coroners Association, but no representative of consultants in general medicine, surgery, obstetrics, or hospital administration.

It was only a few days before oral evidence was to be given to the Brodrick Committee that Dr. Ivor Jones was pressed to accept a representative of the C.C. and S. Committee, and then agreed only "on the understanding that it would not be possible to depart from the general tenor of the evidence which had already been submitted to the Brodrick Committee."

The C.C. and S. Committee took note of this situation and sent my memorandum to the Brodrick Committee.

The Forensic Subcommittee, by virtue of its composition and the autocratic way in which it acted, lays itself open to a charge of special pleading. The members of the Association should have been given the opportunity of deciding whether they would continue to support the present systems of coroners' jurisdiction or would prefer a system similar to the procurator fiscal in Scotland.—I am, etc.,

London W.1. H. A. KIDD.

Aversion Therapy of Homosexuals

SIR,—Dr. M. J. MacCulloch and Dr. M. P. Feldman (3 June, p. 594) state: "The rate of improvement achieved by experienced psychotherapists in comparable series of homosexual patients has in no instance exceeded 27% (Bieber *et al.*, 1962). In our opinion the approximately 60% rate of improvement achieved in our series is mainly due to the use of an aversion therapy technique. . . ."

The 27% statistic refers to the 29 cases in our series of 106 psychoanalytically treated male homosexuals who became exclusively heterosexual. A valid comparison may be made between the group that shifted to exclusive heterosexuality—and only these cases—and the 13 recovered cases (30%) in the authors' series. In our study an additional 16 cases (15%) became actively heterosexual though not exclusively so, bringing the total rate of improvement as judged by sexual status to 42%. In the authors' series seven cases were heterosexual though not exclusively so, bringing their total rate of improvement to 46%, a statistic similar to our own findings. However, the other five cases they list as improved sexually would not be so considered by our criteria. "Two were mixing socially with females and were beginning to approach active heterosexual practice. . . . Three out of the five were improved in the homosexual area and were using strong heterosexual fantasy." The large majority of male homosexuals in the United States, and all the patients in our study, mix socially with females. This does not indicate an ability to have a sexual or romantic relationship with a woman. Nor are heterosexual fantasies, wishes, or beginning approaches to women considered by us to be reliable indicators that a shift in actual sexual behaviour will occur.

The statistics available to MacCulloch and Feldman as reported in our volume,[1] represented the sexual status of 106 patients as of June 1960. In February 1965 I conducted a follow-up study reported at the annual meeting of the American Psychiatric Association on 6 May 1965. Data on the sexual status of 79 of the original 106 cases were obtained. At the outset of treatment 68% had been exclusively homosexual, 28% were bisexual, and 4% were inactive sexually. In February 1965 39% were exclusively homosexual, 21% were bisexual, 34% were exclusively heterosexual, and 6% were inactive. Of the 29 patients who had become exclusively heterosexual as of June 1960 information on 15 was obtained. Of these men 12 had remained exclusively heterosexual for a minimum of five years, while the other three had experienced occasional homosexual episodes during periods of stress, but were married and predominantly heterosexual. There were seven additional patients reported as exclusively heterosexual in 1965 who had not yet become so in June 1960.

The authors state that 30 of their 43 cases had no abnormal psychogenic development. This evaluation is not in accord with our data, where in each of the 106 cases gross psychogenic development and a psychopathological current adaptation were easily discernible. Further, I have personally interviewed at least 200 male homosexuals since the research study and in all instances there were notable disturbances in development as well as in the current life situation. The paucity of data on abnormal aspects of development may reflect the same sort of psychiatric naiveté that, regrettably, is also shown by the authors' use of a simplistic personality typology which includes categories such as "self insecure," "weak willed," "attention seeking."

In developing a relatively new treatment technique the authors would do well to report results factually and in greater detail. Many questions remain unanswered—a primary one being, how many of the 24 cases who had been practising homosexuals for ten years or longer were among the 13 cases who became exclusively heterosexual? We shall await the results of a longer follow-up period with interest before drawing any conclusions about the long-term effectiveness of aversion therapy for long-term homosexuals.—I am, etc.,

IRVING BIEBER.

New York Medical College,
New York City, U.S.A.

REFERENCES

[1] Bieber, I., *et al.*, *Homosexuality. A Psychoanalytic Study*, 1962. New York.

Self-expulsion of a Nasal Polypus

SIR,—A man of 70 presented me with a small container, explaining that he had expelled the contents from his nose that morning. It had been accompanied with a mild cough and only very slight epistaxis. On opening the container I found the mass to be a fairly typical nasal polypus, pearly greyish pink in colour and the size of a brazil nut. It had a jelly-like consistency, with one thin lateral blood vessel. It was not freely supplied with blood vessels as is common with polypi and there was no evidence of the existence of a pedicle. I did not find much muco-pus, and examination of the nasal fossae revealed clean mucous membrane and a free airway.

This in my experience is the first occasion of the self-expulsion of a nasal polypus (or it might be the less common papilloma ?). Incredibly, he had no previous symptoms of any nasal obstruction. My patient had unknowingly at the time saved himself from the nuisance of having to undergo a polypectomy.

I write about this case to inquire whether this in fact is indeed a much more common occurrence than has hitherto been realized, and I would be happy to be enlightened by readers who have had similar cases.—I am, etc.,

Woodford Wells,
Essex. BENJAMIN GREEN

Muscle Stiffness and Vitamin C

SIR,—Dr. I. H. Syed's regimen for the prevention and treatment of muscle stiffness following unaccustomed exercise (30 July 1966, p. 304) has also been assessed in a small double-blind trial, which, like that of Drs. J. L. Corbett and A. Barr, reported in your columns recently (8 July, p. 113), has demonstrated no effect.

Seventy-eight young students at a Scottish police college were subjected to a vigorous 50-minute bout of physical exercises under the supervision of an instructor, whose experience was that such a stint invariably produced severe stiffness and discomfort in a majority of his victims the following day. It was decided, therefore, to make the trial period short and compare the effect of ascorbic acid and lactose only on the condition of the subjects the morning following the exercise and later on in the day.

Tablets containing 100 mg. sodium ascorbate or lactose (flavoured with small amounts of bicarbonate to render them indistinguishable from the ascorbate on chewing) were randomly allocated with instructions to take 5 tablets one hour before the exercise and 4 tablets immediately after. Subjects were only required to fill in a simple questionary. The following morning each recorded the degree of muscle stiffness, if any. Those who had recorded stiffness or discomfort took a further 800 mg. of vitamin C over a period of six hours, recording whether the stiffness subsequently wore off or not.

Analysis of results showed that 40 subjects (35 male and 5 female) had ascorbate and 38 (35 male and 3 female) had lactose. Average age of the two groups was 22.8 and 23.7 years. Although the *degree* of muscle stiffness had been recorded, this purely subjective classification was in fact ignored in the final analysis, as it was felt to be unreliable. No significant differences were demonstrated between the two groups in respect of either "morning after" discomfort or the subsequent six-hour trend.

The trial was carried out with the most helpful co-operation of Col. R. C. Robertson-MacLeod, Commandant of the Police College, and the on-the-spot practical assistance of Sgt. Duff, to whom, together with the students who willingly volunteered, I am most grateful.—I am, etc.,

N. T. POLLITT.

Vitamins Ltd.,
London W.6

SIR,—We were interested to read the comments (8 July, p. 113) by Drs. J. L. Corbett and A. Barr, as we too have recently completed a small trial to assess the value of ascorbic acid in relieving the muscular pain of unaccustomed physical exercise. The trial was designed so that one of us (P. T. L.) received an oral dose of either ascorbic acid (1 g.) or placebo. These were randomly distributed and given immediately before severe exercise. The following day the subject was asked to state whether he thought he had taken the placebo or vitamin, on the basis of the effectiveness in prevention of muscle stiffness. The test was performed 12 times at weekly intervals. Nine out of the 12 doses were correctly assessed, but the ratio of 9 correct to 3 incorrect is not statistically significant.

Thus our findings are in line with those of Drs. Corbett and Barr, indicating the ineffectiveness of large doses of ascorbic acid in preventing muscle pain after exercise.—We are, etc.,

P. T. LASCELLES.
D. DONALDSON.

Department of Chemical
Pathology,
National Hospital,
Queen Square,
London W.C.1.

Difficult Knee-jerks

SIR,—It is occasionally difficult to elicit a knee-jerk that is not absent. The following tip has been found useful.

The patient sits on the couch with his legs dangling but not touching the floor. Place a hand under the big toe (preferably unshod) and ask him to press it firmly on to your resisting hand; now tap the ligamentum patellae.—I am, etc.,

C. B. FRANKLIN.

Newcastle,
Staffordshire.

The Wheel Turns

SIR,—It would seem that the application of cold water is hailed as the most modern first-aid treatment for burns. Past treatments have led us through the days of vinegar, rum, olive oil, tea infusions, carron oil, tannic acid, and many more up-to-date medicaments till, at last, we have found cold water. But could it be that there are some Rip van Winkles among us who have regained consciousness at last and are talking?

The following quotation from a textbook on surgery may be of interest.[1] It is taken from Chapter V, page 441, entitled "Of Burns." The heading reads: "Sect. II. Of the treatment of burns by the application of cold.

"The means recommended by Sir James Earle consist in the speedy application of cold water, or water cooled by ice, which is to be renewed as often as it becomes warm. The cuticle of the burnt or scalded part is not to be removed; all stimulant and oily applications are to be avoided. By this means, he says, the cure will be accomplished without leaving scars or lameness of the part."

Sir James goes on to point to the advantages of this form of treatment which followed in cases under his care.—I am, etc.,

C. W. A. EMERY.

St. Annes-on-Sea,
Lancashire.

REFERENCE

[1] *The Edinburgh Practice of Physics, Surgery and Midwifery,* 1803. London.

Gluten-free Diets

SIR,—I was very interested to read the letter from Dr. R. F. Fletcher and Miss Cathryn E. A. Hood (13 May, p. 445). The National Pharmaceutical Union has in voluntary membership approximately 11,500 (over 96% of the total) of "private" retail pharmacies in the United Kingdom, and recent experience in our information department, which supplies information on a very wide range of subjects to N.P.U. members, has shown that there is an increased demand for information about gluten-free flour and products. That such information is being sought is a clear sign that N.P.U. members are taking particular interest in patients who need gluten-free flour and biscuits. I was therefore concerned to see that these two groups of products were mentioned in the letter as being available from branches of a large multiple pharmacy. This gives the impression that the products are not available from "private" pharmacies, and this certainly is not the case in our experience.—I am, etc.,

J. WRIGHT,
Secretary.

The N.P.U. Group,
London N.14.

Carcinogenicity of Tobacco and Tobacco Smoke

SIR,—Numerous laboratories have shown that tobacco smoke condensates and extracts of tobacco are carcinogenic when applied to the skin of mice and rabbits; they induce papillomas and carcinomas. These findings have been regarded as another piece of evidence in the case against cigarette-smoking. It has been argued that any agent that can produce cancer in an animal can do so in man. Epidemiological experience on a global scale in the only test animal of any real consequence—namely, man himself—does not, however, support this. Is it not surprising, and indeed significant, that among the millions of tobacco-stained fingers that have been continually contaminated with tobacco smoke condensates and tars in heavy cigarette smokers (20 cigarettes and more per day for 20 years or more) that not a single instance of "cigarette-smoker's finger" (papilloma or carcinoma) has ever been seen or reported? As not all heavy cigarette smokers develop lung cancer, does not this argue for some other essential factor, besides cigarette smoke, for the evolution of malignant disease in any particular heavy cigarette smoker?—I am, etc.,

M. GLASS.

Medical Centre,
Cape Town,
Republic of South Africa.

Unexpected Foreign Bodies

SIR,—I have great sympathy with Dr. G. B. Stein (1 July, p. 51), his patient, and the hospital staff concerned. Mr. Derek Stafford and I are just completing a survey of cases where foreign bodies have been swallowed or inhaled in Scotland, Wales, Ulster, Eire, and England in 1964. In 1936 Chevalier Jackson reviewed the 3,612 cases he had treated during the preceding 20 years.[1] In our small series the objects are just as bizarre, but the cases involving dentures are more complicated, since the object cannot usually be seen on *x*-rays. Dr. Stein's castigation of dangerous dentures is quite justified and all the more remarkable since so little attention has been paid to the very many articles, reports, and letters on this subject. Certainly the practitioners and dental laboratory technicians can be blamed for not using a readily available radio-opaque dental plastic; but the blame rests also with teachers of prosthetics in dental schools and the advisers to the British Standards Institute and the Minister of Health. Perhaps the importers and manufacturers of toys will give a lead by insisting on using radio-opaque materials.—I am, etc.,

WARREN HARVEY.

Glasgow Dental Hospital
and School,
University of Glasgow.

REFERENCE

[1] Jackson, C., and Jackson, C.L., *Diseases of the Air and Food Passages of Foreign Body Origin,* 1936. Philadelphia and London.

Policlinic: Medical Teaching at the Bedside

SIR,—I enjoyed the middle article, "A Look at Swedish Medicine and Neurology," by Dr. Bryan Ashworth (6 May, p. 367). But, though he is writing about Sweden, his use of the word "polyclinic" raises a question of nomenclature with which we in English-speaking countries may have to concern ourselves. The related word "policlinic" is beginning to be heard in this country, and "polyclinic" is sometimes written when "policlinic" is meant; both are entertainingly discussed s.vv. in the *Oxford English Dictionary,* 1909, volume VII.[1]

It is evident that Dr. Ashworth is referring to a city (πόλις) or outpatients' clinic that is headed by consultants, a "policlinic" (in Swedish, as in German, "poliklinik"), and not to a clinic for the diagnosis and treatment of diseases of many (or all) kinds (πολύς, κλίνη). Nowadays, if not quite in Jonathan Hutchinson's time (vide the dictionary, which quotes his definition), the name "polyclinic" would suggest a general practitioner's surgery or dispensary; and, since no practitioner or group of practitioners is likely to have any use for it, should we not ban it? And should we not resist any move to call an outpatients' department a "policlinic"? If we wished to confound patients and staff alike and upset *The Times*, as Jonathan Hutchinson did (vide the dictionary's quotation from the issue of 16 December, 1898), we could of course call that part of it staffed by resident or junior doctors whose duty it is to send patients to the appropriate part of the "policlinic" a "polyclinic." It might then seem odd to *The Times* that titles, whatever they have "come to denote," should be chosen which suggest that the sick rise from their various beds in order to occupy a communal one provided by the city.—I am, etc.,

Peppermint Grove, Western Australia. GERALD C. MOSS

REFERENCE

[1] *A New English Dictionary*, 1909, ed. J. A. H. Murray, Oxford.

Local Government Reform and the Health Services

SIR,—Since Miss Elizabeth Burney's article (1 July, p. 41) I have been scanning the columns of your journal in order to see if any of my colleagues in the public health service, whom I felt sure would be able to draft a far better letter than I could do myself, had seen fit to reply. After an interval of three weeks a letter has at last appeared, from the pen of Dr. P. O. Nicholas, of Bolton (22 July, p. 239), and I can only endorse the general tenor of his remarks.

When one has spent a not inconsiderable proportion of one's own, albeit relatively short, medical lifetime in acquiring experience and knowledge in order to be the better able to administer the community health services, one does indeed wonder who are these "others" who are going to guide these selfsame services.

I would venture to say that many of my colleagues, who have been similarly engaged in the same pursuits as myself, would seriously question the soundness of further fragmenting these services and the suitability of anyone else to run them in a sufficiently realistic and understanding manner.—I am, etc.,

Shire Hall, Cambridge. PETER SYLVESTER.

Annual Representative Meeting

SIR,—May I endorse Dr. J. D. Shapland's letter concerning the Annual Representative Meeting? It is deplorable that a limited number of "microphone hogs" were allowed to take up the time of the A.R.M. over details which should have been thrashed out elsewhere. This sort of thing has been progressively more noticeable over a number of years, and I am disgusted at the way hospital matters are rushed through in the last hours of the meeting. What hope is there of getting a better deal for hospital doctors? As far as I am concerned the A.R.M. has fallen into disrepute and only drastic reforms will restore its reputation.—I am, etc.,

Epsom District Hospital, Epsom, Surrey. E. N. CALLUM.

*** The Secretary of the B.M.A. states: The Chairman of the Central Committee for Hospital Medical Services has decided to call a special meeting of his Committee in order to debate the motions under "Hospital and Consultant Services" which were not debated at the A.R.M. at Bristol. The Divisions that proposed the motions will be invited to send representatives to the meeting.—ED., *B.M.J.*

Degrees of Seniority

SIR,—Senior hospital medical officers will welcome the news that the Central Consultants and Specialists Committee has agreed to support the resolution from the S.H.M.O. Group Executive Committee that in the event of any future pay award to medical assistants the existing differential between the salary scales of the S.H.M.O. grade and the medical assistant grade should be maintained (*Supplement*, 15 July, p. 67).

The reason for this resolution should be made clear—namely, that senior hospital medical officers are recognized as of senior status with duties and responsibilities above those of medical assistants, the latter being responsible to named consultants and of intermediate grade (H.M. (67) 26).—I am, etc.,

NORMAN V. WILLIAMS.

Cefn Mably Hospital, St. Mellons, Nr. Cardiff.

B.M.A. as a Negotiating Body

SIR,—The Representative Body at Bristol debated for two hours on Saturday morning, 8 July, a dispute with the Junior Hospital Doctors Association (22 July, *Supplement*, p. 69). It was revealed in the debate that the J.H.D.A. had previously published actionable matter about B.M.A. negotiations, but neither had action been taken against the J.H.D.A., nor, apparently, had the J.H.D.A. been warned about the effect repetition would have on future negotiations.

Now, if the B.M.A. is going to speak to outside bodies, and subsequently negotiate on their behalf, then surely it must establish a code of conduct as a prologue to any such negotiations. If outside bodies are going to use B.M.A. personnel and their resources to help achieve a common objective then the B.M.A. is entitled to, and indeed must, place some restriction on published criticism for the duration of the negotiations.

It was ironical that on Monday, 10 July, the Representative Body should have voted heavily against having non-B.M.A. members on regional councils. The R.B. thus refused to give these non-members the advantages of the resources of the B.M.A. Yet it would appear that what they had refused to do at regional level was already being done with the J.H.D.A. centrally, at the highest level, even to the extent of negotiating on their behalf with the Minister. The status of these negotiations with the J.H.D.A. needs defining.

I do not advocate that the B.M.A. should refuse to negotiate with and on behalf of outside bodies, but I do believe that outside bodies must first recognize their responsibilities towards the B.M.A. in terms of their own behaviour and publications.—I am, etc.,

Leeds. JOHN D. SINSON.

Radio Communication and the G.P.

SIR,—I was surprised that in the interesting article "Radio Communication and the Emergency Department" (15 July, p. 170) by Dr. M. H. Hall and Mr. R. S. Garden there was no mention of a link with the general-practitioner service. More and more family doctors like myself are availing themselves of the great help of a radio transceiver in their cars. This is particularly true in areas where the Emergency Treatment Service is active.

It would be of benefit to general practitioner and hospital alike if there was a means of communicating with the hospital directly from the general practitioner's car. In many hospitals there is a relay unit for direct communication with the ambulance service. It would be easy to adapt this system to communicate with the family doctor, except for the fact that the frequencies used are usually too dissimilar.

It is hoped that the committee considering the equipment of the ambulance service, and bodies controlling other medical radio links, will bear in mind the general practitioner and his needs in this connexion.—I am, etc.,

Glasgow. KENNETH HARDEN.

Points from Letters

Opportunities in British Medicine

Dr D. C. G. BETT (Farnborough Hospital, Kent) writes: I see in your issue of 15 July (p. 128) that the Ministry of Health intends to send a team to North America to try to persuade British doctors there to return home.

I think many of us still in Britain would be interested to know what this team is going to say to these expatriates. We have listened to many fine words from the Ministry, but when these have been translated into actual practice the result is usually very far short of the original promise. If Dr. R. H. Barrett and his colleagues have anything real, which is likely to attract doctors back to Britain, I feel that the good news might be made public now.

Casualty Department—or G.P. Service?

Mr E. P. ABSON (Ryde, Isle of Wight) writes: It is circumstances and not the diagnosis which determines attendance, and the casualty department must be capable of dealing with the immediate needs in many different specialties (1 July, p. 46). Well over 50% of the work and the main responsibility are in making the diagnosis, and, more difficult and important, eliminating more serious diagnoses over a wider spectrum. A man who has fallen 50 ft. (15 m.), and (if the "missed injury" is not to be missed) any case of general trauma, requires full examination and perhaps observation, even though the final conclusion may be "bruise—no treatment."

Obituary Notices

H. STOKES, O.B.E., M.D., F.R.C.S.I.

Mr. H. Stokes, a past-president of the Royal College of Surgeons in Ireland, and the last of his line to be associated with the Meath Hospital, Dublin, died there on 3 July at the age of 88.

Henry Stokes was born in India on 11 January 1879, his father being in the Indian Civil Service. He was brought up and educated in Dublin. He had five sisters and two brothers: of the latter, Brigadier "Bill" Stokes is still alive, and Adrian, the youngest, having won distinction for his bacteriological and pathological work in the first world war, died in West Africa of the yellow fever which he was investigating. Henry was educated at Trinity College, Dublin, where he graduated M.B., B.Ch. in 1903, proceeded M.D. in 1905, and obtained the Fellowship of the R.C.S.I. in 1907. He studied in Berne, Leysin, and Basle on a surgical travelling prize, and later in the Mayo Clinic, U.S.A. He was elected surgeon to the Meath Hospital in 1912, and was later consultant surgeon to the National Children's Hospital, St. Ultan's Infant Hospital, and Cork Street Fever Hospital, Dublin. He eventually resigned his appointments in 1956. During the first world war he served in the R.A.M.C. as lieutenant-colonel, and was appointed O.B.E. in recognition of his services. He was president of the Royal College of Surgeons in Ireland from 1940 to 1942.

He was very appropriately M.D., and his approach to his patients was that of the medical adviser who was ready and able to operate if necessary. He was a sound and versatile surgeon who loved to improvise instruments to meet special cases, such as using the rib of an umbrella to follow the track of a bullet through the abdomen before opening it. As a teacher he kept his students well aware of the history of medicine and the Meath Hospital.

Henry had many interests. He was a keen shot, and was a good and keen fisherman; he was an antiquarian, and a collector of many things from old books to the skeletons of the extinct giant Irish elk, of which he discovered quite a large number; he amassed friends, and had very many in and out of the medical profession. He was the least commercial of surgeons, devoting his best attention to the poor in Dublin, and is remembered with affection by his patients, colleagues, and all who knew him.

He married in 1911 Kitty Franks, and had a son, a daughter who is a doctor, and another daughter who is an excellent artist.
—B. O'B.

S. W. MASLEN-JONES, M.S., F.R.C.S., F.R.C.O.G.

Mr. S. W. Maslen-Jones, adviser to overseas candidates for the Royal College of Obstetricians and Gynaecologists and a former vice-president of the College, died at his home in Tettenhall on 17 July. He was 75.

Samuel Walter Maslen-Jones, the son of a Baptist missionary, was born in Simla on 6 September 1891, and was educated at Eltham College, and at the Middlesex Hospital, London, where he qualified with the Conjoint diploma in 1914. During the first world war he joined the R.A.M.C., and saw four years service in Egypt, where he was mentioned in dispatches, and where—in Cairo—he met and married Sister Kate Wilde, Q. A. I. M. N. S. After demobilization he graduated M.B., B.S. in 1919, and took the M.S. and the F.R.C.S. in 1920. He went to Wolverhampton to work with Frederick Edge, and in 1921 was appointed to the staff of the Women's Hospital there. During the years of his work in the West Midlands he gained an outstanding reputation, founded not only on his ability and skill as a diagnostician and operator but on the sympathetic understanding and kindliness of approach to all with whom he came into contact. He was a past-president and honorary Fellow of the Birmingham and Midland Obstetric and Gynaecological Society, a one time chairman of the South Staffordshire Division of the British Medical Association, and president of the Staffordshire Branch from 1937 to 1940. In his own specialty he was a foundation member of the British College of Obstetricians and Gynaecologists—as it was then called—and in 1931 was elected to the Fellowship. He was chairman of the building committee responsible for the construction of the new college house in Regent's Park, and was a vice-president of the College from 1958 to 1961. Among his many interests outside medicine, he was on the governing council of the Royal Masonic Boys' School, and for the year 1966–7 was president of the Old Boys' Association of Eltham College.

Maslen's interests and hobbies were innumerable, as were his friends. He had a great capacity for making and retaining friends, and his popularity was immense. He was also considered one of the best after-dinner speakers in his part of the country. In his student days he played rugby for the Middlesex Hospital, he was a good tennis player, and for years played off a handicap of 12 at golf. His annual ski-ing holiday was a great joy to him, his support of the "Wolves" keen and regular, and for the last 25 years he had become an ardent trout and salmon fisherman. Even in the gardening with which he had interested himself since retirement, he was, as ever, a perfectionist.

There are many who mourn Maslen. To his widow and three sons and their families a very real sympathy is extended.—H. J. M.

Dr. VICTOR RUSSELL writes: Maslen, as he was affectionately known to us all, was not only a great man, a prominent Freemason, and a fine surgeon but also a warm and friendly person, and a true friend. His kindness and helpfulness will be long remembered, and I think his general-practitioner colleagues in Wolverhampton will never forget the strong support than he, together with two or three others, afforded them in the struggle before 1948; and this at a time when most consultants, well satisfied with the terms of service they had been able to negotiate, had little time or sympathy to spare for their general-practitioner brethren. Those of us who knew him well feel that we are the better for having known him, and that the world is diminished by his passing.

W. DUNLOP, O.B.E., M.B., CH.B. D.T.M.&H.

Dr. W. Dunlop, a former professor of clinical therapy and lecturer in diseases of children at the Royal College of Medicine, Bagdad, died at his home at Tillingham, on 30 June. He was 80.

William Dunlop was born on 14 September 1886, and received his medical education at the Universities of Dublin and Edinburgh, graduating M.B., Ch.B. in 1909. He had a varied career, much of it being abroad. On the outbreak of the first world war he joined the R.A.M.C., and most of his service was in Mesopotamia, where he commanded various hospitals and took part in the advance on Bagdad, and was promoted major. He was three times mentioned in dispatches, and was appointed O.B.E.(Mil.) in November 1918. He transferred to the Civil Administration, and was appointed chief medical officer, civil hospitals, in March 1919, and in April of that year was appointed director of the Bagdad General Hospital, a post which later included being professor of clinical therapy and lecturer in diseases of children at the Royal College of Medicine. In 1924 he took the D.T.M.&H. He remained in Iraq until 1935 and for his distinguished services there he was given the Order of the Nahdhah by the Iraq Government. On his retirement he was presented with the Order of the Rafidain by the King of Iraq.

On the outbreak of the second world war he again returned to the R.A.M.C., and remained in it until July 1945, after which he was appointed a member of the Pensions Appeal Committee, and in 1947 chairman. He retired in 1956.

Willie, as he was known to all his friends, had many interests apart from his profession, which always came first. He was widely read, and probably his main hobbies were bird-watching and shooting. He was an outstanding authority on the birds of Iraq, and we were always amused at his little " pocket duck book," which he carried to identify the remarkable number of migrant ducks which visited the country. There was rarely a shooting day (once a week) when the guns were not asked back to his house, and entertained by his wife to a sumptuous tea.

I cannot imagine him being ruffled by anything, and impatience, anger, or neglect were not in his character. Above all, he had a great sense of humour, probably due to his Irish blood. He was a great man, beloved by British and Arabs alike.—T. H. McL.

H. J. GIBSON, M.D., D.P.H.

Dr. H. J. Gibson, consulting pathologist and director of the Bath clinical area central laboratory, died on 6 June. He was 62.

Hubert John Gibson was born in King's Lynn, Norfolk, on 22 October 1904, but his family moved to Isley, Argyllshire, where the firm foundation of a Scottish education was laid in the village school. In 1914 the family moved again, this time to Edinburgh. There he continued his education, first at George Watson's College and later at Edinburgh University, where he graduated M.B., Ch.B. in 1926. In the postwar era the large backlog of able medical graduates gave rise to delays in obtaining house appointments at the Royal Infirmary. Gibson decided, therefore, to fill in the waiting time in general practice. This took him to the West Riding coalfield of Yorkshire, where he experienced the difficulties of the general practitioner working divorced from the help of ancillary medical services. He was also moved by the plight of those with advanced rheumatoid and allied diseases, which he now met for the first time. Undoubtedly these experiences influenced his future career, both as regards his continuing interest in the clinical side of pathology, which in turn enabled him to help his colleagues at the bedside, as well as his special interest in the pathology of rheumatic conditions.

In 1927 he returned to Edinburgh, took the D.P.H. in 1929, and was invited to join the university staff in the department of bacteriology under the late Professor T. J. Mackie, where he soon made his mark, becoming lecturer in the department. During this period he published work on the natural antibodies of man and animals, on the isolation of enteric organisms from sewage, and on the transmission of louping-ill virus. He proceeded M.D. with high commendation in 1935. In the 1930s his work with streptococci directed his interests to the rheumatic diseases. Although by this time he had every prospect and promise of going further in academic bacteriology, he accepted an invitation to establish a department of pathology at the Royal National Hospital for Rheumatic Diseases at Bath, and in 1935 crossed the border. From this time onwards he made numerous regular contributions to the literature of the pathology on rheumatic disorders and established a world-wide reputation. He was an excellent administrator, and after the second world war was appointed area pathologist. In this capacity he was responsible for planning an area central laboratory capable of providing laboratory services for the Bath clinical area. The laboratory was built in 1952.

Among the many offices he held were Chairman of the Bath Division of the British Medical Association in 1948–9, president of the Clinical Society of Bath, and chairman of his hospital's medical staff committee. He was a founder member of the Bristol Bone Tumour Registry, a founder Fellow of the College of Pathologists, and a member of the Heberden Society.

Hubert Gibson happily combined his first-class brain with a pleasing personality and an outsize sense of humour. He had a most infectious laugh. If at times inclined to be quick-tempered, and unwilling to bear fools lightly, his innate kindliness would quickly reassert itself, and it is true to say that he had many friends and no enemies. By any standards a first-class general pathologist, he will be remembered widely as one of the last of the true clinical pathologists, always interested in the patient, and always preferring to work at the bedside. The logical marshalling of the evidence presented in his detailed reports, invaluable to the harassed clinician, was a further illustration of his clarity of mind. He was always up to date as the result of prodigious reading, extensive travelling to other centres, and a generally inquiring mind. He had the quality, unfortunately rare nowadays, of enthusiastically embracing new ideas and the new scientific approach to medical problems, without relinquishing his attachment to bedside medicine. He loved travelling, and was as interested in the contemporary scene as he was in the relics of bygone civilizations. He had an abiding interest in music, and was a loyal Churchman.

In 1934 he married Enid Spurrier, a talented musician, who survives him with their three children. His only son, Derek, is a member of the medical profession.—D. W. P. and L. C. H.

I. N. S. writes: Having known Hubert Gibson since we were at school together in the early 1920s, I know what a fine man we have lost. He was then that rare bird a boy of English parentage at a Scottish school, and it was interesting to see how keen, for instance, he was on cricket, which is not so popular in Scotland. He himself was no mean cricketer. Another abiding interest which he shared with his wife was music; and they had marvellous summer holidays in far away and unusual places. Many will miss him.

M. C. MACQUEEN, M.B., CH.B. F.F.A. R.C.S.

Dr. M. C. Macqueen, a consultant anaesthetist at the Royal Infirmary, Edinburgh, died on 27 June at the age of 59.

Malcolm Campbell (Callum) Macqueen, a son of the manse, was born on 4 October 1907, and was educated at the Royal Academy, Inverness, and at Edinburgh University, graduating M.B., Ch.B. in 1935. For some years he practised in Elgin and Inverness, until the second world war, when he joined the R.A.M.C. and served in the Middle East and in Italy. On demobilization he pursued his special interest in anaesthetics, took the D.A. in 1947, and the F.F.A. R.C.S. in 1955, and thereafter devoted his whole professional life to his chosen specialty. His services were greatly in demand by his colleagues in Edinburgh, where it was quickly recognized that his technical skill was matched by his sympathetic interest in the human problems of his patients.

Outside his profession he had many interests, and throughout his life maintained a tremendous enthusiasm and zest for living; in spite of failing health he remained a keen supporter and office bearer of the Scottish Gun Club, and was for many years president of the Edinburgh University Shinty Club and the University Hockey Club. Callum Macqueen was an outstanding individualist who will be remembered by his associates for his fearless and outspoken debunking of the bogus and insincere. His many friends will cherish the memory of his constant thoughtfulness and simple acts of kindness, his stout opposition to injustice, his hospitality, his courage, and his integrity.

We offer our sincerest sympathy to his devoted wife and two sons.—G. K. M.

J. H. MELLOTTE, M.B., B.CH., B.A.O.

Dr. J. H. Mellotte, a well-known London ophthalmologist, died in his sleep on 8 July at his home at Walton-on-Thames, where he had practised ophthalmology since 1940. He was 74.

James Henry Mellotte was born in Co. Mayo on 3 October 1892, and after leaving school at Rochestown, Co. Cork, went on to the National University in Dublin to read law. He switched from law to medicine, and graduated M.B., B.Ch., B.A.O. in 1920. Soon after graduating he came to live in England, but after general practice in London until 1936 decided to specialize in ophthalmology, and was subsequently for many years chief clinical assistant at the Royal Eye Hospital, and in the ophthalmic department of the Royal Waterloo Hospital, in London.

Within his chosen specialty Mellotte concentrated his considerable abilities in the art of refraction, and it is not too much to say that he was at one time rightly regarded as a master in this field. He also made a special study of migraine at a time when there was little interest in the subject. His contributions to the medical press were of value in both diagnosis and treatment of this devastating and common complaint.

Throughout his professional life Mellotte was deeply concerned with medical politics, and was for years a much valued B.M.A. representative and committee-man. He served not only on the Ophthalmic Group Committee but also on the Public Medical Services Subcommittee and the Standing Subcommittee on Ophthalmology. He was chairman of the Lambeth and Southwark Division of the B.M.A. from 1931 to 1934. As one of the very early members of the old National Ophthalmic Treatment Board (which through the B.M.A. formed and administered the National Eye Service until the advent of the N.H.S.), he became in turn one of the first ophthalmic medical practitioners to form, with the dispensing opticians, the N.O.T.B. Association. This association he served as a council member until his death. It was inevitable that in these spheres his strong controversial views and outspokenness should bring him into open conflict with a number of his colleagues, with whom he was ever ready to enter the fray, but always with wit and obvious enjoyment.

A man who had an undeniable fondness for the good things of life, and one in whom it was always possible to discern the Dublin medico of the St. John Gogarty tradition—he wrote for the *B.M.J.* a memorable obituary notice of Gogarty in 1957—Mellotte was none the less a lifelong and devout churchman, and was well known in the Catholic community in England. He served also in the Territorial Army as a captain in the R.A.M.C.

There is no doubt about Mellotte's considerable professional and intellectual attainments, and these should perhaps be seen and remembered in the light of what he himself wrote of his old friend, St. John Gogarty—namely, that he was "very Irish in temperament and character"—words which certainly applied to James Mellotte himself, and which he would no doubt be happy to have for his own epitaph. In spite of the burden of increasing years and failing health he worked tenaciously and bravely to the end, and in fact saw his last patients on the very morning of his death. We shall always remember him.

Mellotte married Hélène, daughter of Sir Robert Wallace Best, K.C.M.G., of Melbourne, and is survived by her, and by their two sons and two daughters. Our sympathy to them, and to the grandchildren, in their bereavement is very sincerely offered.—V.P.

C. DE W. KITCAT, M.R.C.S., L.R.C.P.

Dr. C. de W. Kitcat, formerly consultant chest physician in the South and West Somerset clinical area, died in Taunton on 4 July at the age of 67.

Cecil de Winton Kitcat was born on 4 June 1900. His education was interrupted by the first world war, in which he served as a midshipman in the Royal Navy, executive branch. After demobilization he entered St. Bartholomew's Hospital, London, qualifying with the Conjoint diploma in 1923. He subsequently held house appointments at the Connaught Hospital, the West End Hospital for Nervous Diseases, and the Brompton Hospital. An appointment as resident medical officer at the Brompton Hospital followed, and he was able to continue his interest in chest diseases when appointed assistant physician at Fairlight Sanatorium, which he combined with general practice at St. Leonards-on-Sea. He later moved to Highgate, in North London, and at the outbreak of the second world war he rejoined the Royal Navy. He saw active service, and had to swim for his life when H.M.S. *Hecla* was sunk in 1943. Finding another vessel floating near by with the stern blown off, he clambered aboard and was subsequently taken to Gibraltar. Serving under Dr. W. D. W. Brooks at the Royal Naval Hospital, Chatham, he renewed his dealings with chest diseases, and after demobilization took up an appointment as tuberculosis officer with the Somerset County Council. This led to his appointment as consultant chest physician with the South-west Regional Hospital Board, covering Taunton and the south and west of Somerset. He retired in May 1965.

His breezy approach and jaunty manner won him wide acclaim. Many patients, and their family doctors, had occasion to bless his shrewd diagnostic acumen and the effective treatment he meted out. About 18 months before retiring he suffered a myocardial infarction, from which he never fully recovered, and which restricted his activities on retirement.

He leaves a widow, Kitty Meg, to whom our sympathy is extended.—B. J. D. S.

J. T. ANDERSON, M.B., CH.B. D.T.M.&H.

Dr. J. T. Anderson, assistant health adviser, Aden, died suddenly in Aden on 14 May, aged 33.

James Terry Anderson was born on 11 November 1933, and received his early education at Robert Gordon's College, Aberdeen, where he distinguished himself both in the classroom and on the sportsfield. He was also an active member of the Army Cadet Force. In his final year at Gordon's he was appointed school captain, and won the Otaki shield as the best all-round boy. This shield carries with it a trip to New Zealand. He received his medical education at Aberdeen University, graduating M.B., Ch.B. in 1957. While a student he took an active part in the students' representative council, and was a very popular participant in the annual student shows—popular both because of his fine baritone voice and because of his comic ability. As a student he won several awards in the local music festivals, where he sang opera and oratorio with the same competence as he did the Scots songs which he loved. Later in his career he also appeared as a singer on Grampian Television. After graduation he was a resident in the City Hospital and the Royal Infirmary, Aberdeen.

On starting his National Service he volunteered for service with Trucial Oman Scouts, during which time he learned to read and write Arabic. On returning to Britain he entered general practice in Bucksburn, Aberdeenshire. He remained in this post for three years, being very much liked by his patients, for whom he worked very hard. Four years ago he decided to return to Arabia, where he did two terms of duty, first in charge of a hospital in Lodar in Aden, and latterly as health adviser in Mukalla. During the period of leave between his two terms he studied at Liverpool University and took the D.T.M.&H. in 1965. He was to have returned to Liverpool University as an assistant lecturer in tropical medicine but for his untimely death. During his term in Mukalla he was undertaking a massive programme among schoolchildren to eradicate tuberculosis.

To those of us who knew Jimmie at school and at University, the loss is irreplaceable.

In 1958 he married Anne Greenwood, and to her and their two children, Susan and John, we extend our sympathy.—G. E. A.

I. DAVIES, L.R.C.P.&S.ED. L.R.F.P.S.GLASG., D.M.R.E.

Dr. I. Davies, formerly a radiologist at Swansea General Hospital and Eye Infirmary, died at his home in Llandyssul, Cardiganshire, on 29 June after a long illness patiently borne. He was 75.

Iwan Davies was born on 7 November 1891, and received his medical education in Edinburgh, qualifying with the Scottish joint diploma in 1917. After holding a resident appointment at the Aberystwyth General Hospital he proceeded to Liverpool to study radiology, a subject he was to adopt as his specialty. In 1922 he was appointed radiologist to the Swansea General Hospital, where he established the first radiotherapy department in Wales and served on the hospital's house committee for 24 years. He took the D.M.R.E. in 1925. He held the appointment of radiologist to Haverfordwest, Carmarthen, Llanelly, Gorseinon, Morriston, and Neath Hospitals. As radiologist to the pneumoconiosis unit he initiated special studies on anthracosis among south Wales coal miners. He was chairman of the Swansea division of the British Medical Association in 1937–8.

Dr. Davies's calm and genial personality endeared him to his patients, whose natural fears he allayed during his special investigations of their diverse illnesses, and whose weakened hope he sustained and strengthened should they prove in need of prolonged radiotherapy. In his earlier years he was a keen golfer, playing off a handicap of two. He was an ardent fisherman, a devoted gardener, a close student of wild life, and a lover of the countryside and its lore. A deacon of his chapel, he possessed a simple and firm faith. He supported wholeheartedly all good causes and befriended the lowly and the needy. In all his dealings he practised the tenets of a wayside religion. He will be missed by a wide neighbourhood, by his relatives and many friends, and especially by his widow, whose loss is greatest.—W. E.

C. E. HARRISON, M.B., B.S.

Dr. C. E. Harrison, formerly in general practice at North Elmham, Norfolk, died in hospital on 21 May. He was 75.

Cyril Edward Harrison, the son of a metal merchant in Drury Lane, was born in London on 6 November 1891. He received his medical education at the Middlesex Hospital, and after qualifying with the Conjoint diploma in 1915 joined the R.A.M.C. and saw active service at Gallipoli and in Malta, India, China, and at Vladivostok. On demobilization in 1919 he graduated M.B., B.S., and in May of the same year married Miss Muriel Rarkham of Q.A.R.A.N.C. In February 1920 he took over the practice of his father-in-law, Dr. A. Rackham, at North Elmham, where he carried on single-handed an extensive rural practice until 1951, when he was joined by his nephew Dr. Esmond Earle. In 1958 he retired from practice to live in the south of England.

Dr. Harrison was an active member of the British Medical Association, serving as chairman of the East Norfolk Division in 1956–7, and as a member of the local committee of that Division. He kept up to date in medical work by regular attendance at meetings of the local medical society.

To those who knew him well Dr. Harrison was a quiet, unassuming, extremely competent, conscientious family doctor with the formal manner of his days. Meeting him in consultation was always a pleasurable experience, and one was impressed by the trust and confidence so obviously given him by all his patients in every situation of life. His hobbies were music—he was a proficient pianist—and gardening, the latter being shared by his wife, to whom in her loss the sympathy of all his friends and colleagues is extended.—B. B. M.

Z. GREEN, L.R.C.P.&S.I., L.M.

Dr. Z. Green, formerly in general practice at Paddington, London, died while on holiday in Eastbourne on 3 July. He was 75.

Zelick Green was born in Dublin on 1 September 1891, and educated at Wesley College, after which he served an apprenticeship with a firm of chemists, qualifying as a dispensing chemist in 1913. At the outbreak of the first world war he volunteered to go to France as a hospital dispenser with the British Red Cross Society, and was awarded the Mons Star for his services. He returned to Dublin in 1915, and received his medical education at the Royal College of Physicians and Surgeons in Ireland, qualifying in 1920. Shortly afterwards he entered general practice in East London, and became a clinical assistant at the London Jewish Hospital. In 1930 he succeeded Dr. A. J. Cronin to the practice in Paddington where he continued until his retirement in 1960. He was also a clinical assistant at the West London Hospital, a member of the disablement panel, and during the second world war medical officer to the Civil Defence services.

An active member of the British Medical Association, he was a representative at the Annual Meeting in 1955–6, and chairman of the Paddington Division from 1954 to 1962. He was a member for some years of the London Medical Committee. His particular interest was the Paddington Medical Society, which he created and organized for many years. He was also the originator of the Irish Jewish Medical and Dental Society, which was his particular invention, and for several years he was chairman at its happy functions. Much of his spare time was given to the activities of the Jewish Lads' Brigade, of which he was medical officer, and he was always ready to help the youngsters in any way he could.

Dr. Green had a happy retirement, and he kept his interests in his friends and family to the end, and, above all, maintained a most delightful sense of humour and kindliness towards those with whom he came in contact from all walks of life. Although latterly his health was deteriorating, he never lost his great qualities, and the end came in the way he would want it, peacefully and quickly.

He is survived by his widow and two sons, the elder of whom succeeded him in the practice in 1960.—L. M. G.

J. G. writes: Dr. Green, affectionately known as "Jack," was held in the highest esteem by patients and friends alike. Even to this day many of his former patients will remember with gratitude the individual care and attention he bestowed upon them. He took a leading part for many years in bringing about in London a reunion of graduates of Irish medical and allied professions. He was a delightful postprandial raconteur, his speeches being full of Irish wit and jocularity. He was proud of his Irish birth.

Sir EARDLEY HOLLAND, LL.D., M.D. F.R.C.P., F.R.C.S., F.R.C.O.G.

A. W. B. writes: Sir Eardley Holland's achievements (obituary, 29 July, p. 313) during a distinguished career are well known to the profession. Having known him as an intimate friend since the early 1920s, I wish to write about his personal qualities. Eardley had a genius for friendship, which was evident in all the gatherings of his colleagues, owing to his lively interest in their affairs and work and a capacity for real affection for his close friends. He was personally attractive by his distinguished appearance, his welcoming smile, and melodious speaking voice. Wide reading had endowed him with powers of discussion and conversation on almost any subject of intellectual interest. I recall the delight of our monthly dinners, alternately at my flat in Wimpole Street and his club in St. James's. After dinner, if at the club, we would return to the flat and enjoy talk on literature, the arts, history, and the career of men until nearly—or even after—midnight. From his knowledge of literature he developed a style of writing English which was almost pedantic in the careful choice of words, phrasing, and composition; elegant, lucid, and to the point. This became very evident to me during the two years or so when Eardley and I were associated in editing the two volumes of *British Obstetric Practice*, and the companion gynaecological volume. Very carefully did he read the chapters of the contributors, ready, occasionally to their annoyance, to correct slipshod or woolly English.

For me Eardley possessed the charm of manner and companionship which made our meetings so enjoyable, but he was not immune to an irritable impatience with what he considered to be inferior work, the slackness of unfulfilled promises, or what he thought were loose, untidy, or thoughtless opinions. During the home and foreign tours of the Gynaecological Visiting Society Eardley was at his best as a cheerful member, mixing with all of us, and sometimes as the efficient manager of a party of 20 or more which included at least one or two who were not renowned for their idea of punctuality.

Despite his recent incapacity, I feel keenly the loss of his friendship over some forty years or more. My sympathy goes out to his beloved wife, Olivia, and to his three daughters.

Sir ALEXANDER MACGREGOR

K.B.E., LL.D., M.D., F.R.C.P.GLASG., D.P.H.

C. M. S. writes: Sir Alexander Macgregor (obituary, 15 July, p. 181) encouraged, and quietly expected, every member of his staff to take a special interest in one particular branch of preventive medicine, and to undertake research. When a paper was submitted Dr. Macgregor, as we then knew him (or "A. S. M.," as he was affectionately referred to), would ask the aspiring young author to meet him after office hours for a light (very light) evening meal in one of the near-by city tea rooms, and then to return for a couple of hours spent on a detailed reading and suggested improvements of the paper—all this after a punishing day's work as head of a huge department. These evening sessions would be repeated until the paper was, in his view, fit for publication. His approach to all would-be contributors was: "Where are your facts ?" Speculation and surmise were blue-pencilled, only facts and reasonable deductions were passed.

He knew how to divest himself of the day-to-day chores of his office, which were handled by a competent lay secretary. One trait I admired: any general practitioner in the city who was asked to speak to him personally on the telephone was put through at once. He was truly one of the great leaders of the public health service, and it was a cherished privilege to have been trained by him.

Sir CLAUDE FRANKAU, C.B.E. D.S.O., M.B., F.R.C.S.

Sir TREFFRY THOMPSON writes: Others have paid tribute to Claude Frankau's skill as a general surgeon (obituary, 8 July, p. 116), but it is to him as the surgical registrar at St. George's before the first world war that I would like to pay special tribute, a period when I knew him first and best. He was a wonderful teacher to whom nothing was ever too much trouble so long as he could make sure that we understood the reason for a diagnosis or the details of an operative procedure. Not that he endured fools gladly. After some particularly fatuous answer to some question he would slightly cock his head to one side and cast a quizzical look at the idiot, and would then make sure that the idiot got the facts or the details right. Even in those days we all owed him a tremendous debt for his teaching.

News and Notes

EPIDEMIOLOGY

Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available.

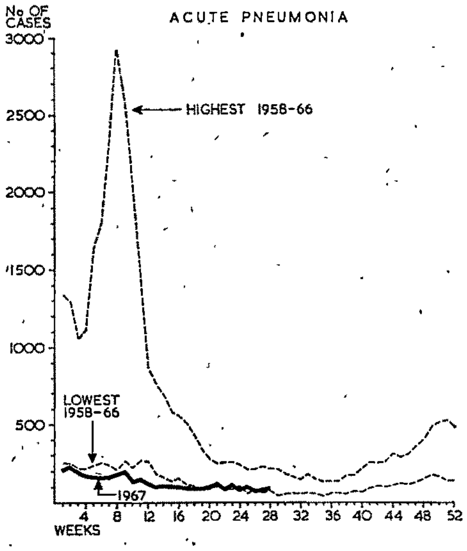
	Week Ending 14 July	Week Ending 21 July
Dysentery		
Greater London	78	**58**
Ealing	13	**12**
Lancashire	66	**51**
Warwickshire	30	**21**
Birmingham C.B. ...	14	**11**
Yorkshire West Riding ...	75	**49**
Bradford C.B.	19	**11**
Leeds C.B.	29	**19**
Edinburgh	19	**24**
Glasgow	15	**25**
Food-poisoning		
Greater London	60	**35**
Hillingdon	30	**10**
Hampshire	0	**35**
Kingsclere & Whitchurch R.D.	0	**34**

Births and Deaths in the June Quarter

The birth rate in England and Wales during the June quarter was 17.9 per 1,000 population and was 0.1 below the rate for the preceding June quarter. Stillbirths reached the low level of 14.6 per 1,000 total births, being 0.4 below the rate for the second quarter of 1966. The death rate was 10.8 per 1,000 population and was 0.2 below the rate for the preceding second quarter. Infant mortality was 18 per 1,000 live births.

Graphs of Infectious Diseases

The graph below shows the uncorrected number of cases of acute pneumonia in England and Wales. Figures for 1967 are compared with the highest and lowest figures for each week in the previous years shown.



INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **15 July** (No. 28) and corresponding week 1966.

Figures of *cases* are for the countries shown and for Greater London. Figures of *deaths* and *births* are for the whole of England and Wales (London included), Greater London, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0		9	0	1	0	
Dysentery ..	447	78	46	5	2	542	86	39	10	4
Encephalitis, acute.. ..	3	0		0		3	0		0	
Enteric fever: Typhoid ..	5	1	2	0	1	7	4	1	0	
Paratyphoid..	2	0	18	0	0	5	1	0	0	
Food-poisoning	219	60	4	1		146	42	9	3	
Infective enteritis or diarrhoea under 2 years				32	24				24	58
Measles* ..	5,181	359	26	106	114	7,855	781	95	86	146
Meningococcal infection ..	3	0	4	0	1	12	4	4	0	1
Ophthalmia neonatorum..	10	1	0	0		13	4	0	0	
Pneumonia† ..	90	10	67	4		75	10	69	1	
Poliomyelitis, acute: Paralytic ..	0	0	0	0		1	0	0	0	
Non-paralytic	0	0	0			0	0	0		
Puerperal fever§	68	18	2	0		100	48	2	0	
Scarlet fever ..	283	46	21	14	9	370	67	22	7	3
Tuberculosis: Respiratory ..	225	51	39	2		243	75	44	7	
Non-respiratory ..	58	19	4	1		49	7	8	3	
Whooping-cough	750	136	74	7	68	423	69	31	6	10

DEATHS	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0		0	0	0	2		0	0	0
Dysentery ..	0	0		0		0	0		0	
Encephalitis, acute.. ..					0					0
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	8	2	0	0	5	2	0	2	0	1
Influenza ..	2	0	0	0	0	3	0	0	0	0
Measles ..	0		0	0	0	0		0	0	0
Meningococcal infection ..			0					0		
Pneumonia ..	616	83	20	6	6	495	65	15	13	6
Poliomyelitis, acute.. ..	0	0		0	0	0	0		0	0
Scarlet fever ..	0		0	0	0	0		0	0	0
Tuberculosis: Respiratory ..	26	9	3	2	1	40	7	1	0	1
Non-respiratory ..				0	1				0	0
Whooping-cough	0	0	0	0	0	0	0	0	0	0
Deaths 0-1 year	273	61	24	5	17	285	59	22	2	8
Deaths (excluding stillbirths)	9,621	1518	475	92	160	8,902	1369	518	101	164
LIVE BIRTHS	15,954	2684	853	218	252	16,296	2820	923	185	298
STILLBIRTHS	220	30	17			266	41	12		

* Measles not notifiable in Scotland, whence returns are approximate. † Includes primary and influenzal pneumonia. § Includes puerperal pyrexia.

MEDICO-LEGAL

Complaints by Patients

[From our Legal Correspondent]

A patient whose complaint is accepted by a service committee under the National Health Service (Service Committees and Tribunal) Regulations, 1956, cannot appeal to the Minister on the ground that the penalty imposed was too small.

Dr. Jacob Ellis, of Barnsley Road, Sheffield, was granted[1] an order of prohibition by the Divisional Court of the Queen's Bench Division ordering the Minister of Health not to hear a purported appeal by Mr. Ernest Harrison, of Neepsend, Sheffield. Mr. Harrison had made a complaint to a service committee. The service committee reported to the executive council that it found Dr. Ellis in breach of his terms of service. It was recommended that £5 should be withheld from Dr. Ellis's remuneration. Mr. Harrison felt that £5 was too small a sum and wanted to appeal to the Minister on that account.

Regulation 7 (2) of the 1956 Regulations provides that any dissatisfied party is entitled to appeal to the Minister against the Council's decision. The Divisional Court held that a party who had in effect won on the only issues that concerned him was not a dissatisfied person within the meaning of the regulation and had no right of appeal. Had the complaint been rejected Mr. Harrison would have had a right of appeal. But the complaint had been found proved. The decision of the Council about what action, if any, should be taken upon that finding was not a matter in which the complainant had an interest. A complainant would have an interest in such decision only if he alleged that he had incurred expenses as a result of the breach and sought to recover them under the regulations. In granting the order of prohibition, the Court allowed Dr. Ellis his costs against the Minister.

Reference

[1] *The Times*, 6 July 1967.

PARLIAMENT

Abortion Bill: New Conscience Clause and Title

[From our Parliamentary Correspondent]

Two of the House of Lords' amendments to the abortion law reform Bill have put it in jeopardy. The House had the Bill before it on the committee stage on 26 July, and passed an amendment requiring that one of the two doctors giving an opinion on lawful termination should be a Health Service consultant or a doctor approved by the Minister of Health. The other amendment, carried by one vote, was to delete the words "or any existing children of her family" (subsection (1) (a) (i)).

Changes in the Bill—and the second change referred to is vital to its structure as M.P.s passed it—require that it shall go back to the Commons for their agreement. This must now be in the single week at the end of October, when Parliament returns from the summer recess to tidy up the odds and ends of legislation before starting on a new session. The time will be shortened by the fact that the Lords have to push the Bill through its report and third reading. An obdurate opposition could still foil the promoters' hopes of seeing this measure become an Act of Parliament before the current session ends.

These considerations were in the mind of **Lord Silkin**, piloting the Bill, when early in the debate he said, "We must face the fact that time is against us, and if we pass any amendments of which another place [House of Commons] does not approve we shall effectively kill the Bill." He asked the House to accept the Bill as it stood.

Type of Doctor

The first issue discussed was the status of the two doctors on whose opinion, as declared in Clause I (I), a termination should be lawful. The clause requires simply two registered medical practitioners.

Lady Summerskill proposed that one of them should be named on a list approved by the Minister of Health. **Viscount Dilhorne** and others wanted one of them to be "employed under the National Health Service as a consultant or approved by the Minister of Health or the Secretary of State for the purpose." **Lady Wootton of Abingdon** thought one of them should be specially qualified in psychological medicine.

For the Government **Lord Beswick** enumerated a number of defects which the Ministry of Health saw in all these proposals, and reminded the House that the Minister had refused to accept the responsibility of making invidious distinctions between doctors. **Lord Silkin** said the Bill as it stood was right, pointing out that the operation must be carried out in a Health Service hospital or an institution approved by the Minister, and approval must include suitable staff.

Lady Summerskill withdrew her amendment; Lady Wootton did not move hers; and Viscount Dilhorne's was carried by 116 votes to 67.

"Serious" Risk

Lord Segal tried to amend paragraph (a) (i) to provide that the risk of continuation of the pregnancy to the life of the woman should be "serious," and that injury to her physical or mental health should be "grave." He had the support of **Lord Parker of Waddington** on the ground that it would enable judges to direct a jury that it was not intended that it should be just "any" risk or slight injury but a serious risk and a real injury.

Lord Stonham, for the Home Office, pointed out that the British Medical Association and the Royal College of Obstetricians and Gynaecologists had said that these requirements could raise considerable difficulties in practice, and might mean that terminations carried out on certain medical indications that were accepted in current medical practice would become questionable in future. It was because of the strong representations of the responsible medical bodies that the words were taken out of the Bill in the Commons.

The amendments were withdrawn.

Health of Existing Children

The most contentious part of the discussion arose on an amendment moved by **Viscount Dilhorne** to leave out "any existing children of her family." The provision, he said, sought to introduce as a justification for abortion a criterion wholly unrelated to the condition of the pregnant woman. Let the test which the doctors could apply be a test of health in its widest sense, but let it be the health of the pregnant woman.

Lord Brock objected that the phrase departed from the medical considerations of abortion as they affected the physical or mental health of the woman. Where family background or circumstances were such as to prejudice her health the natural compassion of the doctor, fostered by his medical experience, would be sufficient to influence him to pay attention to these matters. But the phrase definitely introduced the problem of social reasons for abortion. It was the fear of many surgeons that they would then be called on to perform abortions for reasons not connected with the health of the pregnant woman herself. Some might be willing to do so for non-medical reasons, but most would not. It would not be right to expect a surgeon and his team to do something against their will and conviction.

Lord Platt said he could not support the amendment. The Bill, if passed into law, should be, with all proper safeguards, more permissive and not more restrictive than the present state of affairs. To rule out the words at this stage was almost tantamount to instructing doctors not to take account of the influence of social factors on the medical state of their patients and their patients' families. It would be a new and wholly undesirable departure from good doctoring.

Lord Molson, supporting Lord Silkin in the task of getting the Bill through, refused to accept the amendment. It had been made plain from the start that the supporters of this Bill were not satisfied that it should be merely a restatement of the doctrine in the Bourne case. It was intended to be a measure of social reform, and to go further than the existing law.

The amendment was carried, on a vote, by 87 to 86.

Conscience Clause

Lord Silkin moved to delete Clause 4 (conscientious objection to operation) and insert a redrafted clause (conscientious objection to participation in treatment). The new clause, which was agreed to, stated:

> (1) Subject to subsection (2) of this section, no person shall be under any duty, whether by contract or by any statutory or other legal requirement, to participate in any treatment authorized by this Act to which he has a conscientious objection:
>
> Provided that in any legal proceedings the burden of proof of conscientious objection shall rest on the person claiming to rely on it.
>
> (2) Nothing in subsection (1) of this section shall affect any duty to participate in treatment which is necessary to save the life or to prevent grave permanent injury to the physical or mental health of a pregnant woman.

Title of Bill

Lord Silkin moved an amendment to change the title to the Abortion Bill, by which, he said, it was known. The amendment was agreed.

He also proposed an amendment that the Bill should come into force six months after it was passed. This period was necessary, he explained, to enable the Ministry of Health to make the necessary preparations. The House accepted this amendment.

If Lord Silkin's fears are not realized, and the Bill is not lost in disagreement between the two Houses, it could obtain the Royal Assent at the end of October and come into operation next April.

S.T.P.

The current dispute on the effects of soft drugs in leading to addiction to hard drugs occupied the early attention of the House of Commons on 28 July, the day the House adjourned for the summer recess.

It was introduced by Mr. P. Channon (Southend, West, Con.), who asked the Government whether the subcommittee of the Advisory Committee on Drug Dependence, which is studying the question of soft drugs, would deal with cannabis.

Miss Alice Bacon, Minister of State at the Home Office, said that the Government was making urgent inquiries about S.T.P. It had not yet been placed under control in America, she said, and preliminary information suggested that its chemical structure would not bring it under British legislation. The Government Chemist was examining a tablet, and the Government was considering the need to bring it under control.

Cannabis was scheduled under the International Convention on Narcotic Drugs of 1961, to which Britain was a party. Since it was banned by virtually every country, it could not be freed from control without international consequences. It would be "entirely mad" for the Government to relax control over the drug without further information. Some 97% of all heroin addicts known to the Home Office had a previous history of taking cannabis.

The Minister stated that the number of convictions for the illegal use of cannabis was 554 in 1964 : 1,119 in 1966 ; and 530 in the first four months of this year.

Service Committees

Mr. G. Fowler (The Wrekin, Lab.) asked the Minister of Health how many cases were heard by National Health Service service committees in each year from 1960 to 1966, inclusive ; how many of these cases were the subject of a further appeal to the Minister or the tribunal ; and how many cases went in favour of the practitioner and how many in favour of the patient.

Mr. K. Robinson, replying on 19 July, stated that a number of the cases considered by service committees resulted from references by executive councils, not from complaints by or on behalf of patients, and separate figures for the latter type of complaint were not available before 1963. They were shown in brackets for 1963 and later years. Appeals were only to the Minister.

Year		Number of Cases	Appeals	Practitioner Found in Breach of his Terms of Service
1960	...	1,191	87	713
1961	...	1,341	95	744
1962	...	1,036	70	486
1963	...	1,086 (706)	94	463 (151)
1964	...	1,236 (836)	93	485 (149)
1965	...	1,159 (883)	95	413 (175)
1966	...	1,006 (738)	85	360 (151)

There were 552 service committees in England and Wales from 1960 to 1964. The number was reduced to 536 following a reduction in the number of executive councils on 1 April, 1965.

Air Pilots Certificates

Mr. Hector Monro (Dumfries, Con.) asked the President of the Board of Trade on 19 July for what reasons the medical examination for a private pilots' licence must in future be carried out by an authorized medical examiner and not by any medical practitioner.

Mr. J. P. W. Mallalieu, Minister of State: "It is desirable that medical certificates that give continuing validity to licences now issued for five years should be given by doctors who are knowledgeable about aviation medicine and the standards to be applied."

MEDICAL NEWS

Control of University Expenditure

In a statement in the Commons last week Mr. Anthony Crosland, Secretary of State for Education and Science, announced that the Government had accepted the Public Accounts Committee's recommendation that the Comptroller and Auditor General should be given access to the books and records of the University Grants Committee and the universities (see *B.M.J.*, 4 February, p. 251). The Government, he said, shared the view of the Committee that this item of Government expenditure, which had risen to well over £200m. a year, "can no longer continue to be the sole major exception to the normal requirements of Parliament regarding scrutiny and report." It would become a condition of grant to universities from 1 January 1968 that their books and records should be open to inspection.

Royal Society of Medicine

The following have been elected Honorary Fellows of the Royal Society of Medicine: Lord Cohen of Birkenhead, Mr. Cuthbert Dukes, Dr. Douglas Guthrie, Sir Robert Macintosh, and Professor Martin Rushton.

U.S. Honours British Dentists

On 27 July Mr. David Bruce, the United States Ambassador in London, presented the Elmer S. Best Memorial Award to Professor Martin Rushton, whose contributions to dentistry he described as "outstanding and of world renown." The award was established in 1961 by the Pierre Fauchard Academy of Cleveland, Ohio, in memory of its founder. Professor Rushton was educated at Cambridge University and Guy's Hospital, graduating in science, medicine, and dentistry. From 1959 to 1962 he was dean of the faculty of dental surgery at the Royal College of Surgeons of England. Other members of the dental profession who were honoured at the ceremony were Professor Bertram Cohen and Professor Bryan E. D. Cooke, who were presented with the honorary membership of the Academy.

Medical Computing Language

The Minister of Health, Mr. Kenneth Robinson, is setting up a committee to consider the need for a standard medical computing language. He has appointed as chairman Mr. D. White, an assistant secretary in the department who is in charge of computer policy and developments. Other members of the committee are: Professor J. Anderson, department of medicine, King's College Hospital ; Professor G. Black, National Computing Centre, Manchester ; Mr. R. A. Brooker, department of computation, Manchester University ; Dr. D. Michie, department of machine intelligence and perception, Edinburgh ; Dr. O. R. L. L. Plunkett, physician superintendent, St. Peter's Hospital, Chertsey ; Major J. B. Ready, medical records officer, Hospital for Sick Children, London ; Dr. B. Richards, department of computation, Manchester

University; and Dr. J. Scott, medical officer, University of Keele.

Education in Management

Wise management of existing hospital resources is the keynote of the annual report of King Edward's Hospital Fund for London. The Fund organizes courses in management for consultant medical staff and senior registrars. The main theme is the efficient use of resources (beds, services, money, and manpower) and ways and means of measuring efficiency. In September next year the four staff colleges will merge to form the King's Fund College of Hospital Management. Grants in 1966 totalled £239,768. About a third (£70,540) was devoted to research, much of it to practical studies designed to improve hospital service. A useful feature of the report is a summary of the Fund's activities in the form of annotated lists of grants, studies, and publications.

Changes in Trusteeship

The trustees of the Medical Commission on Accident Prevention have appointed Mr. Norman Capener, F.R.C.S., scientific director of the Commission, to succeed Sir Arthur Porritt when he resigns as chairman in September. Mr. Capener will be succeeded by Dr. C. A. Boucher. Copies of the annual report for 1966–7, recording the work of the various committees, can be obtained from the Commission's Executive Offices, 50 Old Brompton Road, London S.W.7, 5s. plus 6d. postage.

Courses for General Practitioners

A B.M.A. list of courses for general practitioners is now available. The courses referred to are being held from September to December and will last a week-end or one or two weeks. Copies of the list can be obtained on application to the Secretary, British Medical Association, B.M.A. House, Tavistock Square, London W.C.1.

People in the News

▶Lord Hill of Luton, chairman of the Independent Television Authority, is to become chairman of the B.B.C. Board of Governors.

News in Brief

On 26 July the Minister of Health, Mr. Kenneth Robinson, laid the foundation stone of the University Hospital of Wales and teaching centre at Heath, Cardiff. The building scheme is estimated to cost £19m.

The Department of Education and Science is seeking evidence of drug-taking by schoolchildren and students. It has written to chief education officers and principal school medical officers asking what steps are being taken to guard against this development and to ensure treatment for those who need it.

Grants and Awards

The Polar Medal has been awarded posthumously to Dr. J. K. Wilson, medical officer, British Antarctic Survey. (An obituary notice was published in the *B.M.J.*, 30 October 1965, p. 1067.)

Recent Publications

A report, *Pharmaceutical Research: The Case for Growth in Britain*, calls for an economic environment in which the industry can expand and compete internationally. Issued by the Office of Health Economics (162 Regent Street, London W.1).

Societies and Lectures

For attending lectures marked ● a fee is charged or a ticket is required. Applications should be made first to the institution concerned.

Wednesday, 9 August

Stoke Mandeville Hospital.—12.15 p.m., Mr. L. Cosin: New Thoughts on the Care of the Old.

Friday, 11 August

Institute of Diseases of the Chest.—5 p.m., Dr. H. Nicholson: clinical demonstration.

Universities and Colleges

ROYAL COLLEGE OF PHYSICIANS OF LONDON

At a quarterly meeting of the College held on 27 July, with the president, Sir Max Rosenheim, in the chair, Mr. D. H. Barran, chairman of the Shell Transport and Trading Co. Ltd., and Dr. J. A. P. Treasure, chairman of the J. Walter Thompson Co., were elected Friends of the College.

Sir John Richardson was elected representative of the College on the General Medical Council.

The appointment of Dr. D. E. Bedford as Harveian Orator and Dr. P. B. Beeson as Bradshaw Lecturer, both for the year 1968, was announced.

The following lecturers were also appointed for 1968: Lumleian Lecture, Dr. A. C. Dornhorst; Goulstonian Lecture, Dr. D. N. S. Kerr; Croonian Lecture, Dr. E. G. L. Bywaters; Bertram Louis Abrahams Lecture, Air Commodore H. L. Roxburgh; Humphry Davy Rolleston Lecture, Dr. Sheila P. V. Sherlock; Langdon-Brown Lecture, Dr. H. Harris. For 1969: FitzPatrick Lecture, Major General A. N. T. Meneces; Watson Smith Lecture, Dr. F. F. Hellier; Marc Daniels Lecture, Dr. W. R. S. Doll.

The Baly Medal was awarded to Dr. Bernard Katz.

The following Fellows of the College were elected Officers for the ensuing year: *Senior Vice-president*, Dr. Clifford Wilson; *Censors*, Dr. Clifford Wilson, Dr. N. S. Plummer, Dr. W. N. Mann, Dr. Cyril Astley Clarke; *Treasurer*, Dr. R. R. Bomford; *Registrar*, Dr. K. Robson.

At a meeting of the College held on 28 July the following, having satisfied the Censors' Board, were admitted members of the College:

A. R. M. A. Awwal, P. Beck, A. N. Bowden, R. L. Bown, C. G. D. Brook, A. S. Burney, J. H. Chamberlain, Mo Wah Chan, P. Cochrane, J. B. Cocking, J. J. Cogswell, P. Collins, Johanna A. Cotter, Gillian M. Craig, R. J. Cryer, D. R. Cullen, G. Danta, P. G. D'Arbela, Judith M. Darmady, J. R. E. Dathan, E. W. Davies, M. J. Dillon, B. O. L. Duke, A. L. W. F. Eddleston, Joy B. Edelman, P. C. Edmondson, C. F. Elliott, P. H. Q. Fernando, D. J. H. Fisher, F. V. Flynn, R. A. Fox, P. Ghosh, N. Gitlin, S. H. Green, Jacqueline Harris, R. Harris, D. R. Hart, P. Hillenbrand, K. Hollinrake, P. R. Hunter, A. F. M. A. Islam, U. S. Jayawickrama, M. B. S. Jones, A. B. Kay, N. Kesaree, A. M. S. I. Khan, M. Z. Khan, N. B. Kirkland, R. P. Knill-Jones, J. Knowelden, G. Lawton, A. W. Lees, A. R. Lo Su Fook, D. M. McCarthy, D. G. McCoy, G. McEnery, V. Mahadev, P. A. Majid, M. N. Marsh, J. S. Marshall, R. T. Maxwell, P. P. Meisner, W. R. J. Middleton, K. Miloszewski, C. M. Morgans, M. G. Moshal, P. Moulik, I. M. Murray-Lyon, J. M. Muscat-Baron, F. Navab, M. J. Noronha, M. D. O'Brien, M. C. L'E. Orme, R. C. L'E. Orme, B. C. Pakrashi, M. C. Pearson, Patricia M. Perera, M. C. Petch, J. M. E. Pinto, H. V. Price, D. J. Pugsley, J L. Quintner, K. W. Ranasinha, R. M. Rash, Margaret H. Retter, Mary A. Rossiter, A. H. Sabah, M. H. A. Sacoor, R. R. Shah, D. G. Shand, H. Shazli, Margot Shiner, B. R. Silk, P. Singh, A. S. Sinnatamby, P. H. Smith, C. J. F. Spry, The Honourable Trevor C. B. Stamp, Sabina T. Strich, R. O. C. Summers, P. K. Talukdar, D. R. Thomas, D. A. Toms, B. K. Toone, Joan M. Trowell, Po Yiu Tso, D. S. Tunstall Pedoe, H. D. Tunstall Pedoe, Sheila L. Waller D. C. Webb-Johnson, G. H. Whitehouse, J. A. Whittaker, S. P. Wickremasinghe, A. Wilson, H. I. Winner, R. C. Wofinden, J. K. Young.

Diplomas

The following diplomas were granted, jointly with the Royal College of Surgeons of England:

Diploma in Child Health.—R. G. Wilson.

Diploma in Industrial Health.—D. M. Davies, M. Y. El-Tonbary, J. H. Elwood, W. R. Esson, J. S. Hall, R. A. Mahmoud, S. P. Mukherjee, El S. M. Saad, F. Sattarzadeh, A. A. Tehranian, A. Vassigh.

Diploma in Laryngology and Otology.—G. R. Gokani, S. Hussain, Y. A. Ismail, Ikram-Ullah Khan, I. Z. Khan, J. McNeill, S. N. Mukherjee. H. E. Porte, P. B. Rajput, T. M. S. Saluja, A. N. Samanta, S. M. S. Senanayake, M. S. A. F. Sheta, N. K. R. Shetty, M. P. Thomson, Eileen J. Vega, F. G. Youssef.

Diploma in Medical Radiodiagnosis.—A. V. Mitchell, A. K. Bose.

Diploma in Ophthalmology.—Margaret H. Brennan.

Diploma in Psychological Medicine.—J. C. Ague, A. Ahad, S. A. Ahmed, S. Bal, R. N. Bale, O. Ben-Arie, Sylvia M. Blunden, R. K. Brahma, P. Busapathumrong, J. J. Byng-Hall, W. H. K. Carpenter, M. Chandra, Evelyn M. Cheongvee, R. S. Curnow, C. J. David, P. Dening-Smitherman, N. Destro, W. Dunn, Janet Y. Eccles, D. J. P. Ellis, D. P. Eyre, I. Freedman, J. B. Frost, A. S. R. Goonetilleke, G. W. Goulden, Joyce Gunawardena, Elizabeth J. Harbott, P. W. E. Hayward, D. W. Hill, G. T. Hollingworth, H. Hpay, D. S. James, Annabel M. Jenkins, M. E. D. Johns, A. M. Jukes, C. H. Kelland, J. A. Kohiyar, O. Kyaw, A. Shiu-Hung Leung, Yolande Lucire, N. C. MacKenzie, R. S. Mackinnon, A. L. McKnight, J. E. Miles, N. Mohit-Mafi, A. B. K. Morrall, Elizabeth McQ. D. O'Brien, E. G. Ostler, R. S. Parmar, S. J. Parthev, S. W. Pendaeli, Gwenllian J. Pryce, Ann Rhys, Nancy M. E. Robertshaw, A. H. Robbins, G. Sakalis, Noeline P. Sebaratnam, U. P. Seidel, D. M. Shaw, Margaret R. Sheridan, Nancy K. Shrubshall, G. J. S. Simpson, Ann C. Spark, T. G. Tennent, E. B. Tompkins, P. M. J. Walsh, R. M. C. Welldon, Joy E. West.

Diploma in Public Health.—V. B. G. Amu, S. Datta, Lillian K. L. Lim, A. W. C. Lobban, June D. Mills, Uma K. Nathwani, K. V. Shah, A. K. B. Svindland, D. P. Upadhya, Elsie L. M. Wallace, G. E. P. Williams.

Corrections

In the leading article on the "Changed Character of Osteomyelitis" (29 July, p. 255), Dr. L. R. I. Baker and his colleagues were said to have reported that "other debilitating diseases such as neutropenia secondary to systemic corticosteroid therapy" might precipitate osteomyelitis. This should have read "rare precipitating causes include systemic corticosteroid therapy and hypogammaglobulinaemia, and debilitating diseases such as neutropenia as recently reported by Dr. L. R. I. Baker and his colleagues."

Drs. E. C. Hutchinson and A. J. McCall write: We regret that there is an omission in the summary of our paper on "Stenosis and Occlusion of Vessels in Cerebral Infarction" (29 July, p. 270). The summary refers only to "Occlusion of the cerebral arteries" and should have read: "Occlusion of cerebral, carotid, or vertebral arteries was found only in the infarct group and the incidence of stenosis in this group is significantly higher than in the controls."

All communications with regard to editorial business should be addressed to The EDITOR. British Medical Journal, B.M.A. House, Tavistock Square, London W.C.1. Telephone: 01-387 4499. Telegrams: *Aitiology, London W.C.1.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs.

ADVERTISEMENT AND SUBSCRIPTION ORDERS should be addressed to The Manager at B.M.A. House, London, or at 415 Bourke Street, Melbourne, Victoria, Australia.

MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the British Medical Association, B.M.A. House, London, or to the Scottish Secretary, B.M.A. Scottish Office, Drumsheugh Gardens, Edinburgh.

BRITISH MEDICAL JOURNAL

LONDON SATURDAY 12 AUGUST 1967

Pointers

Ethics of Clinical Experiment: In institutions the Royal College of Physicians favours group approval of projects (p. 429). Leader at p. 385.

Future of General Practice: Conditions for survival debated by G.M.S. Committee (*Supplement*, p. 111) and discussed on this page.

Drug Addiction: Dr. Griffith Edwards relates American practice to British scene (p. 425). Medlars search for papers on Cannabis (p. 430). Letters (p. 435).

Autistic Children: Survey in Middlesex by Dr. J. K. Wing and colleagues reveals that this handicap is twice as common as blindness (p. 389).

Obstructive Airways Disease: Forced expiratory volume estimation showed progressive fall in group of chronic bronchitic patients followed over four years by Dr. Peter Howard (p. 392).

Epidural Analgesia: Drs. D. D. Moir and J. Willocks found that with this management caesarean section rate was only 3.8% in delayed labour due to incoordinate uterine action (p. 396).

Paediatric Neurology: Rectal biopsy as a diagnostic test evaluated by Drs. E. M. Brett and C. L. Berry (p. 400).

Postpartum Anaemia: Iron-dextran by total dose infusion technique improved iron nutrition but retarded folate nutrition in a trial conducted by Dr. J. Metz and colleagues in Johannesburg, S. Africa (p. 403).

Influenza: Scottish schoolchildren showed immunity to type B infection in concurrent A and B epidemics report Dr. J. C. Taylor and colleagues (p. 406).

"Long-acting" Corticotrophin: Dr. M. Friedman found duration of activity of carboxymethylcellulose preparation less than that of gelatin preparation (p. 409).

Rare Cause of Claudication: Symptoms cured by removal of popliteal artery cysts by Mr. G. J. T. Lewis and colleagues (p. 411).

Chronic Thyrotoxic Myopathy: Involvement of respiratory and bulbar muscles (p. 415).

Autoimmune Disease: Dr. G. L. Asherson outlines present state of our knowledge in the first of two "Growing Points" articles (p. 417).

Motion Sickness: Management (p. 421).

Thyrocalcitonin and B.P.: Letter from Professor J. H. Burn (p. 432).

Hospital Doctors: Negotiating machinery (*Supplement*, p. 117).

Future of General Practice

Perhaps the holiday season brought relaxation to the General Medical Services Committee's discussion (reported in the *Supplement*) on the future of general practice, or perhaps a fear, voiced by more than one speaker, of the demise of this branch of medicine served wonderfully to concentrate the Committee's mind. Whichever it was, the subject had a good going over. That no definite conclusions were reached is relatively unimportant. What matters is that in holding the debate the Committee showed that it is getting its priorities right.

General practice has been examined often enough—some would say too often. Certainly too much scrutiny may have aggravated in it a tendency to neurosis if not to hypochondria. In such cases one opinion after another is commonly sought. Had the National Health Service not intervened individual general practitioners over the past 19 years would have had to work out their own salvation. Left to themselves it may be assumed that most, out of sheer necessity if for no other reason, would have made their practices efficient. It will never be known how they would have compared with what exists today. But it can be said that the nationalized medical service, in which individual action is governed largely by collective decisions, has been singularly ineffectual in equipping general practice for a modern role.

The G.M.S. Committee is the recognized spokesman for general practitioners and it voices the profession's views on general practice—two functions that are not always the same. If in the past the Committee has spoken more loudly for general practitioners it was doing what was expected of it by doctors whose professional way of life had been revolutionized and whose livelihood had become dependent almost wholly on the State as a monopoly employer. It took threats of resignation, an arbitration, a royal commission, and the setting up of a special body to review doctors' pay to instil into successive Ministers of Health and their administrations some idea of their responsibilities towards their medical employees. The publicity surrounding these disputes did nothing to enhance the reputation of either side. And neither the Government nor the profession foresaw the intolerable strains that a free medical service available to all on demand was bound to exert on doctors under contract to provide it. New terms and conditions of service for family doctors have now been agreed which, if they are not the final answer, at least dispose of the worst features of the old. General practitioners can now more freely turn their attention to promoting the much-needed reforms in the organization of their work—a pursuit that will enlist the sympathy of the public.

General practice in the future must be such that it can offer keen doctors well trained in medicine a continuing opportunity to practise and to improve their skills. Only when general practitioners can get back into the stream of medicine will they regain their confidence and their branch of practice its prestige. The basic requirements for these are

© *British Medical Journal*, 1967. All reproduction rights reserved.

clear, even if the ways for getting them are not. Firstly, general practitioners must have a sound knowledge of medicine. Secondly, the conditions in which they practise must be such that they can apply their knowledge to the full. Thirdly, they must have time for unhurried clinical work. Fourthly, they must have time to keep up to date. Fifthly, their pay must be enough to ensure for them a fair standard of living. Doctors must in the main learn as they earn, and there is no greater stimulus to keeping abreast than working alongside colleagues in the same and in other branches of medicine. The trend must be towards practice in groups and closer association with hospitals. It is for consideration whether that might lead naturally to a unified medical service based on hospitals and with a common career structure for doctors.

Fears that in the demand for greater efficiency in medical practice the more human needs of the patient may be forgotten are not groundless. One of the finest features of British general practice is the admirable relationships which have bound doctors and patients together. Some of the art in medicine, so essential when science was lacking, is outworn. But modern medicine takes patients as well as doctors anxiously into unfamiliar ground. If courtesy, kindness, and gentleness form part of the art of applied medicine then there will be more need than ever in the future for the exercise of these qualities in the doctor–patient relationship. It is never out of time for doctors to remind themselves that if one of their prime duties is to cure when possible so it is also to comfort always.

Penicillin Encephalopathy

Not long after penicillin first became available it was realized that it could cause epileptic fits if injected directly into the brain or if too concentrated a solution was introduced into the ventricles or the subarachnoid space.[1] [2] This led to the use of diluted solutions in the intrathecal treatment of, for instance, pneumococcal meningitis. And despite long-term treatment in high dosage given by mouth or intramuscular injection to thousands of patients toxic effects on the nervous system have been rare. They have included occasional hypersensitivity reactions and the disastrous results of direct injection into a nerve trunk. The protective action of the blood–brain barrier and the efficiency of clearance mechanisms no doubt prevent toxic levels being reached in or around the nervous tissue. However, if either or both of these mechanisms break down, and if in addition the penicillin is given intravenously in very high dosage, as in the treatment of some relatively resistant Gram-negative organisms, then a much more dangerous situation may arise.

Since 1952 nine cases have been reported of an encephalopathy developing under such circumstances, and H. A. Bloomer, L. J. Barton, and R. K. Maddock[3] have now added four of their own. By describing these in conjunction with six of the previously reported cases they have built up a remarkably uniform clinical picture. All the patients except one were in their sixth to eighth decade, and all had renal insufficiency at the time of the onset of toxic symptoms. Penicillin was being administered intravenously for infections with resistant Gram-negative organisms in a dosage amounting to at least 25 million units per day, and often considerably more. After two to three days the patients' conscious level became depressed, some becoming comatose, and this was rapidly followed by myoclonic jerking, affecting particularly the face, pectoral muscles, and limbs. The jerks were at one time focal, at another generalized, sometimes occurring in bouts resembling a status epilepticus. In between these bouts some patients were able to communicate normally, but in others generalized convulsions also occurred. Phenobarbitone gave little benefit, but liberal and repeated use of paraldehyde controlled the myoclonus. In seven patients on discontinuing the penicillin the syndrome settled down, but coma persisted in the remaining three and death ensued. Few of these patients had any history of disease affecting the central nervous system, and they were not overhydrated, hypertensive, or suffering from electrolyte disturbance. The same authors refer to a similar syndrome, developing under similar circumstances, in a uraemic patient on intravenous sodium cephalothin and point out that renal failure potentiates the toxic effects of chloramphenicol, streptomycin, and polymyxin.

Clearly it is necessary to bear in mind the danger to the nervous and vestibular system of antibiotics given intravenously in high dosage to patients in renal failure, a point emphasized only a few weeks ago in this journal by the studies of J. R. Curtis, S. J. McDonald, and J. H. Weston[4] on the use of gentamicin. Indeed the symptoms may be mistaken for uraemic convulsions rather than for an effect of the treatment. For such patients it is possible that bactericidal levels of the antibiotic may be obtained on lower dosage and with less danger to the nervous system. And if, as it seems, penicillin G is particularly apt to produce such an encephalopathy, other antibiotics might be considered as first choice in treatment. When a preparation is as safe as penicillin there is a danger of becoming a little careless about its use, and this recent study sounds a timely note of warning.

---

[1] Johnson, H. C., and Walker, A. E., *J. Amer. med. Ass.*, 1945, **127**, 217.

[2] Walker, A. E., and Johnson, H. C., *Arch. Surg.*, 1945, **50**, 69.

[3] Bloomer, H. A., Barton, L. J., and Maddock, R. K., *J. Amer. med. Ass.*, 1967, **200**, 121.

[4] Curtis, J. R., McDonald, S. J., and Weston, J. H., *Brit. med. J.*, 1967, **2**, 537.

Rheumatic Fever in Scotland

In 1939 2.6% of London schoolchildren under 15 years of age had had rheumatic fever,[1] though its incidence had been falling for many years. The crude annual death rate from rheumatic fever in England and Wales was 67 per million living in 1901, 23 per million in 1939, and 2 per million in 1965.[2] [3] The fall continues, but the disease still presents important problems, for its victims are mainly children and young adults, and with proper application of our present knowledge it could be largely eliminated. In addition, though new cases are now uncommon, there are still a large number of patients with heart disease resulting from rheumatic fever.

In 1962 the Standing Medical Advisory Committee of the Scottish Health Services Council appointed a subcommittee "to consider the problem of rheumatic fever and rheumatic heart disease in Scotland with particular reference to the incidence of these diseases and the means of prevention." Its report,[4] recently published, gives the facts in Scotland, largely from the mortality returns of the Registrar General for Scotland and the morbidity statistics of the Scottish regional hospital boards and school medical service. A special survey of schoolchildren was attempted but proved unfruitful and was abandoned.

Deaths from rheumatic fever in Scotland fell from 0.9 per 100,000 living in 1953 to 0.3 in 1962 and 0.1 in 1963. The 1962 figure is comparable with that in many "developed" countries—for example, England and Wales, Australia, and the United States. By contrast the figure for Northern Ireland is 1.8. Deaths from chronic rheumatic heart disease show the expected preponderance of females. Scotland had 19.2 per 100,000 deaths of females and 9.5 per 100,000 deaths of males from chronic rheumatic heart disease in 1962, a slight drop from the 1953 figure. The English figures are about the same as the Scottish, in fact slightly higher, but those for Northern Ireland are distinctly lower. Most of the deaths still occurring were of people in the latter half of life. The classical relation between rheumatic fever and poverty, probably overcrowding, is shown by the relatively high frequencies in the Glasgow and Lanarkshire areas.

School medical examinations showed a fall in the incidence of acquired organic heart disease (synonymous with rheumatic heart disease at that age) from 361 per 100,000 examined in 1949 to 95 in 1964. By contrast the incidence of congenital heart disease rose over the same period from 221 per 100,000 to 376. The report ascribes this to greater interest in and better diagnosis and treatment of congenital heart disease in recent years. This is probably true, though difficult to assess quantitatively. Experience with rubella and more recently with thalidomide should warn us of the danger of regarding all congenital anomalies as genetically caused.

In their recommendations on means of prevention the authors of the report advise chemoprophylaxis,[5] the reduction of overcrowding, and the further use of questionaries by the school medical service. The value of chemoprophylaxis is well documented. It is disappointing that the committee did not take the opportunity to find out why it is not more used. Is it lack of information or of enthusiasm by those who should be prescribing it? Or is it fear of producing penicillin-resistant strains of bacteria? Penicillin-resistant β haemolytic streptococci have not been reported in children on prophylactic penicillin,[6] but resistant *Streptococcus viridans* organisms have. Thus subacute bacterial endocarditis with the resistant organisms is a rare possibility.[7] It would also have been interesting to discover to what extent the chemoprophylaxis already prescribed was being actually taken, for reluctance to receive prolonged undramatic prophylaxis may have to be overcome.[8]

Trousseau wrote[9]: "So distinctively characterized a disease as rheumatism ought to have only one remedy; but no such specific is within our reach." We still have no remedy, but prophylactic measures deserve more attention.

---

[1] Bach, F., Hill, N. G., Preston, T. W., and Thornton, C. E., *Ann. rheum. Dis.*, 1939, **1**, 210.

[2] Glover, J. A., *Lancet*, 1939, **1**, 465.

[3] *The Registrar General's Statistical Review of England and Wales for the Year 1965*, Part 1, Tables, Medical, 1967. H.M.S.O.

[4] *Rheumatic Fever in Scotland*, 1967. H.M.S.O.

[5] *Prevention of Initial Attacks and Recurrences of Rheumatic Fever*, revised May 1965, Ministry of Health. H.M.S.O.

[6] Naiman, R. A., and Barrow, J. G., *Ann. intern. Med.*, 1963, **58**, 768.

[7] Garrod, L. P., and Waterworth, P. M., *Brit. Heart J.*, 1962, **24**, 39.

[8] Taranta, A., *Ann. Rev. Med.*, 1967, **18**, 159.

[9] Trousseau, A., *Lectures on Clinical Medicine*, 1871, **4**, 451. New Sydenham Society, London.

Experiments on Man

Traditionally British institutions have tried to meet problems as they arise rather than legislate for them in advance. Thus medical institutions have never sought to lay down hard and fast rules of ethical conduct for research projects on man. True, valuable guidance has been forthcoming from both the Medical Research Council[1] and the World Medical Association,[2] but the final responsibility has always been held to rest squarely on the individual worker undertaking the research. Recently, however, some medical men have claimed that this practice, in Britain and elsewhere, does too little to safeguard the patient's interests, and that stricter controls are necessary.

The U.S. Public Health Service has already acted.[3] Since November it has declined to support investigations unless they have first been approved by a professional committee of the institution concerned. Subsequently the committee continues its scrutiny of the project and gives advice to the research workers. In a lecture in London on human experimentation Professor W. B. Bean,[4] of Iowa, proposed that any research project should be assessed by a group of the doctor's peers, though he insisted that legislation was undesirable. And M. H. Pappworth[5] has suggested that consultation committees should be formed for each large hospital or hospital group, and that these in their turn would be responsible to the General Medical Council and to Parliament.

It is against this background that a recent report by a special committee of the Royal College of Physicians (p. 429) must be viewed. It divides "clinical investigations" into those with diagnostic or therapeutic relevance and those from which the subject cannot expect direct personal benefit. Like previous commentators, the College sees the second as the type more likely to present ethical difficulties. Formal codes, it states, can provide only general guidance, and their application to particular problems is often a matter of opinion. The report rightly rejects rigid or central bureaucratic controls, because these would deter doctors from undertaking research and retard the growth of medical knowledge. Like the U.S. Public Health Service, the College is in favour of scrutiny by committee, proposing that in any institution in which clinical investigations are done a group of doctors should satisfy itself that a project is ethical.

Obviously some kind of guidance should be welcomed by the research worker who is inexperienced or in genuine doubt about the issues concerned. The right of consultation among colleagues is one of the most prized possessions of the professional man. Scrutiny by committee might well prove to be a valuable complement to the statements by the M.R.C. and the W.M.A. But today there must be relatively few research projects which are not first extensively discussed with fellow workers. It is questionable whether the more difficult, basic problems can be solved by a committee—particularly a committee having the deliberately vague terms of reference laid down by the Royal College. Such a system will not deter the very person at whom it is aimed—the man determined to finish a project unrestrained by any scruples. But it could cause appreciable delay to workers whose ethical integrity cannot be questioned. Furthermore, the mere creation of a committee will do little to satisfy those laymen or medical men who have called for more far-reaching action.

---

[1] *Brit. med. J.*, 1964, **2**, 178.

[2] Ibid., 1964, **2**, 177.

[3] U.S. Public Health Service, P.P.O. 128, 1966.

[4] *Lancet*, 1967, **2**, 252.

[5] Pappworth, M. H., *Human Guinea Pigs*, 1967. London.

[6] Biörck, G., *Brit. med. J.*, 1965, **2**, 7.

Two years ago, surveying the next ten years in medicine, Professor Gunnar Biörck[6] prophesied the probable decline of the importance of the individual at all levels—what he termed a change from the "individual-centred" attitude to the "group-centred" one. Some might feel that the College's proposals are a step in that direction. Whatever the system for supervising the ethical aspects of research the ultimate safeguard must be the conscience of the individual worker. Medical teachers have a prime responsibility to instil this into their students and junior staff, particularly by their example. Medical journals can also play a part by refusing to publish papers when the propriety of the work is questionable. It is important, too, that the issues should be publicly and constantly debated. But in the final reckoning the decision about a particular project is one for the doctor concerned, and for him alone.

New Light on Leprosy

Leprosy constitutes one of the biggest health problems in the world, and probably about four million patients in tropical Africa and three million in the Indian subcontinent are suffering from the disease. It is an uncommon condition in Britain and only about 50 new cases are notified each year. Though the acid-fast organisms discovered by Hansen in 1872 were the first bacteria to be aetiologically associated with human disease, scientific proof that *Mycobacterium leprae* is the cause of leprosy is still lacking because Koch's postulates have not yet been fulfilled. Despite numerous attempts by successive generations of research workers the organism has still not been grown in vitro.

In 1960 C. C. Shepard[1] inoculated nasal washings from lepromatous patients with highly positive smears into the footpads of mice and succeeded in producing limited multiplication of *Myco. leprae*. Shepard's results were confirmed and extended by R. J. W. Rees[2] as well as by other workers, and for the first time a technique was available to test antileprosy drugs in animals and to confirm cases of presumed resistance to dapsone.[3] Unfortunately this experimentally produced infection remained localized and multiplication of bacilli occurred only on a small scale; moreover, the histological appearance of the lesions produced was different from that seen in patients with leprosy and the animals suffered no general reaction to the disease.

There are two well-defined forms of leprosy: firstly, diffuse lepromatous leprosy, characterized by unrestrained multiplication of *Myco. leprae*; and, secondly, self-healing tuberculoid leprosy in which few bacilli are present. These differing patterns are probably the result of little-understood differences in the patient's immunological state; indeed, little is known also about the interplay of humoral, cellular, genetic, and other factors in leprosy. Since Shepard's pioneer experiments numerous other attempts to reproduce the disease in animals have been made with varying success, the ultimate object being to achieve progressive infection with systemic dissemination and the production of lesions resembling the disease in man.

Recently Rees and his colleagues[4] have succeeded in reproducing in mice a picture very similar to the human disease. The immunological capacity of these animals was reduced by a combination of thymectomy and total body irradiation before they received injections of leprosy bacilli. Rees and his colleagues describe four main findings. Firstly, there was an appreciably higher yield of bacilli from the footpads and ears of the mice, compared with the untreated animals. Secondly, a year after inoculation dissemination of the initial local lesion had occurred. Furthermore, the infected footpads in some of the animals had become swollen, and the overlying skin was covered with small nodules. Thirdly, the histological picture in the ears, footpads, and cutaneous nerves was comparable with that in skin and cutaneous nerves of patients with lepromatous leprosy. Lastly, intravenous injection of a suspension of bacilli produced for the first time a systemic infection in the ears and footpads of the mice.

These results represent a substantial advance in the experimental study of leprosy, and further progress in this field will be awaited with interest.

---

[1] Shepard, C. C., *J. exp. Med.*, 1960, **112**, 445.
[2] Rees, R. J. W., *Brit. J. exp. Path.*, 1964, **45**, 207.
[3] Adams, A. R. D., and Waters, M. F. R., *Brit. med. J.*, 1966, **2**, 872.
[4] Rees, R. J. W., Waters, M. F. R., Weddell, A. G. M., and Palmer, E., *Nature (Lond.)*, 1967, **215**, 599.

Psychogenic Vomiting

There are many causes of vomiting, itself a common disorder. And because the metabolic effects of depletion of water, electrolytes, and calories may have serious consequences for the patient, it is essential if the cause is not obvious after a complete clinical examination to proceed to full biochemical and radiological investigation.

Exclusion of pyloric and small bowel disease is most important, and this is aided by *x*-ray examination. Gastric lavage is an important preliminary to this, because as well as lessening the risk of vomiting during the examination it allows better visualization with a small amount of contrast material—an important factor if subsequent surgery is required. Toxic causes, such as those associated with uraemia, cortisol deficiency, and hypercalcaemia are usually discovered as a result of determination of serum and urinary electrolytes, blood urea, and blood 11-hydroxy-corticosteroids. The group of cases associated with raised intracranial pressure or lesions of the inner ear and brain stem are not usually misdiagnosed because of the other symptoms which accompany the vomiting—for example, headache, tinnitus, and vertigo—and of the physical signs these disorders produce.

Though many conditions are quickly diagnosed, there are some patients, particularly those with chronic vomiting over a number of years, in whom an adequate diagnosis is never made; the vomiting is then usually labelled "functional." Patients in whom this diagnosis is made are either given sedative drugs or drugs aimed at preventing vomiting, or conveniently a phenothiazine preparation with both properties. It is popularly believed these people do not as a rule develop any of the complications, such as dehydration or hypokalaemia, seen in those with organic vomiting.

According to O. Hill[1] the concept of the psychogenic vomiter remaining in reasonably good health is not always true. He gives examples of severe potassium depletion leading to paralysis of voluntary and smooth muscles in three patients with psychogenic vomiting, and stresses that the paralysis may be considered hysterical unless studies of potassium metabolism are made. A low serum level of potassium, a raised alkaline reserve, and a raised blood *p*H usually substantiate the diagnosis of chronic potassium deficiency. The finding of a low urinary level of potassium excretion, provided the patient does not have renal tubular disease, and of electrocardiographic changes (ST depression and U waves) are further supporting evidence of this state, and a dramatic response to potassium supplements completes the diagnostic picture.

---

[1] Hill, O. W., *Gut*, 1967, **8**, 98.

Patients with psychogenic vomiting are more commonly female than male, and the history may date back to childhood. Psychiatric problems may not be obvious unless a long and exhaustive history is taken, and patients with this disorder will admit to their difficulties only if their problems are sympathetically and carefully handled. A carefully taken history will often disclose conflicts at home and in particular an unhappy relationship with parent or spouse. Hill records that during one interview one of his patients was " overcome by nausea " when the interviewer mentioned the particular member of the family with whom the patient was in conflict. Such a spot diagnosis from the history stresses the important factor that the answer lies in the patient's story. The well-worn phrase " You make me sick " really does have a meaning, for vomiting is a physical expression of unhappiness in a disturbed family environment.

We are used to functional diarrhoea and abdominal pain, functional loss of weight, and anorexia seen at its most extreme in anorexia nervosa. Likewise, functional vomiting can be diagnosed in some cases. Potassium supplements and psychiatric help may bring good health to these troubled patients once organic disease has been excluded.

Ruptured Chordae Tendineae

Chordae tendineae tether the fine edges of the mitral valve cusps to the papillary muscles. Rupture of them presents a syndrome that is being distinguished with increasing accuracy from that of chronic rheumatic mitral insufficiency. Accurate diagnosis is important because the prognosis, indications for surgery, and surgical management of the two are different.

This condition may complicate mild rheumatic insufficiency or may arise in a previously normal heart. The exact mechanism that causes a chorda to rupture is usually not obvious,[1] but subacute bacterial endocarditis and trauma may sometimes be implicated. Myocardial infarction affecting the posterior papillary muscle causes a similar picture to that of rupture of chordae tendineae.[2]

Either or both of the mitral valve cusps may be left unsupported by the ruptured chordae. The centre of the cusp becomes flail and forms a hood that balloons back into the left atrium in systole. In the case of the posterior cusp a jet of blood is directed forwards against the atrial septum and root of the aorta, while in the case of the anterior cusp it is directed backwards.[3] The haemodynamic disturbance is therefore one of acute and severe mitral incompetence in a previously normal or nearly normal heart. The left atrium is small and uncompliant, and the giant " v " wave in systole is transmitted directly to the pulmonary capillaries.

The clinical picture is characterized by the early onset of severe and progressive effort dyspnoea, often with attacks of pulmonary oedema. The physical signs are those of severe mitral insufficiency, but in contrast with chronic rheumatic mitral disease the patient is usually in sinus rhythm, and the pansystolic murmur has a mid-systolic accentuation. The anteriorly directed jet associated with a flail posterior cusp causes radiation of the murmur to the aortic area and carotid arteries, which, combined with the " diamond " shape of the murmur's distribution, may give rise to confusion with aortic valve disease.[3]

The chest radiograph shows the small heart and left atrium and cardiac catheterization the huge " v " wave in the left atrium. An only slightly raised end-diastolic pressure in the left ventricle suggests that the ventricle has not been significantly affected by rheumatic fever or subjected to a long-standing volume overload. Injection of contrast medium into the ventricle confirms the severity of the mitral incompetence but seldom shows the exact valvular lesion.

The prognosis is poor, and, again unlike chronic rheumatic mitral disease, the downhill course rapid. If medical treatment fails to relieve incapacitating symptoms surgery is advisable. Recommendation of surgical treatment is made more readily than in rheumatic disease because the lesion can often be cured without having to use a prosthetic valve, the long-term endurance of which is not yet established.

The operative techniques available are basically of three types—replacement of the entire valve with a prosthesis,[2 4] the formation of artificial chordae from prosthetic material,[5] and plication of the flail cusp so that it becomes supported by the remaining chordae (the McGoon procedure).[6] The substitution of artificial chordae has been almost uniformly unsuccessful because of late recurrence of incompetence,[4] which has left surgical practice divided into two schools. One recommends prosthetic valve replacement in every case, and the other finds the McGoon plication operation satisfactory in both the short and long term. There is no doubt now that the latter is correct, particularly when the posterior leaflet is involved. The surgical results of both procedures are considerably better than those for chronic rheumatic mitral disease, probably because the left ventricle is in much better condition.

Hirsuties

Hirsuties may be defined as an excessive growth of body hair, or hair at body sites other than those of the head, the pubis, and the axillae. The definition is also conventionally restricted to its appearance in women.

One question immediately raised by this definition is, " What is an excessive growth of hair ? " The growth of hair on the body is a graded characteristic, and its degree varies widely among individuals. Moreover, while the amount of growth is generally greater in men than in women, some overlap between the sexes does occur.[1] Theoretically, therefore, it might seem difficult to draw a line between normal and excessive hair growth—though in clinical practice this is not usually a real problem.

---

[1] Sanders, C. A., Scannell, J. G., Harthorne, J. W., and Austen, W. G., *Circulation*, 1965, **31**, 506.

[2] Raftery, E. B., Oakley, C. M., and Goodwin, J. F., *Lancet*, 1966, **2**, 360.

[3] Osmundson, P. J., Callahan, J. A., and Edwards, J. E., *Proc. Mayo Clin.*, 1958, **33**, 235.

[4] Sanders, C. A., Austen, W. G., Harthorne, J. W., Dinsmore, R. E., and Scannell, J. G., *New Engl. J. Med.*, 1967, **276**, 943.

[5] Morris, J. D., Penner, D. A., and Brandt, R. L., *J. thorac. cardiovasc. Surg.*, 1964, **48**, 772.

[6] McGoon, D. C., ibid., 1960, **39**, 357.

Two factors appear to be concerned in the degree of hair growth. One is hormonal, probably related to the amount of circulating androgen. The marked differences in the amount of hair found at various sites of body hair suggests that sensitivity to the action of circulating androgen plays a part in this distribution. The nature of the circulating androgen has been the subject of considerable speculation. Testosterone was an obvious explanation of hair growth in man, but some other explanation had to be found in women. Though some androgenic compounds are secreted by the adrenal gland, with the possible exception of androstenedione they are weakly androgenic, and it seemed doubtful whether they would explain excessive growth of body hair in women.[2] Pointing out that testosterone was much the most potent androgen known, R. I. Dorfman[3] suggested that amounts circulating in the blood undetectable by methods previously available would be enough to cause growth of body hair in women. Subsequently, using a highly sensitive method M. Finkelstein and his colleagues[4] were able to demonstrate that a small amount of testosterone is present in the plasma of women. This was quickly confirmed by a number of other workers, and many authorities now appear to accept testosterone as the physiological androgen in both sexes. The precise site of origin in women remains uncertain. There is evidence for its production by the ovary and the adrenal, and for its production from other androgenic compounds after secretion into the blood stream.

The other factor in hirsuties is constitutional, affected subjects representing one end of a biological range. All other causes of the condition are unusual. They include corticotrophin-producing tumours of the pituitary, congenital adrenal hyperplasia (including a form that first manifests itself at puberty), bilateral adrenal hyperplasia of later life, tumours of the adrenal cortex, various masculinizing tumours of the ovary (including arrhenoblastoma, Leydig, and hilus cell tumours, and the rare hilus-cell hyperplasia[5]), and finally iatrogenic hirsutism produced by giving androgenic compounds in therapy. Nevertheless, hirsuties in much the largest group of patients is of unknown aetiology. No clear-cut biochemical abnormality is demonstrable, though there is indirect evidence that testosterone production is above normal.[2]

Differential diagnosis can be difficult and require specialist assessment. Clinically, age may be an important pointer; thus excess hair appearing at puberty and in the 'teens is likely to be constitutional in origin; appearing in childhood or later life it is probably due to other causes. Pituitary and adrenal causes are usually, though not invariably, associated with a raised excretion of 17-oxosteroids. Pregnanetriol excretion is increased in some forms of congenital adrenal hyperplasia. Normal levels of 17-oxosteroid excretion are found in ovarian forms of hirsutism.

Treatment of the constitutional type of hirsutism is essentially cosmetic, the administration of hormones being ineffective. Shaving, plucking, depilatory creams, removal by wax, and bleaching—all have a role in treatment, though none of them can produce permanent improvement. The most effective and permanent relief is obtained by electrolysis—but this is tedious, time-consuming, and expensive, and it is usually reserved for treatment of the beard area.

---

[1] Ferriman, D., *Proc. roy. Soc. Med.*, 1965, **58**, 802.
[2] Prunty, F. T. G., *Brit. med. J.*, 1966, **2**, 605.
[3] Dorfman, R. I., *Acta. endocr.*, Suppl. No. 50, 1960, p. 211.
[4] Finkelstein, M., Forchielli, E., and Dorfman, R. I., *J. clin. Endocr.*, 1961, **21**, 98.
[5] Joplin, G. F., and Fraser, R., *Proc. roy. Soc. Med.*, 1962, **55**, 999.

Blood Changes in Manned Space Flights

When we see pictures of astronauts preparing to take their part in manned space flights the "medical check" always features prominently. We know too from the daily press that elaborate medical and physiological checks are carried out when the astronauts return to earth. But the results of all this work have hardly been made known at all to the general medical reader. Now C. L. Fischer, P. C. Johnson, and C. A. Berry have published[1] an account of the changes they have detected in red cell mass and plasma volume in the astronauts manning three Gemini space flights. The three flights differed in length: the Gemini IV flight lasted some 97 hours, Gemini V 191 hours, and the Gemini VII flight, which was most extensively studied, lasted 330 hours. In the shortest flight plasma volumes were measured before and after flight, in the 191-hour flight plasma volumes and red cell mass were determined, and in the longest flight these measurements and the survival of red cells, as estimated by the radio-chromium test, were determined.

The results are interesting even if the data were, in the authors' opinion, not as complete as could be wished. "Because of the problems of scheduling, and the safety requirement that no blood be drawn from the astronauts for three days prior to lift-off, all venepunctures were kept to a minimum. The blood studies on recovery were accomplished with makeshift facilities on the recovery aircraft-carriers. The radioisotope studies were only a small part of the demands on the astronauts' time. This precluded the use of more refined techniques and drawing more frequent blood specimens to obtain die-away plots of injected radioactivity for estimation of erythrocyte survival." With these very understandable limitations they were able to show that in the Gemini IV and V flights there was a decrease of plasma volume of the same order as would be expected from similar periods of bed rest. In one of the Gemini VII astronauts, however, the plasma volume actually rose. This may be because the conditions of flight were different, for the Gemini VII astronauts were not only in space for a longer period but also spent some days out of their space suits. The red cell masses also decreased during the period of flight by amounts varying from 7 to 20%. The values returned to normal later; in the Gemini VII crew this took three weeks.

But the most interesting finding is that there was a mild but definite increase of red cell destruction in the crews of the Gemini V craft and in one of the crew of the Gemini VII craft. This mild haemolysis appeared not to be compensated for by an increase in red cell production during the period of the flight. After the flight findings returned to normal in about three weeks. The cause of this mild haemolysis is so far not determined, but it will be studied further, because clearly in long flights such an effect might become important. The detailed data about these results have been described in published reports of the proceedings of conferences held after the flights. Perhaps we can now expect further summary reports of the results of the medical and physiological studies that are of interest to the medical profession everywhere.

---

[1] Fischer, C. L., Johnson, P. C., and Berry, C. A., *J. Amer. med. Ass.*, 1967, **200**, 579.

On 29 July Sir John Peel was re-elected president of the Royal College of Obstetricians and Gynaecologists.

Papers and Originals

Autistic Conditions in Early Childhood: A Survey in Middlesex

J. K. WING,* M.D., PH.D., D.P.M.; N. O'CONNOR,* M.A., PH.D.; V. LOTTER,* PH.D.

Brit. med. J., 1967, 3, 389–392

Kanner (1943, 1957) was the first to point out that one particular syndrome of abnormal behaviour could be separated from the previously undifferentiated group of childhood psychoses. Children with the syndrome (called early infantile autism) were distinguished by three outstanding characteristics: lack of responsiveness to other human beings—that is, "autism"—an insistence on the preservation of sameness in the environment, and an onset in the first two years of life. The children were attractive and alert in appearance, and Kanner believed they were not intellectually subnormal, though their functional abilities were grossly impaired. Their parents in most cases seemed vocationally successful and intelligent.

In retrospect the syndrome had already been brilliantly described by Itard, whose account of the "Wild Boy of Aveyron," written in the early years of the nineteenth century, has never been bettered (Humphrey, 1932). Itard did not agree with Pinel's diagnosis of severe subnormality and evolved an educational technique which is now being rediscovered by psychologists (Lovaas, 1966).

Subsequent writers have not been able to improve upon Kanner's clinical acumen. The best recent descriptions, unmarred by interpretations of what might or might not be going on in the child's mind, are by Rutter (1966a) and Wolff and Chess (1964, 1965). These writers, as well as Creak and Ini (1960), confirmed certain of Kanner's findings, but in children in whom onset was sometimes later than the age of 2 years. Like Kanner, Rutter and Wolff and Chess emphasize the importance of the speech disorder, which in many cases seems impossible to differentiate from the receptive type of developmental aphasia (Pronovost *et al.*, 1966). In Creak's (1963) and in Rutter's (1966b) series, followed up into late adolescence or adulthood, there was no evidence of any development into schizophrenia. Kanner has also pointed out the lack of genetic relationship between schizophrenia and early infantile autism.

No epidemiological study has been made and the prevalence of the condition is unknown. The present survey was undertaken at the suggestion of Dr. Guy Wigley, then Medical Officer of Health for Middlesex and now Deputy Medical Adviser to the Greater London Council. Funds were generously provided by the Middlesex County Council.

Terminology

The term "autistic" can reasonably be applied, descriptively, to a much wider range of conditions than those included in the present series, just as this series contains some children without an onset in early infancy and some who had evidence of gross organic illness. No doubt, eventually, a more exact terminology will be possible which differentiates groups of children. All we can do at this stage is to describe as precisely as possible the basis for selection of a series and to assign a name arbitrarily. The term "autistic condition of early childhood" is used in this article to emphasize that, in addition to those with Kanner's syndrome, some children have been included who showed characteristics which Kanner might have considered a basis for exclusion (notably, an onset between 2 and 5 years, and the presence of gross organic features). However, the other substantial group of conditions, also sometimes called "autistic," in which the main symptom is social withdrawal, in the absence of the central features described here, has been excluded from this series and our conclusions do not refer to them.

Aims and Method

The major aims of the survey were to estimate the prevalence of "autistic conditions in early childhood" in Middlesex and to investigate certain assumptions which had been made about the male : female ratio, birth order, parental occupation and intelligence, and the prevalence of mental disorder in close relatives.

The method has been described in detail by Lotter (1966a). Briefly, the whole population of Middlesex aged 8, 9, or 10 on 1 January 1964 (78,000) was screened by means of a specially developed behavioural questionary based on an amplified and modified version of the Creak Committee's "Nine Points" (Creak *et al.*, 1961). This was completed by school-teachers, occupation centre supervisors, nurses, or parents. Only 1% of the population at risk could not be screened. Special attention was given to children in ordinary schools reported as showing any kind of deviant behaviour which might possibly be part of the syndrome, and to all children known to the local authority as handicapped in any way, physically or mentally.

The 135 children who were selected by the first screening process were then examined and given psychological tests, and further information on behaviour was obtained from a trained informant. As a result of this second screening process 61 children were retained in the series and a detailed social, medical, and developmental history was obtained from the parents, who were also tested on the Progressive Matrices and Mill Hill Vocabulary Scale.

Finally, all the available medical and social records were examined and the 54 children for whom sufficient information was available were divided into three groups according to a standard procedure. The "nuclear autistic group" all showed Kanner's two essential symptoms (but not necessarily the onset pattern) in marked degree—that is, lack of responsiveness to people and insistence on the preservation of sameness. The "non-nuclear autistic group" showed one or other of

---

* Medical Research Council Social Psychiatry Research Unit, Institute of Psychiatry, London S.E.5.

these symptoms but not both: all showed many other characteristics of the syndrome as well. The remaining "non-autistic group" showed only minor fragments of the syndrome.

The screening procedures used at each stage were assessed for reliability in various ways and found to be satisfactory. Several details of the mothers' accounts (motor milestones, birth weight, and presence or absence of certain behaviours) could also be checked, and were found to be reasonably reliable.

Results

Children

Table I shows the prevalence of affected boys and girls aged 8, 9, and 10 on the census day. If the nuclear and non-nuclear groups are combined the overall prevalence is 4.5 per 10,000 children of this age group, about twice that for blindness. There was an excess of boys in all groups, the highest male : female ratio occurring in the nuclear group (2.75 : 1). This is much higher than the highest ratio reported for subnormal children—for example, 1.7 : 1 (Malzberg, 1954).

TABLE I.—*Prevalence on 1 January 1964 Among Children Aged 8, 9, and 10 Residing in the County of Middlesex*

	Boys	Girls	Both sexes	Rate per 10,000
Nuclear autistic group	11	4	15	2·1
Non-nuclear autistic group ..	12	5	17	2·4
Total autistic children	23	9	32	4·5
Non-autistic group	13	9	22	—

Of the 15 children in the nuclear group five had an I.Q. above 55; the rest were untestable or below 55. Five of the 17 non-nuclear autistic children also had I.Q.s above 55. All these 10 children were boys.

Considering the nuclear and non-nuclear groups together, 22 children had a gradual onset from an early age, while 10 had a definite and recognizable setback in development, eight of the latter having a low I.Q. or being untestable at the time of the survey. Delay in motor or speech development (15 out of 32 had marked delay in sitting or walking) was also associated with functional level at the time of the survey.

Nine of the 32 autistic children were mute and a further 10 had only a very limited use of speech: all these were functioning at a low level of intelligence. Five of the eight children whose speech was less severely affected and all the five whose speech was almost normal had intelligence quotients above 55.

There was no evidence of any special likelihood for an autistic child to be first-born (17 out of 32, compared with an expected 15.3) or to have any other specific birth rank. Most autistic children had normal siblings. These was no deviation from the expected frequencies of maternal age at the time of birth of the autistic children. There was no excess of children weighing less than 5½ lb. (2,500 g.) at birth in the autistic children or their siblings, but one-quarter of the children in the non-autistic group were immature according to this criterion. Their siblings had a similar median birth weight but no excess of immaturity.

Significant complications during pregnancy and delivery were reported in 6 out of 28 autistic children for whom medical records were available, compared with 3 out of their 44 siblings (Fisher's exact probability=0.073). Nine (28%) of the 32 autistic children had recorded evidence suggesting neurological abnormality: four had convulsions (three of them beginning in the first year), three had abnormal E.E.G.s, one was deaf (due to rubella), and one had congenital protrusion of one eye and a history of severe coal-gas poisoning. Eleven of the 22 non-autistic children had an equivalent range of abnormalities.

Parents

The distribution of fathers' occupations is shown in Table II. (In the general Middlesex population there were 5.0% in class I, 18.5% in class II, 57.2% in class III, and 19.3% in classes IV and V.) The fathers of nuclear autistic children are particularly likely to have occupations in the upper two classes (9 out of 15).

TABLE II.—*Occupation of Fathers Classified by Social Class*

Social Class	Nuclear Autistic	Non-nuclear Autistic	Non-Autistic
I	5	2	0
II	4	3	5
III	4	9	12
IV, V	2	2	4
Total	15	16	21
Not known	—	1	1

The education of the parents differentiates the three groups of children even more clearly, as can be seen from Table III. The parents' scores on the Mill Hill Vocabulary Test confirm these results.

TABLE III.—*Actual and Percentage Distribution of Parents (Mothers and Fathers Combined) According to Educational Level Reached, For the Three Survey Groups*

Educational level	Nuclear Autistic		Non-nuclear Autistic		Non-Autistic	
	No. (1)	%	No. (2)	%	No. (3)	%
School up to 15 years only	7	25	19	59	34	81
School after 15, or technical or other formal training	12	43	9	28	7	17
Professional education or university graduate	9	32	4	13	1	2
Total	28	100	32	100	42	100

Data not known for two parents in each group.

The adoptive parents (father, graduate; mother, school after 15) were included for one child in the nuclear autistic group.

Significance (1) *v.* (2) *v.* (3): $\chi^2 = 24{\cdot}15$, d.f. 4, $P < 0{\cdot}001$.

Data on the mental health of parents were obtained for 28 of the 30 parents of nuclear autistic children (three admitted to psychiatric hospital), 32 of the 34 parents of non-nuclear autistic children (two admitted to hospital), and 42 of the 44 non-autistic children (one admitted to hospital). None of the parents of autistic children had suffered from schizophrenia, though affective disturbances were not uncommon. Information was also obtained about 283 siblings of 97 parents of children in the three groups, only one of whom was reported to have had an illness resembling schizophrenia (one of the mothers of a nuclear autistic child had a sister who had been admitted to an institution in the United States, and treated by leucotomy).

Thus of 189 parents, uncles, and aunts of the autistic probands, 6 (3.2%) had been admitted to hospital for psychiatric illness, a figure very little different from that for the general population. In addition, out of 86 siblings of autistic children three showed behaviour disorder and an I.Q. in the E.S.N. range, though none had a clear-cut autistic disorder.

Services

The Middlesex County Council (like the Greater London Council, of which it now forms part) was outstanding in its efforts to provide special facilities for handicapped children. It is inevitable, however, that facilities for autistic conditions, where education and medical procedures are still experimental, should lag behind those for children with other handicaps such as blindness or deafness.

In most cases the problem was picked up early enough, though eight children were not referred to specialists till after the age of five, when earlier referral might have been helpful. Roughly half the parents of autistic children were strongly critical of the advice they received about diagnosis, management, and placement when they saw a specialist (see Table IV).

TABLE IV.—*Mothers' Opinions on the Advice Received About Diagnosis, Management, and Placement of Their Autistic Children*

	Diagnosis		Management		Placement	
	No.	%	No.	%	No.	%
Satisfied	6	21	5	17	9	31
Dissatisfied but not strongly critical	9	31	11	38	4	14
Strongly critical	14	48	13	45	16	55
Total	29	100	29	100	29	100

Three mothers could not be interviewed.

These criticisms were not casual or unfair—many mothers made explicit allowance for the special diagnostic and placement difficulties posed by their children. Inadequate guidance about placement attracted most comment—patients felt they were not given sufficient information about the alternatives available and the possible consequences of any decision they might make. Many mothers felt that they should have been given a better account of what was the matter with the child, and nearly half said that they were offered little or no helpful advice about how to manage their children at home. One mother, for example, said that she was told at a paediatric clinic about her 3-year-old son: "He's mentally defective; there is no hope for him whatsoever," and that thereafter she was left on her own, "like a leper, a young mother with a young baby, clueless about what to do. The only advice I ever got was 'let him play in the garden with a ball.'" This might have been an extreme example, but many of the mothers gave accounts which indicated that the medical and social work specialists they saw had not always been able to devote sufficient time to skilled counselling (Lotter, 1966b).

Only 16 of the 32 autistic children were receiving education (half of them in Steiner schools). The rest had not been given a trial in a special education unit; in fact, most had received no schooling at all. The decision to place these children in a non-educational setting cannot therefore have been based on adequate information about their response to skilled teaching methods in classes specially designed to contain and manage their difficult behaviour.

Discussion

The true incidence of autistic conditions in early childhood would be higher than the prevalence estimated from the results of this survey if some children with mild autistic disorders improved to such an extent that they would not have been picked up at the age of 8, 9, or 10 by the methods used. In addition, there may well be an excess mortality in very severely affected children. On the basis of the present results there are about 1,400 children aged 5–14 with the nuclear syndrome in England and Wales and another 1,600 autistic children with a rather less clear-cut clinical picture. Of these 3,000, at least 1,000 have a testable intelligence quotient above 55, and many of the others would undoubtedly benefit from remedial education. These figures compare with 1,400 blind children, and 2,100 partially sighted children, receiving special education, in January 1962, in schools approved by the Department of Education.

The high male–female ratio, the greater likelihood of paranatal complications, the high proportion suffering from physical abnormalities, together with the symptoms of the condition (particularly the speech disorder), suggest an organic aetiology. It is interesting in this connexion that Ingram (1960) also found a high male–female ratio and a substantial proportion of upper-middle-class parents in his series of children with developmental aphasia. The speech difficulties of children with receptive aphasia are closely similar to those found in psychotic children (Rutter, 1966a).

There is clearly no genetic or familial relationship to schizophrenia; a finding which has been paralleled in every well-documented series. Adults resident for long periods in a mental hospital tend to develop the syndrome of institutionalism (Barton, 1959; Wing, 1962) and thus acquire an artificial clinical homogeneity. Autistic children are particularly vulnerable to an understimulating environment (Rutter, 1965), so that if they grow up in an institution they may come to look like other institutionalized patients. These behavioural analogies have no diagnostic implications, and in any case do not hold for children brought up in their own families and given adequate education. None of the positive features of schizophrenia, such as delusions or hallucinations or specific catatonic phenomena, occur in autistic children, nor do they develop in later life (Rutter, 1966b). Adult schizophrenics do not have a history of Kanner's syndrome in childhood nor a raised incidence of autistic conditions in their relatives. There seems to be no reason why the two classes of disorder should be confused.

The unusual distribution of parental occupations requires explanation, but no plausible hypothesis is immediately evident. It has usually been assumed that this distribution is due to educated parents seeking advice more efficiently and refusing to accept a diagnosis of mental subnormality. There is no evidence for this in our data. Since there were 14 autistic children whose fathers had occupations in classes I and II, there would have to be 46 in classes III, IV, and V in order to achieve the same distribution as in the general population, whereas only 17 were found. It is extremely unlikely, in view of the very thorough search of local health and education authority records, that as many as 29 children in classes III–V could have been missed.

Rimland (1964) argued that the child with infantile autism might be a homozygote for high intelligence but carry a high vulnerability to various noxia during pregnancy and delivery. In the past, explanations have been based on an assumption that educated women are less likely to give their children expert and loving care during the first few months of life. There is little sociological evidence for this view, and in any case most educated women do not have autistic children; indeed, most parents of autistic children also have normal children. Finally, there is no evidence from any of the numerous series of children who were *really* deprived of maternal love during early infancy—for example, those raised in unsuitable institutions from birth—that such conditions produce a high incidence of childhood autism. The aetiology of the condition therefore remains obscure, though one report suggests that tryptophan metabolism may be abnormal (Heeley and Roberts, 1965).

Services leave a great deal to be desired, though most of the problems experienced by parents in the survey were also mentioned by the parents of children of severely subnormal intelligence (Tizard and Grad, 1961). The special nature of the disorder, however, gives some of the difficulties extra weight. The child may appear alert and attractive in spite of his odd behaviour. When the specialists seem puzzled and offer little helpful advice, and adequate educational and other services are not available, the parents may become profoundly isolated. The recent special units that have been set up in the London area (for example, Elgar, 1966) should help to relieve this problem, as will the growing experience of paediatricians, psychiatrists, and social workers. The parents should, of course, always be put into touch with the appropriate voluntary organization (the National Society for Autistic Children).

Summary

A survey of children aged 8, 9, and 10 resident in the former County of Middlesex on 1 January 1964 showed that 4.5 per 10,000 had "autistic conditions of early childhood." This means that there are about twice as many autistic children in the country as there are blind children. There was a raised male–female ratio but no special birth order. Autistic children were more likely to have suffered from complications during pregnancy and delivery than their siblings, and one-half had marked delay in motor milestones. It was confirmed that the parents of autistic children (particularly those in the "nuclear group") were likely to be above average in educational attainment, occupational level, and intelligence. There was no evidence for a genetic or clinical relationship between early childhood autism and schizophrenia. Clinical and educational services still leave much to be desired.

REFERENCES

Barton, R. (1959). *Institutional Neurosis.* Bristol.
Creak, M., and Ini, S. (1960). *J. Child Psychol.*, 1, 156.
—— *et al.* (1961). *Brit. med. J.*, 1961, 2, 889.
Elgar, S. (1966). In *Early Childhood Autism,* edited by J. K. Wing, p. 205. Oxford.
Heeley, A. F., and Roberts, G. E. (1965). *Develop. Med. Child Neurol.*, 7, 46.
Humphrey, G., and Humphrey, M. (1932). Translation of *The Wild Boy of Aveyron*, by J. M. G. Itard. New York.
Ingram, T. T. S. (1960). In *Child Neurology and Cerebral Palsy* edited by M. C. O. Bax, E. Clayton Jones, and R. C. Mac Keith. Oxford.
Kanner, L. (1943). *Nerv. Child*, 2, 217.
—— (1957). *Child Psychiatry*, 3rd ed. Springfield, Illinois.
Lotter, V. (1966a). *Soc. Psychiat.*, 1, 124, 163.
—— (1966b). In *Early Childhood Autism*, edited by J. K. Wing, p. 241. Oxford.
Lovaas, O. I. (1966). Ibid., p. 115.
Malzberg, B. (1954). *Amer. J. ment. Def.*, 58, 301.
Pronovost, W., Wakstein, M. P., and Wakstein, D. J. (1966). *Exceptional Children*, 33, 19.
Rimland, B. (1964). *Infantile Autism.* New York.
Rutter, M. L. (1965). In *Children with Communication Problems*, edited by A. W. Franklin. London.
—— (1966a). In *Early Childhood Autism*, edited by J. K. Wing, p. 51. Oxford.
—— (1966b). Ibid., p. 83.
Tizard, J., and Grad, J. C. (1961). *The Mentally Handicapped and their Families.* London.
Wing, J. K. (1962). *Brit. J. soc. clin. Psychol.*, 1, 38.
Wolff, S., and Chess, S. (1964). *Acta psychiat. scand.*, 40, 438.
—— —— (1965). *J. Child Psychol.*, 6, 29.

Evolution of the Ventilatory Capacity in Chronic Bronchitis

PETER HOWARD,* M.A., B.M., M.R.C.P.

Brit. med. J., 1967, 3, 392–395

The forced expiratory volume (F.E.V.) and its derivative the indirect maximum breathing capacity (M.B.C.) are used as indices of airways obstruction in patients with chronic obstructive airways disease. Prevalence studies of particular populations or groups of normal subjects have shown the F.E.V. to decline linearly with age. It is agreed that the ventilatory capacity declines further with progression of obstructive airways disease, but little information is yet available about the rate and mode of decline, particularly in relation to the phase of illness. The results of a long-term follow-up study are now reported in which the changes in the F.E.V.$_{0.75}$ have been carefully observed in a group of patients with established chronic obstructive airways disease attending an outpatient clinic. Particular attention has been paid to the long-term changes in individual patients and also to the effects of acute exacerbations of symptoms. It was hoped that the information might lead to a better understanding of the progress of airways obstruction, which is generally believed to be the chief cause of disability in chronic bronchitis.

Methods of Study

A study was made of 112 men and 13 women attending the clinic on account of frequent exacerbations of chest illness or breathlessness, usually the latter. Patients were included who had been followed regularly for at least two years, and this was the major criterion for admission to the study. In 1962 the patients answered the Medical Research Council (1960) short questionary on respiratory symptoms. All except two patients admitted to a productive cough, but a further 10 thought it occurred less often than on "most days for three months of the year" (grade 0). Of these 10 patients, five had attacks of bronchial asthma defined as sudden attacks of reversible severe wheezing and breathlessness not associated with cardiovascular disease, one had hay-fever in the summer months, and four said they experienced frequent attacks of chest illnesses but denied the persistent production of sputum between attacks. Twenty-four patients said they produced sputum only in the mornings (grade 1) and 89 said that it was raised both in the mornings and throughout the day (grade 2). Therefore 123 patients could be classified as cases of chronic bronchitis of some severity (Medical Research Council, 1965). One hundred complained of breathlessness which limited them to their own pace on the level or of more severe disability, and only four denied any breathlessness. Of the 125 patients, 106 had suffered at least one attack of chest illness in the previous three years, but most of them experienced more frequent exacerbations than this. Three patients have developed congestive cardiac failure (cor pulmonale) during the period of observation.

The patients usually attend the clinic at monthly intervals or less in the winter-time and every two or three months in the summer. In the four years up to the end of 1965 the F.E.V.$_{0.75}$ and the forced vital capacity (F.V.C.) were measured by means of a Poulton spirometer (McKerrow, McDermott, and Gilson, 1960) on each visit by one of three trained technicians. The F.E.V. was read directly off this instrument as the indirect M.B.C. in litres per minute. Five serial recordings were taken, the result being recorded as the mean of the best three readings. Before 1962 the same measurements were made annually with a Collins–Gaensler spirometer. From this machine the absolute F.E.V.$_{0.75}$ was measured, corrected for temperature, and then multiplied by 40 to derive the indirect M.B.C. In a comparison of the two instruments no significant difference was found between consecutive readings on the same patients ($t=16.6$, $P<0.001$).

Since the initiation of these studies the indirect M.B.C. has become a less popular method of recording this type of measurement. Thus in the analysis of the data the figures have been divided by 40 to convert them to the F.E.V.$_{0.75}$ as they were originally measured. Though formulae are available for

---

* Department of Medicine, University of Sheffield, the Royal Hospital, Sheffield 1. Present address: Department of Environmental Medicine, Johns Hopkins University, 615 North Wolfe Street, Baltimore, Maryland 21205, U.S.A. Requests for reprints to Sheffield.

converting F.E.V.$_{0.75}$ to F.E.V.$_1$ this was not done in the present study, as such a conversion cannot easily be made without criticism (Pearson, Ashford, Brown, and Morgan, 1966). A regression of the change in F.E.V.$_{0.75}$ with time (in months) was calculated for each patient together with the standard deviation about the regression and the standard error of the slope. The connotation F.E.V. is used in this paper to represent F.E.V.$_{0.75}$. Ninety-seven patients have been followed for more than four years and their measurements were taken with both instruments. In 28 patients the Poulton spirometer alone was used.

At each attendance the patient was examined and treatment prescribed. Most patients were treated with aerosol sprays of isoprenaline and/or adrenaline and atropine and an oral bronchodilator drug such as theophylline monoethanolamine, choline theophyllinate, or orciprenaline. Courses of tetracycline (1 g. daily for seven days) or ampicillin (1 g. daily for seven days) were dispensed to treat individual acute exacerbations of symptoms as they occurred. In the past three years extra courses have been given as reserve supplies for the patient to take himself as soon as he felt that a further exacerbation was developing. A small number of patients also received prednisolone for associated bronchial asthma or chlorothiazide diuretics for congestive heart failure.

Results

The mean age of the patients was 60.7 (S.D.= ±9.86) years and Table I shows the age distribution. The mean period of follow-up was 7.1 years (range 2–13 years) and the mean initial F.E.V. 1.2 (S.D.= ±0.165) litres. Fig. 1 shows the distribution of the initial F.E.V. The regression coefficients were expressed in litres per year, and only four out of the 125 patients had a positive regression coefficient. The mean regression coefficient for the whole group was −0.0834 (S.D.= ± 0.0667) litre per year. Fig. 2 shows the distribution. The mean standard deviation about this slope was ±0.162 litre and the mean standard error of the slope ±0.0221 litre per year. The death rate has been followed since 1962, and up to the end of 1965 13 patients had died. Their mean age at death was 64.7 years and their mean regression coefficient −0.0930 litre per year, values which were slightly larger than those of the group as a whole.

TABLE I.—*Age Distribution of the* 125 *Patients*

Age in 1965	<39	40–49	50–59	60–69	70–79
No. of patients ..	5	7	33	62	18

The regression coefficients were plotted against age in 1965, the mean F.E.V. (calculated from the sum of all measurements divided by the number of measurements on each individual), and the years of follow-up. A statistically significant regression was obtained with age in 1965 (t=2.57, P<0.02) and with the mean F.E.V. (t=4.95, P<0.001). The regression equations were:

$$y = -0.00154 \text{ age} + 0.0101$$

$$y = -0.0648 \text{ mean F.E.V.} - 0.0308$$

The regression coefficients were plotted on the ordinate. Thus the rate of fall of ventilatory capacity showed a small decline with age in this particular group of hospital patients. The rate of fall was also related to the mean F.E.V. The mean point was used rather than the initial F.E.V. as the use of the latter is apt to give spurious correlations (Oldham, 1962). The mean F.E.V. was not related to age (t=0.6, P>0.6) and was therefore an unlikely explanation of the age effect. Fig. 3 shows the plot of regression coefficient against years of follow-up, for which a regression was not calculated on account of the changing

FIG. 1

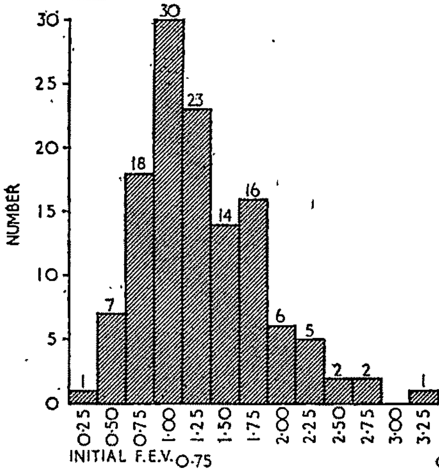


FIG. 2

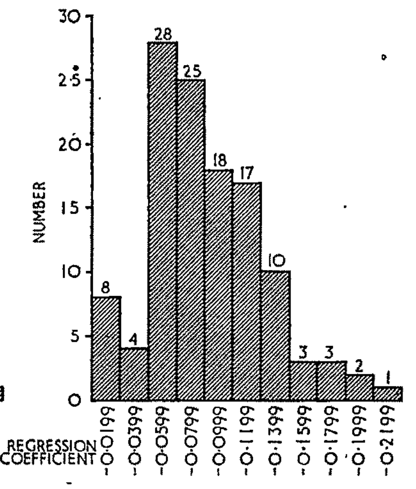


FIG. 3

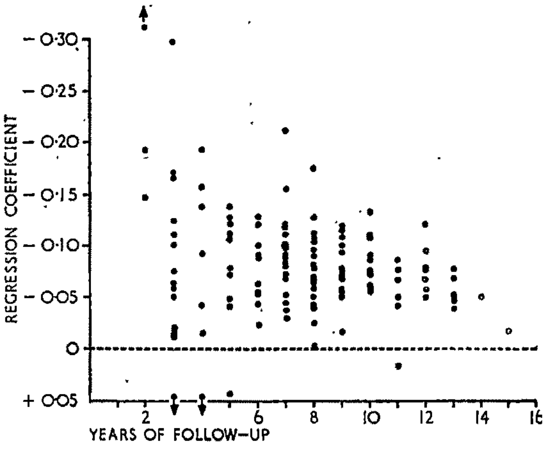


FIG. 4

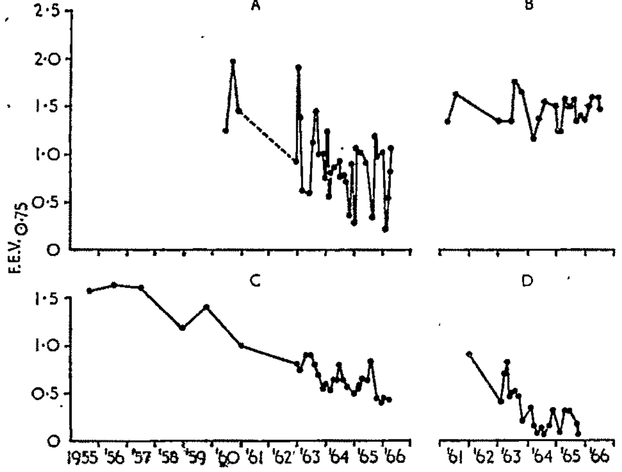


FIG. 5

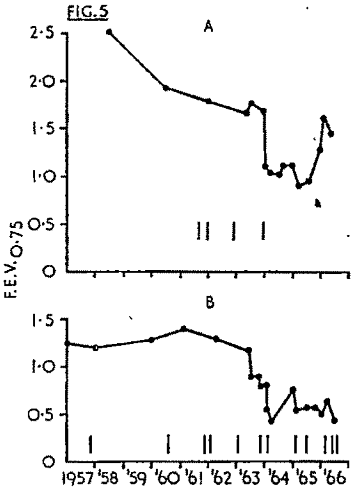


FIG. 1.—Distribution of the initial F.E.V.$_{0.75}$ in the 125 patients. FIG. 2.—Distribution of the regression coefficients. All patients with a negative coefficient are included except two with values of −0.2958 and −0.5658 respectively. The four patients with positive coefficients are also not included. FIG. 3.—Plot of regression coefficient against years of follow-up. FIG. 4.—A selection of F.E.V. curves. A, Bronchial asthma. B, Chronic bronchitis. C, Chronic bronchitis, showing a marked seasonal variation in the past three years. D, Chronic bronchitis with severe emphysema. The dots on the abscissa represent 1 January of each year. FIG. 5.—F.E.V. curves of two patients who have shown sharp alterations of ventilatory capacity. The dots on the abscissa represent 1 January of each year and the short vertical lines the time of occurrence of an exacerbation for which a course of antibiotics was given.

variance. The variance would be expected to be higher in those followed for only a short period, simply on account of the smaller number of observations possible, but also because of the tendency for those with higher rates of decline of ventilatory capacity to die or leave the clinic after being followed for only short periods. This may also be a factor in the explanation of the reduced rate of fall of ventilatory capacity with increasing age.

Inspection of the individual curves, particularly from the past four years when more measurements were available, revealed several points of interest. Seven patients (Fig. 4A) showed wide fluctuations of the F.E.V. All of these patients had bronchial asthma, and despite the large swings of F.E.V. many had large regression coefficients. In the remainder, forming the majority of patients and excluding those who improved, the F.E.V. declined at various rates with a variable fluctuation about the regression. Fig. 4B illustrates this picture. The "fluctuation" in 25 patients showed a seasonal variation, with troughs of low F.E.V. appearing in the winter months and the peak values in the summer (Fig. 4C). In half of the total number of patients no specific pattern to the variations could be discerned (Fig. 4D), but their amplitude remained relatively constant in any individual.

Disregarding the seasonal and spontaneous fluctuations, the rate of decline of F.E.V. in any one patient tended to remain constant for long periods, in some throughout the whole of the period of their observation. For example, in 19 out of 28 patients who had been followed for more than 10 years a straight line could easily be drawn by eye through the values obtained throughout the whole period. However, in a number of cases, excluding the "asthmatic" curves, there occurred sharp falls of F.E.V., arbitrarily defined as a loss of F.E.V. within six months or less, greater than two standard deviations from the regression. Twenty-one such incidents have occurred in 19 patients during the past four years. Fig. 5 gives two examples. Seven recovered completely within a year, usually within three months, three recovered between one and two years (Fig. 5A), four made a partial recovery, and in seven there was no recovery at all. The curves of the last-mentioned group thus showed a downward step, and the path of the regression usually intersected the step some way about its mid-point. The ruling of a departure by two standard deviations from the regression had to be relaxed on this account in some of these cases, but in all a step in the function curve was clearly visible. Fig. 5B was such a case. The pattern of the F.E.V. curve has continued after the sharp fall in the same manner as before. The patients showing the sharp falls of ventilatory capacity did not differ clinically, as judged by the replies to the M.R.C. questionary, from those who did not show these changes.

The cause of the 21 sharp falls of function was investigated, and Table II shows the various illnesses which could be associated with them in time. In only 10 patients could an acute exacerbation, however mild, be implicated, and in six no change in clinical status had apparently occurred. Some even maintained that they were as well as they had ever been. Though the sharp falls of function appeared slightly more often in the winter months (Table III), there was no significant seasonal factor. Smoking habits were not recorded in detail at the time of occurrence, but appeared to be a factor in that replies from the questionaries completed in 1962 (Table IV), indicated that those patients showing the sharp functional alterations were more persistent smokers than those who did not have these changes.

Table II.—*Illnesses Associated with the 21 Sharp Alterations of Ventilatory Capacity in Time*

Illness	No.
Acute exacerbation	10
Peritonsillar abscess	1
Cold	1
Hay-fever	1
General condition worse but no clear evidence of an exacerbation	2
None	6

Table III.—*Seasonal Occurrence of the 21 Sharp Alterations of Ventilatory Capacity*

Month	No.	Month	No.	Month	No.
January	1	May	—	September	2
February	2	June	2	October	2
March	2	July	3	November	—
April	4	August	—	December	3

Table IV.—*Smoking Habits in 1962 of Patients Who Subsequently Had Sharp Alterations of Ventilatory Capacity Compared with Smoking Habits of Those Who Did Not Exhibit These Changes. Figures in Parentheses are Percentages*

Patient Group	No.	Cigarette Smokers		Ex-Smokers	Pipe Smokers	Non-Smokers
		0–14 Daily	15+ Daily			
Patients with sharp falls	19	11 (58)	4 (21)	3 (16)	—	1 (5)
Remaining patients	106	34 (33)	11 (10)	43 (41)	8 (7)	10 (9)
Total	125	45 (36)	15 (12)	46 (37)	8 (6)	11 (9)

The relation between acute exacerbations of symptoms and the rate of fall of the F.E.V. was examined further. In each patient the time of occurrence during the past four years of acute exacerbations for which antibiotics were given was marked on the F.E.V. curve. The majority showed no more than a minor fall of the F.E.V. The regression coefficients were plotted against the number of courses of antibiotics prescribed per year in the past four years for all patients, and the relation was just significant at the 5% level of probability ($t=2.04$, $P<0.05$).

Finally, the change in F.E.V. was compared with the change in F.V.C. in those patients showing the sharp falls of function. F.E.V./F.V.C. and F.V.C. were plotted against time, and in 16 patients out of the 19 both fell, indicating that the decline in F.E.V. could be partly accounted for by a fall in vital capacity. In a number of the remaining patients picked at random the same trend was evident throughout the period of follow-up.

Discussion

The patients in this study are a highly selective sample of those with chronic obstructive airways disease. Most of them were referred to the clinic only when they became breathless, when they became unable to work, or when their symptoms were difficult to control. Many of these patients had the most severe forms of the disease. A minimal period of follow-up of two years, preferably three, was arbitrarily fixed in order to accumulate enough observations to plot a reasonable regression. This policy discriminated against a few patients with steep regressions who presented to the clinic with a low F.E.V. (<1). The death rate was underestimated, as it was not recorded before 1962 and patients followed up from that period would constitute a survivor population. Both of these factors, however, would tend to lead to an underestimation of the mean regression coefficient. Despite these difficulties, several important features are shown. Firstly, the average rate of fall of ventilatory capacity is very much higher than other figures reported so far; secondly, the rate of decline is very variable even in patients with established disease, some patients having particularly steep rates of fall; and, thirdly, though most patients appear to lose function in a reasonably linear manner, a number exhibit sharp drops which do not recover. These points are discussed below in more detail.

The progressive deterioration of function occurred in all but four patients. It could not be accounted for by the ageing of the population, and it continued despite careful symptomatic treatment administered in the clinic. The mean regression coefficient of -0.0834 litre per year is larger than other reported figures. Higgins and Oldham (1962), in a five-year follow-up of miners and non-miners in the Rhondda Fach, found an overall loss of 0.0472 litre per year. Age correlations from prevalence studies have been used to calculate the rate of deterioration of ventilatory capacity. Baldwin, Cournand, and

Richards (1948) thus found a fall of 0.013 litre per year (calculated from the direct M.B.C.), Kory, Callahan, Boren, and Syner (1961) a fall of 0.025 litre per year (calculated from F.E.V.$_{1}$), and Ferris, Anderson, and Zickmantel (1965) a fall of 0.024 litre per year (also calculated from F.E.V.$_{1}$), all in healthy males after standardizing for body size. Preliminary figures from a companion study of a slightly younger male group of 142 workers from a Sheffield steel and chemical plant followed since 1956, using the same spirometers, reveal a mean regression coefficient of the order of -0.03 litre per year up to the end of 1965. The expression of the decline in ventilatory capacity as a regression coefficient is a useful index of the overall decline and one measure of the severity of the disease.

Though a detailed follow-up of the ventilatory tests has been in progress for only four years, it would appear that the path of the mean F.E.V. does fall in a reasonably linear manner in many patients for periods of at least several years. The slope is very variable, but sufficient clinical and physiological information is not yet available to compare and contrast patients with differing rates of deterioration of ventilatory capacity. The sharp alterations of ventilatory capacity seen in some patients were surprisingly infrequent, as it was expected that the exacerbations of the disease would have had a much greater effect on the F.E.V. curve. It is true that in outpatient clinics attendances may have been missed at the peak of illness and some sharp falls therefore gone unnoted. However, many exacerbations were observed in the acute phase and most at some stage during recovery, and still significant decreases of F.E.V. were relatively infrequently found, and closer study is warranted.

The significance of the sharp falls of function that were observed cannot yet be fully evaluated. In particular, information is needed to determine how often they occur during the natural history of the disease, and whether they develop in persons with completely normal function. The findings suggest that chronic bronchitis is associated with some pathological process which is responsible for a steady erosion of ventilatory capacity, but that the same or a different process exacerbates the decline at certain times. Since a complete recovery of function was observed in only half of the instances where steep falls occurred, the latter must contribute to at least part of the overall decline.

Several factors are thought to play a part in the cause of chronic bronchitis, such as smoking, atmospheric pollution, and bronchial infection. Tobacco consumption has not been studied in detail, but it was clear from the replies given to the questionary in 1962 that those who subsequently showed the steep falls of ventilatory capacity were more persistent smokers than those who exhibited a steady deterioration. It is hoped, at a later date, to prepare a more detailed analysis of the relation between smoking habits and the decline of ventilatory capacity.

The significance of bronchial infection is difficult to assess. The acute exacerbations so characteristic of the disease have been attributed to bronchial infection on clinical grounds and by the isolation of pathogenic organisms such as *Streptococcus pneumoniae* and *Haemophilus influenzae* from the sputum. Pathologists looking at the terminal phases of the disease have suggested that bronchial infection plays an important part in the development of destructive lung changes (Leopold and Gough, 1957; Reid, 1961). In controlled trials of the prophylactic use of antibiotics the total period of disability from exacerbations has been found to be reduced but the number of exacerbations unaffected (Murdoch, Leckie, Downie, Swain, and Gould, 1959; Francis and Spicer, 1960; Francis, May and Spicer, 1964). This suggests that the acute exacerbations are initiated by factors unrelated to bacterial infection but may be prolonged by its secondary effects.

Whatever the causes of the acute exacerbation, this study shows that the majority had very little effect on the individual F.E.V. curves but there was some correlation between the rate of deterioration of function and the number of courses of antibiotic prescribed. Though the establishment of a correlation does not prove a causal relation, it is possible that bronchial infection is a factor in the steady erosion of ventilatory capacity. But in a controlled trial of chemotherapy undertaken by the Medical Research Council (Fletcher, 1965; Medical Research Council, 1966) no difference was found in the deterioration of function between patients showing a large number of respiratory illnesses and frequent periods of mucopurulent sputum and those without these features. In a quarter of the patients in the present study who exhibited sharp falls of ventilatory capacity clinical evidence of a coincident exacerbation could not be obtained. Thus, although bacterial infection recognizable on clinical grounds and frequent exacerbations of disease may contribute, they do not seem to be essential to the decline of ventilatory capacity.

Summary

A follow-up study of the F.E.V.$_{0.75}$ in 125 patients with chronic obstructive airways disease attending an outpatient clinic is presented. The mean age of the group in 1965 was 60.7 years and the mean period of follow-up 7.1 years. The mean rate of fall of F.E.V. expressed as a regression coefficient was 0.0834 litre per year and considerably greater than that so far reported in normal subjects or other populations.

In the past four years a detailed study has been made of all patients whose F.E.V. was measured on every attendance at the clinic. Several varieties of F.E.V. curves are described. The size of individual regression coefficients was very variable even in patients with severe disease. There was some relation between the size of the regression coefficient and the number of acute exacerbations of the disease requiring antibiotic therapy, but, in individual plots, acute chest illnesses in the majority had no more than a minor effect on the F.E.V. curve. Yet on 21 occasions in 19 patients in the past four years steep falls of the F.E.V. (a loss greater than two standard deviations from the regression occurring within six months or less) were observed. One-quarter of these episodes could not be associated with any chest illness, however mild, and in only half was a good recovery of function observed. These results are discussed in regard to the aetiology of obstructive airways disease.

I am grateful to Professor C. H. Stuart-Harris for his encouragement and constructive criticism of this work. I also thank Miss Victoria Home, who made most of the measurements of forced expiratory volume. This work was supported in part by grant No. H.E. 04775 from the National Heart Institute, U.S. Public Health Service, and in part by the Board of Governors of the United Sheffield Hospitals.

REFERENCES

Baldwin, E. de F., Cournand, A., and Richards, D. W. (1948). *Medicine (Baltimore)*, 27, 243.

Ferris, B. G., Anderson, D. O., and Zickmantel, R. (1965). *Amer. Rev. resp. Dis.*, 91, 252.

Fletcher, C. M. (1965). In *Bronchitis 2*. International Symposium held at Gröningen, 1964, edited by N. G. M. Orie and H. J. Sluiter. p. 372. Springfield, Illinois.

Francis, R. S., May, J. R., and Spicer, C. C. (1964). *Brit. med. J.*, 1, 728.

—— and Spicer, C. C. (1960). Ibid., 1, 297.

Higgins, I. T. T., and Oldham, P. D. (1962). *Brit. J. industr. Med.*, 19, 65.

Kory, R. C., Callahan, R., Boren, H. G., and Syner, J. C. (1961). *Amer. J. Med.*, 30, 243.

Leopold, J. G., and Gough, J. (1957). *Thorax*, 12, 219.

McKerrow, C. B., McDermott, M., and Gilson, J. C. (1960). *Lancet*, 1, 149.

Medical Research Council (1960). *Brit. med. J.*, 2, 1665.

—— (1965). *Lancet*, 1, 775.

—— (1966). *Brit. med. J.*, 1, 1317.

Murdoch, J. McC., Leckie, W. J. H., Downie, J., Swain, R. H. A., and Gould, J. C. (1959). Ibid., 2, 1277.

Oldham, P. D. (1962). *J. chron. Dis.*, 15, 969.

Pearson, N. G., Ashford, J. R., Brown, S., and Morgan, D. C (1966). *Amer. Rev. resp. Dis.*, 94, 64.

Reid, L. (1961). In *Bronchitis*, International Symposium held at Gröningen, 1960, edited by N. G. M. Orie and H. J. Sluiter, p. 137. Springfield, Illinois.

Management of Incoordinate Uterine Action under Continuous Epidural Analgesia

DONALD D. MOIR,* M.B., CH.B., F.F.A. R.C.S., D.A., D.OBST.R.C.O.G. ; JAMES WILLOCKS,* M.D., M.R.C.O.G.

Brit. med. J., 1967, 3, 396–400

British anaesthetists and obstetricians have made little use of epidural analgesia in obstetrics. From time to time small series have been reported by British workers who have used caudal or lumbar epidural analgesia in incoordinate uterine action (Galley, 1949 ; Johnson, 1952, 1954, 1957 ; Arthur and Johnson, 1952 ; Ball and Chambers, 1956 ; Tunstall, 1960) and in pre-eclampsia and eclampsia (Bryce-Smith and Williams, 1955 ; Scott, 1955).

In contrast, epidural techniques are extensively used for obstetric analgesia in many North American centres (Bush, 1959 ; Hingson *et al.*, 1961 ; Hellmann, 1965 ; Moore, 1966) following on the pioneer work of Hingson and Edwards (1943). The reasons for this difference in practice are several.

Firstly, British obstetric opinion is generally in favour of encouraging spontaneous delivery where this can safely be achieved, and most spontaneous deliveries are conducted by midwives in hospital and at home. Epidural analgesia, because it produces perineal anaesthesia and so abolishes the reflex expulsive efforts of the second stage of labour, is usually associated with a high forceps delivery rate.

Secondly, epidural analgesia may be required at any time of the day or night, and its safe conduct necessitates the presence of an anaesthetist experienced in the technique for as long as the block is maintained. This demands a 24-hour obstetric anaesthetic service by experienced anaesthetists who are not committed to other duties. This service exists in few hospitals in Great Britain today, though in our experience the benefits are substantial and not confined to the administration of epidural analgesia.

Finally, there exist anaesthetists and obstetricians who believe, despite impressive evidence to the contrary, that epidural analgesia is a difficult and dangerous technique. With experience the success rate can approach 100%, particularly in younger women without spinal deformities or the ossification of the supraspinous ligament which may develop in the elderly. The potential dangers of epidural analgesia should not be minimized, but with awareness of these dangers and constant attention to details in technique and management by a team of anaesthetists, obstetricians, and midwives the method is acceptably safe. The vast experience of others confirms this safety. Norris *et al.* (1960) reported over 9,000 epidural blocks in labour, and Hellmann (1965) reported over 26,000 cases. In neither series was there any foetal or maternal mortality attributable to epidural analgesia, and the incidence of complications was very low. Continuous observation is essential for safety, and an extra burden is thereby placed on nursing staff, who, in our experience, accept this willingly when convinced of the value of the procedure.

It is not our intention, however, to advocate the routine adoption of epidural analgesia for relief of pain in normal labour. In the Queen Mother's Hospital, Glasgow, continuous lumbar epidural analgesia is used in just over 4% of all labours and, in addition, "single-shot" epidural analgesia is used for 9% of mid-cavity forceps deliveries. During the last two and a half years 246 continuous epidural blocks have been given to patients in labour. In the 100 cases reported here the indication was incoordinate uterine action. The present review was undertaken to assess the contribution made by epidural analgesia to the management of these cases.

Anaesthetic Technique

The lumbar rather than the caudal approach to the epidural space is preferred because of the higher success rate, the lower dose of local anaesthetic drug, and because the skin of the lumbar region seems less open to contamination than the skin over the sacral hiatus. The caudal approach is used when abnormalities of the lumbar spine are present.

Lumbar epidural puncture is performed with the patient in the sitting position to encourage spinal flexion, which may be difficult to achieve in the lateral position because of the gravid uterus. A 16 S.W.G. Tuohy needle is used and the epidural space is identified by the loss-of-resistance technique. A plastic catheter (Lee, 1962) with a blunt tip (Moir and Hesson, 1965) is then advanced into the epidural space, the needle is withdrawn, and the catheter is connected to a sterile plastic 50-ml. syringe filled with local anaesthetic solution. This syringe is now sealed inside a transparent bag (Cole, 1964) and strapped to the abdominal wall. This system allows top-up injections to be given without scrubbing-up and seems to avoid the risk of accidental overdosage associated with at least one of the drip techniques (Edmonds-Seal, 1964). Free mobility is permitted as there is no infusion apparatus connected to the patient.

The drug used is 2% lignocaine with 1:200,000 adrenaline added. Doses are varied slightly with maternal height and range from 6 to 9 ml. (120 to 180 mg.) of lignocaine. A larger dose of 10 to 12 ml. (200 to 240 mg.) is given before operative vaginal delivery to ensure perineal analgesia and relaxation of the pelvic floor muscles. The use of 2% lignocaine permits more injections to be made from the 50-ml. syringe than would be possible if weaker solutions were used. The percentage strength of lignocaine solution injected does not greatly influence the extent of analgesia obtained (Bromage, 1962).

Doses of lignocaine are kept as low as possible to minimize the risk of hypotension and because the free spread of solutions in the epidural space of the pregnant woman is recognized and probably attributable to engorgement of the epidural veins (Bromage, 1962). Prilocaine (Citanest) is not used, because repeated injections would be expected to produce considerable methaemoglobinaemia (Adamson and Spoerel, 1966).

Complications

The following complications were observed in the 100 cases reported here.

Dural Puncture.—This occurred in two patients. In one case the epidural catheter probably punctured the dura (Moir and Hesson, 1965) and spinal anaesthesia resulted. In the other case no injection was made. In neither case did mother or infant suffer harm.

Puncture of an Epidural Vein.—This was observed three times after passage of the catheter. No injection was made

---

* Queen Mother's Hospital, Glasgow C.3.

until the catheter had been displaced from the vein (in one case by repuncture at another interspace) and there were no harmful consequences.

Paravertebral Passage of the Catheter.—This occurred once. Only a narrow unilateral area of cutaneous anaesthesia developed and it was presumed that the catheter had passed out through an intervertebral foramen. Repeat puncture was satisfactory.

Toxic Effects of Lignocaine.—None was observed. The dose of lignocaine, with adrenaline, was always less than 250 mg. at each injection.

Hypotension.—Transient falls in systolic blood pressure to below 90 mm. Hg were seen on 15 occasions in 100 epidural blocks in which almost 600 injections were given. This represents an incidence of about 2.5 per 100 injections. In 13 instances the hypotension responded immediately to turning the patient into the left lateral position and was attributed to the supine hypotensive syndrome. In the other two cases an intravenous injection of methoxamine 3 mg. restored normal blood pressure. This drug is better avoided because it can cause foetal bradycardia and tetanic uterine contraction (Vasicka *et al.*, 1964) and constriction of uterine arteries (Greiss and Wilkes, 1964), and vasopressor drugs have not been used in our hospital during the last year.

Other Complications.—Retention of urine may, of course, complicate any labour, but is more likely to occur when bladder sensation is lost under epidural analgesia.

Lumbar-puncture headaches do not occur after epidural analgesia. No foetal or maternal mortality is attributable to the anaesthetic technique.

Tachyphylaxis

This has been discussed elsewhere (Moir and Willocks, 1966). We use this term to mean a substantial reduction in the duration of analgesia obtained after repeated injections of local anaesthetic drug. The phenomenon was seen in over 60% of cases where four or more top-up injections were required, and in 70% of these cases analgesia eventually lasted less than half as long as it had after the initial injection. This rather troublesome phenomenon is unexplained and has seldom been noted by others, though Bush (1959), Bromage *et al.* (1964), and Cox and Spoerel (1964) refer to it. Perhaps tachyphylaxis has been infrequently observed because epidural analgesia is not commonly given for the prolonged periods used in these incoordinate labours (average duration 10½ hours) where pain may be increasing rather than decreasing during the block.

Description of Cases

Continuous epidural analgesia was administered to 100 women with incoordinate labour in the Queen Mother's Hospital from March 1964 to July 1966—1.4% of the deliveries in that time.

In this highly selected group of abnormal cases conventional treatment had failed and the decision had to be taken whether to perform caesarean section without further prolongation of labour. Maternal distress and failure to respond to analgesic drugs, combined with incoordinate uterine action, were the criteria for the use of epidural analgesia. Incoordinate uterine action was a clinical diagnosis—contractions of varying frequency and strength which failed to dilate the cervix and bring the presenting part down in the normal way; most cases were of the hypertonic type associated with distressing pain and backache, but often hypertonic and hypotonic periods occurred in the same labour, as observed by Jeffcoate (1961). When periods of hypotonic uterine action were prominent an oxytocin drip was used: 29 patients had an oxytocin drip at some point after the institution of continuous epidural analgesia. As there was no consistent policy on the use of oxytocin, further comment on this aspect of treatment is difficult. Our impression is that in some cases a more liberal use of oxytocin would have been beneficial.

In a few cases the abnormal pattern of uterine contractions was confirmed by tocodynamometry.

On reviewing the cases thus selected we found that they exhibited many of the general features classically associated with incoordinate labour, such as short stature, postmaturity, large size of foetus, and occipitoposterior position (Table I). Ninety-two of our patients were primigravidae; the remaining eight were in their second pregnancy and all of them had a history of prolonged labour, five having previously been delivered by caesarean section early in labour. Eighty-eight patients were under the age of 30 and none was over 35. Fifty-three patients had labour induced by rupture of the membranes, pre-eclampsia and postmaturity being the most common indications. The average duration of labour before the block was given was 23 hours. Vomiting, pyrexia, tachycardia, and ketonuria were common and intravenous glucose was freely used (Table II). When the membranes had been ruptured for more than 24 hours an antibiotic was given—usually ampicillin 500 mg. every six hours by intramuscular injection.

TABLE I.—*Features Associated with Incoordinate Labour in This Series*

Primigravidae	92%
Age <30 years	88%
Height <61 in. (155 cm.)	40%
Gestation >41 weeks (287 days)	50%
Foetal weight >8 lb. (3·63 kg.)	49%
Occipitoposterior position	65%
Surgical induction of labour (amniotomy)	53%

TABLE II.—*Physical Findings in* 100 *Patients with Incoordinate Uterine Action*

Tachycardia (over 100/minute)	66%
Pyrexia (over 37·5° C.)	38%
Ketonuria	78%
Vomiting	34%
Intravenous drip given	86%

The average duration of labour after epidural block was 10.2 hours and the average total duration of labour 33,25 hours.

Effect of Epidural Block on Progress of Labour

Epidural block was given only after the cervix was 4 cm. dilated; once begun, analgesia was maintained continuously until delivery. Progress in labour was estimated by recording the frequency, duration, and intensity of uterine contractions by abdominal palpation and by assessing cervical dilatation by rectal and vaginal examination.

To obtain an objective assessment of the rate of progress in labour before and after epidural block we prepared, in retrospect, a graph or "partogram" (Rodesch *et al.*, 1965) for each of our cases, employing the method of Friedman (1955), who has made extensive studies of the graphic analysis of labour (Friedman, 1954, 1956; Friedman and Sachtleben, 1961a, 1961b, 1962a, 1962b, 1963a, 1963b, 1965). Friedman assesses progress of labour by graphing cervical dilatation against time because "the dilatation of the cervix is the result of all the driving force of uterine contractions acting upon the uterine contents and against the resistance of the maternal soft parts," and thus is the best index of progress in labour (Friedman, 1965). In the normal primigravida, Friedman (1955) has shown that cervical dilatation in the "active phase" of the first stage of labour (after 3 cm.) progresses in an almost linear fashion.

In our cases we compared (*a*) the rate of cervical dilatation in the time from 3 cm. (when the "active phase" usually begins) until the epidural block was given with (*b*) the rate from epidural block until delivery. We avoided any comparison which included the "latent phase" before 3 cm. dilatation, as this would have given a false impression of an increased rate of dilatation after epidural block. In all cases the records of vaginal rather than rectal examinations were used to construct the graphs.

In three cases there was insufficient information to make a calculation, but the results for 97 cases were that the rate of dilatation after epidural block was increased by at least one and a half times in 68 cases (70%). Dilatation proceeded at an unchanged rate in 18 cases (18.6%) and was slowed in 11 cases (11.3%) (see Table III).

TABLE III.—*Rate of Cervical Dilatation After Epidural Block in 97 Cases of Incoordinate Uterine Action*

Rate	No. of Patients	Percentage
Increased by more than 3 times ..	44	45·4
Increased by 1½ to 3 times	24	24·7
Unaltered	18	18·6
Slowed	11	11·3

As has already been pointed out, only a minority of patients had oxytocin drips, usually for short periods, and there was no consistent policy on the use of oxytocin. The response of the uterus to epidural block did not seem to be related to the use of oxytocin.

The method of delivery is shown in Table IV. Caesarean section was performed in 26 cases: five of these had already reached the second stage of labour and an attempt at vaginal delivery had failed because of mechanical difficulty, while in another two cases an attempt at vaginal delivery was thought inadvisable though the cervix was almost fully dilated. The findings regarding progress in labour and eventual method of delivery should be interpreted in the light of the presence or absence of cephalopelvic disproportion.

TABLE IV.—*Method of Delivery in 100 Cases of Incoordinate Uterine Action Treated by Epidural Block*

Caesarean section	26	Vacuum extraction	21
Forceps	48	Spontaneous	5

Effect of Cephalopelvic Disproportion on Results

Glasgow was at one time notorious for its high incidence of contracted pelvis, and dystocia from this cause is still commoner than in most areas in the United Kingdom, though severe and obvious pelvic contraction such as that caused by rickets is now seldom seen and the diagnosis of cephalopelvic disproportion is often made only in labour or at delivery. Antenatal examination had already excluded major degrees of contracted pelvis in the patients of this series, but in 29 cases it was found that disproportion, usually associated with malposition of the foetal head (particularly occipitoposterior), caused appreciable mechanical difficulty in labour or at delivery.

Jeffcoate (1965) reiterated that small women with large babies are liable to have incoordinate labours. Forty of our patients were 61 in. (155 cm.) or less in height: disproportion was present in 16 (40%) of these and 10 of the 16 babies weighed 8 lb. (3.63 kg.) or more, while in the remaining 24 short women (60% of the group) disproportion was not present though 10 of the babies weighed more than 8 lb. (3.63 kg.).

There were 60 patients whose height was more than 61 in. (155 cm.). Disproportion was present in 13 (22%) of these, and 8 of the 13 babies weighed more than 8 lb. (3.63 kg.), while in the remaining 47 (78.3% of the taller group) there was no disproportion and 21 of the 47 babies weighed more than 8 lb. (3.63 kg.).

The rate of cervical dilatation before and after epidural block in cases with and without cephalopelvic disproportion is shown in Table V, from which it appears that disproportion did not significantly alter the improvement in uterine action in response to epidural block.

In contrast Table VI shows that disproportion was the most important factor influencing the method of delivery, the caesarean section rate being 55.2% in cases with, and 14.1% in cases without disproportion.

TABLE V.—*Rate of Cervical Dilatation After Epidural Block in Cases With and Without Disproportion*

Rate	70 Cases Without Disproportion	27 Cases With Disproportion
Increased by more than 3 times ..	34 (48·6%)	10 (37·0%)
Increased by 1½ to 3 times ..	18 (25·7%)	6 (22·2%)
Unaltered	12 (17·1%)	6 (22·2%)
Slowed	6 (8·6%)	5 (18·6%)

TABLE VI.—*Method of Delivery in 100 Cases of Incoordinate Uterine Action Divided According to Presence of Disproportion*

	29 Cases With Disproportion	71 Cases Without Disproportion
Caesarean section	16 (55·2%)	10 (14·1%)
Forceps	11 (37·9%)	37 (52·1%)
Vacuum extraction	2 (6·9%)	19 (26·8%)
Spontaneous	0	5 (7·0%)

When an increased rate of dilatation followed epidural block in cases with disproportion the caesarean section rate was 27.6%, whereas if the rate of dilatation was increased and no disproportion was present the caesarean section rate was only 3.8%.

Blood Loss at Delivery under Epidural Block

The average blood loss, recorded accurately by a haemoglobin-dilution technique, at forceps delivery in 33 of our cases was 371 ml. Only 2 (6%) of these patients lost more than 500 ml. These figures compare favourably with blood loss at forceps deliveries under general anaesthesia (where the average loss was 412 ml. and the incidence of postpartum haemorrhage was 29%) (Moir and Wallace, 1967).

It is our impression that the principal source of bleeding at delivery under epidural block is the episiotomy rather than the placental site and that uterine retraction is excellent. There is no evidence that the management of incoordinate labour under epidural analgesia predisposes to postpartum haemorrhage.

Foetal Mortality and Morbidity

There was one stillbirth and one neonatal death in the series, giving a perinatal mortality of 2%. An account of these deaths is given in the discussion.

The Apgar score of the 99 liveborn babies was estimated two minutes after birth. Sixty-six babies (66.6%) had a score of 7 or over. Seventeen babies (17.1%) had a score of 4 or less. The number requiring active resuscitation (by intubation or hyperbaric oxygenation) was 15. There were three cases of intrauterine pneumonia or meconium aspiration syndrome and three cases of transient cerebral irritation. No other serious complications occurred and all 98 surviving babies were dismissed apparently well.

Maternal Morbidity

The stay of the mothers in hospital after delivery was of normal duration.

Puerperal pyrexia of 37.6° C. (99.7° F.) or over occurred transiently in 24 patients. One patient was readmitted two weeks after delivery with a genital infection.

Discussion

One hundred women were given continuous epidural analgesia because they were having painful incoordinate labours. Review of these cases showed a high incidence of young primigravidae, short maternal stature, large foetal size, and occipitoposterior position (Table I).

Twenty-nine patients had appreciable mechanical difficulty in labour or at delivery because of minor degrees of disproportion, often in association with occipitoposterior position. Mechanical difficulty of this kind has proved to be the most important factor influencing the method of delivery, and if such cases could be excluded treatment would be much simplified and the results would be better. Experience with this series, however, has confirmed our belief that it is seldom possible to predict mechanical difficulty in labour by antenatal examination except in gross cases of disproportion. The position and attitude of the foetal head are important, but in the borderline case it is the action of the uterus which is the most important factor, and in the primigravida this is completely unknown until labour begins. Often it is only after labour is far advanced that the mechanical problem becomes evident; if pain is abolished by epidural block there is usually nothing to lose by waiting until the diagnosis is clear.

With relief of pain, the patient's general condition may be improved out of recognition, but the obstetrician should always remember the dangers of disproportion and should not strive too zealously for a vaginal delivery. Even "trial of forceps" with the theatre set for caesarean section is not always a safeguard, as the following case illustrates.

A primigravida aged 27 had an incoordinate first stage of labour lasting 45½ hours, the last 20 hours being managed under epidural analgesia. After an hour in the second stage a trial of vaginal delivery was attempted. The vacuum extractor was applied without success and rotation and traction with Kielland's forceps produced no advance. For the first time disproportion was now detected. Caesarean section was performed and the child (weight 3.9 kg.) died five hours later of intracranial haemorrhage from tentorial tears.

When the fault in labour is principally one of uterine action epidural analgesia helps considerably in allowing labour to continue painlessly and with a likelihood of improving uterine action until the second stage is reached, and there is a low caesarean section rate in such cases. It is difficult to assess whether epidural block has a stimulating effect on the progress of labour, even though a graphic analysis showed an increased rate of dilatation in 70% of cases, for some patients also had oxytocin drips and all had dehydration and acidosis corrected as required. Both clinical experience and in-vitro evidence (Mark, 1961) suggest that acidosis impairs uterine action.

Two infants have been lost. One, already described, died from intracranial haemorrhage. The details of the other case are as follows:

A primigravida aged 23 had labour induced at 41½ weeks. She had a hypertonic incoordinate labour (with marked dehydration, acidosis, and bowel distension) for 28 hours, when epidural analgesia was induced. Two hours later the foetal heart was not heard. At no time was maternal hypotension detected and there was no warning irregularity of the foetal heart or meconium staining. A stillborn child was delivered 19 hours later with considerable difficulty, the vacuum extractor being used as the cervix was not yet fully dilated. This case illustrates the need for greater information about the condition of the child in utero, particularly when labour is prolonged. Few other patients in our series have had perhaps an equally unsuitable environment for the baby.

The perinatal mortality rate for the hospital is 3.8%. The present series is small and a foetal loss of 2% is probably acceptable for those difficult cases, but it must be remembered that few premature babies were included. Comparable figures for foetal loss are 2.5% for labours lasting more than 24 hours (Royal Maternity Hospital, Belfast, 1963), 4.1% for labours longer than 30 hours (National Maternity Hospital, Dublin, 1964), and 7.6% for labours longer than 48 hours (Glasgow Royal Maternity Hospital, 1962). Separate figures for incoordinate labour are difficult to obtain, as this does not usually appear as an entity in hospital reports.

The acceptable condition of most infants in the series is shown by the Apgar scores and the low incidence of serious complications already quoted.

It is unnecessary to give depressant analgesic drugs to patients under epidural block, and this means that the child is more easily stimulated to take his first breath.

The value of antibiotic treatment in preventing the child becoming infected in utero is not precisely known, but further studies will probably soon elucidate this. Ampicillin, which is probably the most effective drug for the purpose (Williams and Felton, 1966; Blecher *et al.*, 1966), was used when the membranes had been ruptured more than 24 hours or when there was pyrexia.

The obstetric policy in this series has been conservative, as is indicated by a caesarean section rate of 26%, but there is no doubt that good results have been obtained in many places by a much wider use of caesarean section. The radical attitude adopted now in some centres is illustrated by the figures from the Royal Maternity Hospital, Belfast (1963), where the caesarean section rate for cases of abnormal uterine action without disproportion was 80%, there being no foetal loss, and the caesarean section rate for cases of contracted pelvis was 91.8%, the foetal loss being 2%.

It is our opinion that such a high caesarean section rate is not justified for incoordinate labour in the young primigravida because the uterine dysfunction is unlikely to recur in a subsequent labour if the cervix reaches at least half dilatation in the first labour (Jeffcoate *et al.*, 1952; Jeffcoate, 1961). In the older patient earlier resort to caesarean section is, of course, justified. The woman who has once been delivered by caesarean section faces a risk at subsequent confinements, whether or not a policy of repeat section is followed. Caesarean section is not always the easy and atraumatic operation that it ideally should be, and the postoperative complications are not negligible, the risk of thromboembolism, for example, being nearly six times greater than after vaginal delivery (Claye, 1961).

Incoordinate labour is often terminated by caesarean section because of maternal distress. Our object in using epidural analgesia has been to abolish pain so that time is available for the problem to be resolved to the extent that the woman either has a safe vaginal delivery or is delivered by caesarean section after the cervix is at least half dilated. When the patient has been completely relieved from pain the obstetrician can review the case more calmly; he may then reflect on the maxim of William Smellie (1752) that "it takes more skill to prevent than to perform an operation."

There is no doubt that the method demands both time and skill from a team of obstetricians, anaesthetists, and midwives.

Of the value of epidural analgesia in the management of incoordinate labour we are entirely convinced. Looking back on the patients whose records we have presented here, we regret that the treatment was applied so late to many of them, but the method was a new one in the hospital and only the most difficult cases were chosen for this series. Few who have seen the transformation epidural analgesia brings to a woman distressed with an incoordinate first stage can fail to welcome it with enthusiasm.

Incoordinate labour remains a major problem in modern obstetric practice. Caesarean section cuts across the problem but does not provide an answer to it. The ideal solution would be to achieve complete control over uterine function and complete pain relief at the same time. We do not claim that epidural analgesia does this, but it is a step towards the ideal.

Summary

One hundred women with incoordinate uterine action had labour managed under continuous epidural analgesia, the average duration of the block being 10 hours. Most of the patients were primigravidae, many were of small stature, and many had large babies, commonly with the occiput in the posterior position. Graphic analysis of labour showed an increased rate of cervical dilatation after epidural block in over 70%. The caesarean section rate remained high (55%) in cases complicated by mechanical dystocia, but where this was not present the caesarean section rate was much lower (14%), while in those patients who had no cephalopelvic disproportion and who showed an increased rate of dilatation after epidural block the caesarean section rate was only 3.8%. With this management, caesarean section is rarely required purely for incoordinate uterine action or maternal distress.

The perinatal mortality in the series was 2%, and there were no serious maternal complications.

Dr. John MacVicar provided the initial stimulus for this work, and our thanks are due to him and to Professor Ian Donald for continued encouragement and help. The work could not have been done without the untiring efforts of the labour room staff, whose cheerful co-operation was much appreciated.

REFERENCES

Adamson, D. H., and Spoerel, W. E. (1966). *Acta anaesth. scand.*, Suppl. No. 23, p. 379.
Arthur, H. R., and Johnson, G. T. (1952). *J. Obstet. Gynaec. Brit. Emp.*, **59**, 372.
Ball, H C. J., and Chambers, J. S. W. (1956). *Brit. med. J.*, **1**, 1275.
Blecher, T. E., Edgar, W. M., Melville, H. A. H., and Peel, K. R. (1966). Ibid., **1**, 137 .
Bromage, P. R. (1962), *Brit. J. Anaesth.*, **34**, 161.
—— Burfoot, M. F., Crowell, D. E., and Pettigrew, R. T. (1964). Ibid., **36**, 342.
Bryce-Smith, R., and Williams, E. O. (1955). *Lancet*, **1**, 1241.
Bush, R. C. (1959). *Anesthesiology*, 20, 31.
Claye, A. (1961). *J. Obstet. Gynaec. Brit. Cwlth*, **68**, 577.
Cole, P. V. (1964). *Anaesthesia*, **19**, 562.
Cox, J. M. R., and Spoerel, W. E. (1964). *Canad. Anaesth Soc. J.*, **11**, 72.
Edmonds-Seal, J. (1964). *Anaesthesia*, **19**, 222.
Friedman, E. A. (1954). *Amer. J. Obstet. Gynec.*, **68**, 1568.
—— (1955). *Obstet. and Gynec.*, **6**, 567.
—— (1956). Ibid., **8**, 691.
—— (1965). In *Obstetrics*, 13th ed., by J. P. Greenhill, p. 832. Philadelphia and London.
—— and Sachtleben, M. R. (1961a). *Obstet. and Gynec.*, **17**, 135.
—— —— (1961b). Ibid., **17**, 566.
—— —— (1962a). Ibid., **19**, 576.
—— —— (1962b). Ibid., **20**, 761.
—— —— (1963a). Ibid., **21**, 13.
—— —— (1963b). Ibid., **22**, 478.
—— —— (1965). Ibid., **25**, 844.
Galley, A. H. (1949). *Anaesthesia*, **4**, 154.
Glasgow Royal Maternity Hospital (1962). Clinical Report.
Greiss, F. C., and Wilkes, D. V. (1964). *Obstet. and Gynec.*, **23**, 925.
Hellmann, K. (1965). *Canad. Anaesth. Soc. J.*, **12**, 398.
Hingson, R. A., Cull, W. A., and Benzinger, M (1961) *Anaesth. Analg. Curr. Res.*, **40**, 119.
—— and Edwards, W. B. (1943). *J. Amer. med. Ass.*, **121**, 225.
Jeffcoate, T. N. A. (1961). *Lancet*, **2**, 61.
—— (1965). *Aust. N.Z.J. Obstet. Gynaec.*, **5**, 222.
—— Baker, K., and Martin, R. H. (1952). *Surg. Gynec. Obstet.*, **95**, 257.
Johnson, G. T. (1952). *J. Obstet. Gynaec. Brit. Emp.*, **59**, 644.
—— (1954). *Brit. med. J.*, **1**, 627.
—— (1957). Ibid., **2**, 386.
Lee, J. A. (1962). *Anaeshesia*, **17**, 248.
Mark, R. F. (1961). *J. Obstet. Gynaec. Brit. Cwlth*, **68**, 584.
Moir, D. D., and Hesson, W R (1965) *Anaesthesia*, **20**, 373
—— and Wallace, G. (1967). In press.
—— and Willocks, J. (1966). *Acta anaesth. scand.*, Suppl. No. 23, p. 144.
Moore, D. C. (1966). In discussion on obstetric anaesthesia at the Second European Congress of Anaesthesiology.
National Maternity Hospital, Dublin (1964). Clinical Report.
Norris, S., Harris, L. J., and Eisen, S. M. (1960). *Obstet. and Gynec.*, **16**, 15.
Rodesch, F., Ehman-Ellinger, C., Wilkin, P., and Hubinont, P. O. (1965). *J. Obset. Gynaec. Brit. Cwlth*, **72**, 930.
Royal Maternity Hospital, Belfast (1963). Clinical Report.
Scott, D. B. (1955). *Lancet*, **2**, 43.
Smellie, W. (1752). *Treatise on the Theory and Practice of Midwifery*, vol. 2, Case 289. London.
Tunstall, M. E. (1960). *Brit. J. Anaesth.*, **32**, 292.
Vasicka, A., Hutchinson, H. T., Eng, M., and Allen, C. R. (1964). *Amer. J. Obstet. Gynec.*, **90**, 800.
Williams, J. D., and Felton, D. J. C. (1966). *J. Obstet Gynaec. Brit. Cwlth.*, **73**, 654.

Value of Rectal Biopsy in Paediatric Neurology: Report of 165 Biopsies

E. M. BRETT,* D.M., M.R.C.P. ; C. L. BERRY,† M.B., B.S.

Brit. med. J., 1967, **3**, 400–403

Biopsy of neural tissue, with subsequent histopathological, chemical, and histochemical examination, plays an important part in the investigation of suspected degenerative disease of the central nervous system in infancy and childhood. For a number of reasons brain biopsy is not always acceptable to parent or clinician.

The possibility of using rectal biopsy as a diagnostic test for progressive degenerative brain disease seems to have been first suggested by the necropsy observation of Globus (1942), who noted similar degenerative changes in neurones of the central nervous system and of the myenteric plexus in a case of amaurotic idiocy. Landing and Freiman (1957) encountered similar necropsy findings in various forms of amaurotic idiocy, Niemann–Pick's disease and Hurler's syndrome; and Nakai and Landing (1960) suggested that rectal biopsy might be used in the diagnosis of neurolipidosis. Kobayashi (1960) proposed the use of biopsy of the rectal wall or appendicectomy for the histochemical demonstration of "the dystrophic deposit in ganglion cells of the myenteric plexus" in gargoylism. A series of 75 rectal biopsies was reported by Martin, Landing, and Nakai (1963), but many of these were from patients with suspected Hirschsprung's disease or were incidental to operations for imperforate anus, and only 11 seem to have been intended primarily to further the neurological diagnosis. No specific neurological diagnoses were reached as a result of these biopsies, but the authors believed that rectal biopsy might be as reliable as brain biopsy in the neural lipidoses, and that it should probably be considered in the diagnostic investigation of any otherwise unexplained degenerative neurological disorder of childhood.

Bodian and Lake (1963) reviewed 21 necropsies in which complete agreement was found between neuronal changes in the central nervous system and in the gastrointestinal tract, and there was also evidence of metachromasia in the latter if present in the brain. They further reported a series of 49 rectal biopsies based on this study; 26 of these were normal and 23 showed abnormalities. The latter included 12 cases with changes regarded as non-specific, and 11 with diagnostic features (seven cases of neurolipidosis and four of metachromatic leucodystrophy. The authors suggested that this

---

* Senior Registrar in Neurology, the National Hospital for Nervous Diseases, Queen Square, and Department of Neurology, Hospital for Sick Children, Great Ormond Street, London W.C.1.
† Lecturer in Morbid Anatomy, the Institute of Child Health, London W.C.1.

investigation "embraces the spectrum of neurolipidosis, metachromatic leucoencephalopathy, and possibly sudanophilic leucodystrophy." They believed that these biopsies were far safer than brain biopsy and might well be obtained at an early stage of the evolution of the various diseases.

In subsequent years many more rectal biopsies have been performed at the Hospital for Sick Children, Great Ormond Street, and in this paper we review the results of 165 biopsies from 164 patients over the five-year period 1962–6. These include 47 of Bodian and Lake's series (but not the two performed at other hospitals) and 118 more recent biopsies.

Methods

Full-thickness rectal biopsies were performed under general anaesthesia. For the initial six months of the period considered, half the tissue obtained was fixed in buffered formalin and then sectioned on a freezing microtome. The remaining tissue from these biopsies and all later material was frozen on solid carbon dioxide. Sections measuring 5–7μ were then cut in a cryostat.

Specimens were stained by haematoxylin and eosin, periodic-acid Schiff (P.A.S.), Sudan black, scharlach red, luxol-fast blue, toluidine blue, cresyl-fast violet, Feyrter's thionine, and, where appropriate, a colloidal iron method for interstitial mucopolysaccharide (for details of methods see Bodian and Lake, 1963).

The sections were reviewed by one of us (C. L. B.) without knowledge of the clinical status of the patients. In a few cases review of the earlier sections has resulted in the original interpretation being altered in the light of subsequent histological experience.

Biopsies with Positive Diagnostic Abnormalities

Of the 165 biopsies 33 (20%) showed positive diagnostic features. The proportion of positive biopsies was 20% for children in the total group, 31% for those under the care of the neurological unit, and 13.5% for those in other wards.

Clinical Diagnosis in 33 Cases with Positive Biopsies.—Thirty of these, or approximately 90%, were from patients with neurolipidosis or metachromatic leucodystrophy, as in the initial series of Bodian and Lake. There were 19 cases of neurolipidosis and 11 of metachromatic leucodystrophy. Hurler's syndrome provided two cases, and there was one case of Niemann–Pick's disease.

Duration of Symptoms at Time of Biopsy.—In neurolipidosis it was less than one year in eight, one year in three, two years in three, three years in two, and four years or more in two. One case was of doubtful duration. Five of the eight cases diagnosed by biopsy after less than one year of symptoms were examples of Tay-Sachs disease. In the cases of metachromatic leucodystrophy the duration of symptoms was less than one year in three, two years in two, three years in two, and four years in three, one case being of uncertain duration.

Clinical Features of Cases with Positive Biopsies

A history of dementia or regression in psychomotor skills was the most prominent feature in the two major diseases, being present in 17 of the 19 cases of neurolipidosis and in 9 of the 11 cases of metachromatic leucodystrophy. Convulsions occurred in seven of the neurolipidosis cases. A family history of an affected sibling occurred in five cases of neurolipidosis with biopsies in two pairs of siblings, and in seven cases of metachromatic leucodystrophy, including three pairs of siblings. The family history was suggestive in one further case of metachromatic leucodystrophy—a child whose sibling had died with a progressive neurological condition but without necropsy.

Macular changes were recorded in seven patients with neurolipidosis, five of whom, regarded clinically as examples of Tay-Sachs disease, showed pathognomonic cherry-red spots, bilateral in four cases. Optic atrophy was noted in a further two patients in this group.

Specific features deserving comment in the 11 cases of metachromatic leucodystrophy include a history of ataxia in four patients. In three of these unsteadiness seems to have been the presenting symptom, preceding dementia, the ages of onset being 6, 11, and 16 months. This conforms to the recognized pattern of infantile form of metachromatic leucodystrophy (Allen, 1964).

The occurrence of convulsions in two siblings with metachromatic leucodystrophy was rather unexpected, since these are regarded as infrequent in this disease (Lyon, Arthuis, and Thieffry, 1961 ; Allen, 1964).

Ancillary investigations pointing to the diagnosis (later proved by biopsy) were most helpful in the 11 patients with metachromatic leucodystrophy. In these the urine showed intracellular metachromatic material in all the eight cases in which it was examined by the method of Lake (1965). The conduction velocity in peripheral nerves was measured in nine cases and found to be substantially decreased in eight ; seven of these were previously reported by Fullerton (1964). Cholecystography by the oral route was performed in one patient with positive urine and abnormal conduction velocity, and the gall bladder showed no concentration of dye.

Laboratory tests proved less helpful in the patients with neurolipidosis. In one recent case the serum fructose-1-phosphate aldolase was found to be deficient (0.3 unit per ml. of serum) (Profesor J. N. Cumings) ; the level of this enzyme has recently been reported to be abnormally low in Tay-Sachs disease (Volk, Aronson, and Saifer, 1964 ; Schneck, Maisel, and Volk, 1964), and its measurement has been suggested as a useful screening test for this condition.

Pneumoencephalography gave evidence of cerebral atrophy in five of the six cases of neurolipidosis in which it was performed. In the two cases of metachromatic leucodystrophy so investigated the results were normal. This, with the finding of cerebral atrophy in 23 of the 35 air encephalograms in patients whose rectal biopsies were normal or showed non-specific changes, suggests that air encephalography is *not* a particularly useful investigation in the selection of patients for rectal biopsy. The situation is different when a cerebral biopsy is considered ; this should be preceded by an air encephalogram in order to exclude a congenital cerebral malformation of a kind which might alter the prognosis and management of the patient.

Biopsies without Diagnostic Abnormalities

On review, 132 biopsies taken from 131 patients were thought to show no abnormality.

Analysis of the major clinical features of these cases shows that, in contrast to the cases with positive biopsies, amentia or very early retardation with or without convulsions was the most frequent feature, occurring in 67 cases. Dementia occurred in only 29 cases, roughly one-fifth of the total. There were 15 patients with infantile spasms and 11 with autistic or psychotic features. In five cases without dementia or epilepsy the indication for biopsy was a family history suggesting a progressive cerebral degeneration or the finding of macular changes raising the possibility of such a condition. There were three patients with epilepsy alone and one in whom acute transient deterioration accompanied the sudden onset of epilepsy.

Biopsies with Non-specific Abnormalities

Fourteen of the 132 non-diagnostic biopsies, taken from 13 patients, were on review thought to show non-specific degenerative changes. These are listed below.[1] One patient, a boy with mental and neurological deterioration in association with intractable epilepsy, had two biopsies performed at an interval of 14 months, and similar non-specific abnormalities were seen in both. Nine of the 12 biopsies reported by Bodian and Lake as showing non-specific degenerative changes were thought on review to be within normal limits.

Analysis of the clinical features of the 13 patients with non-specifically abnormal biopsies shows that there were six with dementia and six with amentia. This contrasts with the predominance of dementia in the cases with positive (diagnostic) biopsies and with that of amentia in those with "negative" biopsies. Epilepsy was prominent in the histories of these patients, occurring in 61%, whereas it occurred in 27% of those with positive and 37% (excluding infantile spasms) of those with negative biopsies. The epilepsy was severe and intractable in many patients in this group, and the non-specific changes seen in their biopsies may perhaps reflect anoxia or other secondary effects of uncontrolled fits over long periods rather than any underlying primary degenerative disease.

Confirmation by Cerebral Biopsy or Necropsy

There were 13 cases in which, usually during the same hospital admission, both rectal and cerebral biopsies were carried out, the rectal usually preceding the cerebral biopsy. In six cases both biopsies were normal. Six patients, four with neurolipidosis and two with metachromatic leucodystrophy, showed diagnostic abnormalities in both biopsies. In one patient with subacute sclerosing leucoencephalitis cerebral biopsy showed diagnostic features of this disease, whereas rectal biopsy was normal.

Adequate necropsy studies are known so far to have been made in only seven patients with diagnostic rectal biopsies. These confirmed the diagnosis, in three cases of neurolipidosis and in four of metachromatic leucodystrophy, made on rectal biopsy. No post-mortem studies are so far known to have been made on patients whose rectal biopsies were normal or non-specifically abnormal.

Morbidity

The only complication encountered with any frequency in this series was rectal haemorrhage, which occurred in 13 cases (8%). Haematoma formation was seen in three patients and required drainage. Five patients needed blood transfusion post-operatively.

Discussion

In this series most of the positive rectal biopsies were from patients with neurolipidosis or metachromatic leucodystrophy. The successful selection of cases for such biopsies would therefore seem largely to depend on a high clinical likelihood of one of these specific diagnoses.

There were clear pointers, clinically or on investigation, to the diagnosis in 11 of the 19 neurolipidosis patients; these included macular changes, a family history of an affected sibling, and deficiency of serum fructose-1-phosphate aldolase. In the other eight patients, all of whom were demented, there were no clear indications, though one showed an exaggerated startle response to sound as described in Tay–Sachs's disease (Schneck *et al.*, 1964).

All 11 patients with metachromatic leucodystrophy showed clear evidence of the disease on investigation by urine examination alone (three cases), nerve-conduction studies alone (three cases), or both (five cases). In one patient with normal conduction velocity the urine contained intracellular metachromatic material. Thus the two tests complemented each other in this series. In the metachromatic leucodystrophy patients biopsy was in fact often used as a *confirmatory* investigation, and it could be argued that its use was unjustified in some cases. With the diagnostic help now available from laboratory investigations in this condition and likely to increase with the wider use of urinary sulphatase estimations (Austin *et al.*, 1964, 1966), biopsy, whether of rectum, brain, nerve, skin, or dental pulp (Gardner and Zeman, 1965), may well become obsolete. If biopsy is thought necessary when metachromatic leucodystrophy is strongly suspected, it would seem logical to biopsy a peripheral nerve as originally suggested by Thieffry and Lyon (1959); particularly if nerve-conduction velocity is slowed, rather than rectum or brain. In metachromatic leucodystrophy rectal biopsy is of value solely in showing changes in nerve *fibres*, and the same is true of appendix and dental pulp biopsy. Yudell *et al.* (1967) at the Mayo Clinic have now discontinued the use of rectal biopsy in metachromatic leucodystrophy in favour of biopsy of the sural nerve, which has so far given no false-negative results.

Diagnostic doubt in the neurolipidosis patients was least among those with Tay-Sachs disease because of the characteristic picture. For this group also, serum enzyme studies may well prove to be very reliable. With other forms of neurolipidosis clinical certainty is usually less, macular changes being less frequent and specific, and it is in this group that biopsy is likely to continue to be necessary, though improved chemical and electroencephalographic methods may in time provide tests of diagnostic reliability.

We cannot comment on the suggestion of Bodian and Lake that rectal biopsy might be of diagnostic value in sudanophilic leucodystrophy, since no cases have been investigated by it at this hospital. In this condition it would seem reasonable to prefer cerebral to rectal biopsy until such time as diagnostic changes have been found in the myenteric plexuses in cases at necropsy.

Rectal biopsy was negative in one patient with subacute sclerosing leucoencephalitis in whom brain biopsy was diagnostic. This boy was Case 8 in Bodian and Lake's series of cases with pathological changes other than neurolipidosis or metachromasia, two P.A.S.-positive cytoplasmic inclusions in rectal neurones being mentioned. This finding is quoted by Paine and Oppé (1966), but the inclusions seen in the rectal biopsy were not in fact typical of those seen in subacute sclerosing encephalitis, and similar inclusions have since been seen in a small number of rectal biopsies from patients not suffering from this condition.

Summary

A series of 165 rectal biopsies performed in conditions other than Hirschsprung's disease at the Hospital for Sick Children, Great Ormond Street, in the five years 1962–6, is reviewed. Thirty-three of these biopsies (20%) showed diagnostic and 14 non-specific abnormalities, 118 being normal. Neurolipidosis and metachromatic leucodystrophy were diagnosed on 30 of the positive biopsies. The clinical features of the positive, "negative," and non-specific abnormal groups are reviewed. It is concluded that rectal biopsy is of particular value in the diagnosis of neurolipidosis and metachromatic leucodystrophy. However, it is suggested that where adequate laboratory facilities exist biopsy in the latter condition may become unnecessary

---

[1] Non-specific degenerative changes included a variable degree of distension of neurones with cytoplasmic granularity, increased eosinophilia, and occasionally vacuolation with no specific histochemical staining reaction. Nuclear changes, including condensation of chromatin around the nucleolus with a ballooned appearance of the remainder of the nucleus, were often present.

The presence of P.A.S.-positive macrophages in the lamina propria has been reported as a non-specific abnormality, but this change, together with those already described, has been seen in cases of chronic constipation, megacolon, epilepsy, fibrocystic disease, Hirschsprung's disease, etc.

and that increasing refinement of chemical and other investigations may in time render biopsy obsolete also in many cases of neurolipidosis.

Pneumoencephalography was of no value in selecting cases for rectal biopsy, since it showed cerebral atrophy with equal frequency in patients whose biopsies later did and did not show diagnostic changes.

No diagnostic abnormalities were found on rectal biopsy in patients without dementia, a positive family history of relevant disease or other features pointing strongly towards a specific neurological condition.

We thank the physicians and surgeons of the Hospital for Sick Children, Great Ormond Street, for permission to publish details of patients in their care.

REFERENCES

Allen, N. (1964). In *Pediatric Neurology*, edited by T. W. Farmer. New York.

Austin, J., Armstrong, D., Shearer, L., and McAfee, D. (1966). *Arch. Neurol. (Chic.)*, **14**, 259.

—— McAfee, D., Armstrong, D., O'Rourke, M., Shearer, L., and Bachhawat, B. (1964). *Biochem. J.*, **93**, 15C.

Bodian, M., and Lake, B. D. (1963). *Brit. J. Surg.*, **50**, 702.

Fullerton, P. M. (1964). *J. Neurol. Neurosurg. Psychiat.*, **27**, 100.

Gardner, D. G., and Zeman, W. (1965). *Develop. Med. Child Neurol.*, **7**, 620.

Globus, J. H. (1942). *J. Mt Sinai Hosp.*, **9**, 451.

Kobayashi, N. (1959). *Amer. J. Path.*, **35**, 591.

Lake, B. D. (1965). *Arch. Dis. Childh.*, **40**, 284.

Landing, B. H., and Freiman, D. G. (1957). *Amer. J. Path.*, **33**, 1.

Lyon, G., Arthuis, M., and Thieffry, S. (1961). *Rev. Neurol.*, **104**, 508.

Martin, L. W., Landing, B. H., and Nakai, H. (1963). *J. Pediat.*, **62**, 197.

Nakai, H., and Landing, B. H. (1960). *Pediatrics*. **26**, 225.

Paine, R. S., and Oppé, T. E. (1966). *Neurological Examination of Children*. London.

Schneck, L., Maisel, J., and Volk, B. W. (1964). *J. Pediat.*, **65**, 749.

Thieffry, S., and Lyon, G. (1959). *Rev. neurol.*, **100**, 452.

Volk, B. W., Aronson, S. M., and Saifer, A. (1964). *Amer. J. Med.*, **36**, 481.

Yudell, A., Gomez, M. R., Lambert, E. H., and Dockerty, M. B. (1967). *Neurology (Minneap.)*, **17**, 103.

Effect of Total Dose Infusion of Iron-dextran on Iron, Folate, and Vitamin B_{12} Nutrition in Postpartum Anaemia

J. METZ,* M.D., M.C.PATH.; T. EDELSTEIN,* M.B., DIP.O.&G.; M. DIVARIS,* MED.TECH.; S. S. ZAIL,* M.D.

Brit. med. J., 1967, 3, 403–406

The efficacy of total dose infusion of iron-dextran (T.D.I. Imferon) in the treatment of antepartum and postpartum iron-deficiency anaemia is well established (Varde, 1964; Basu, 1965; Bonnar, 1965). Detailed studies on the effect of T.D.I. Imferon therapy on the iron, folate, and vitamin B_{12} nutritional status of iron-deficient women have, however, not yet been reported. Such information is necessary in view of the poor response to T.D.I. Imferon noted in folate-deficient women (Basu, 1965; Bonnar, 1965), and the suggestion that reactions to T.D.I. Imferon may be related to folate deficiency (Clay *et al.*, 1965; Lane and Scott, 1965). In the present study comprehensive tests of iron, folate, and vitamin B_{12} nutrition were carried out before and after administration of T.D.I. Imferon therapy to postpartum anaemic subjects. This therapy generally resulted in restoration of normal nutrition, but the postpartum improvement in folate nutrition, shown in untreated control subjects, was retarded.

Material and Methods

All subjects were Bantu admitted to Baragwanath Hospital, Johannesburg (altitude 5,760 ft.; 1,756 m.). Consecutive patients with haemoglobin levels of less than 10 g./100 ml. and decreased marrow iron stores on the third postpartum day were included in the study. A total of 81 patients received T.D.I. Imferon, and 61 of them returned for follow-up six weeks later; 12 of these 61 received folic acid as well as Imferon. Control subjects consisted of 18 patients who received no therapy. The control group is much smaller than the group receiving therapy, for during the course of the study pronounced differences between the groups became apparent, and it was not felt warranted to leave more patients untreated.

Procedure

Before therapy on the third postpartum day venous blood was drawn for measurement of haemoglobin, haematocrit, serum iron, unsaturated iron-binding capacity (U.I.B.C.), serum folate activity, serum vitamin-B_{12} concentration, and for the preparation of films. Blood for serum iron and U.I.B.C. estimation was allowed to drip direct from the needle into iron-free containers. Films were prepared from bone marrow aspirated from the sternum.

Imferon was administered as follows. The dose for each patient was calculated as described by the manufacturers. The Imferon was diluted in normal saline, not more than 20 ml. being added to a litre of saline. The infusion was started at 10–15 drops a minute until 100 ml. had been administered, and thereafter at 45 drops a minute. Before infusion basal readings of the pulse and blood pressure were made, and these were repeated at hourly intervals during the infusion. Any untoward symptoms occurring during the infusion were recorded. Forty-eight hours after completion of the infusion the site was examined for pain, tenderness, swelling, and redness, and the lower limbs were examined for evidence of venous thrombosis. The 14 patients who were to receive folic acid were then given folic acid tablets (5 mg.) and instructed to take at least one tablet daily for a period of 40 days.

The patients were studied again six weeks later. All previous investigations, including bone-marrow-puncture, were repeated. Patients were re-examined for symptoms or signs of venous thrombosis at the site of infusion and in the legs. After withdrawal of the blood and marrow samples the investigation of the patients was complete; those who had received only Imferon therapy were supplied with folic acid tablets, and those who had received no therapy since delivery were treated with iron and folic acid by mouth.

Laboratory Methods

Haemoglobin was estimated as cyanmethaemoglobin, a commercially obtained standard being used. The haematocrit was

---

* Department of Haematology, South African Institute for Medical Research, and Department of Obstetrics, Baragwanath Hospital, Johannesburg.

measured in a microhaematocrit centrifuge, and the mean corpuscular haemoglobin concentration (M.C.H.C.) calculated in the usual way. Serum iron and unsaturated iron-binding capacity were measured by the methods of Bothwell and Mallett (1955) and Charlton *et al.* (1965) respectively. Serum vitamin B_{12} was assayed with *Lactobacillus leichmannii* (Brandt and Metz, 1961) and serum folate activity with *L. casei* (Herbert, 1961; Waters and Mollin, 1961). Blood films were stained with Wright's stain and examined for hypochromia, and for hypersegmented neutrophils. When more than 3% of the neutrophils showed five or more lobes in the nucleus, a "shift to the right" was regarded as being present. Wright's stained bone-marrow films were examined for the presence of megaloblasts and giant myeloid cells. In addition, marrow films were stained for haemosiderin by the Prussian-blue reaction, and iron stores in the particles graded from 0 to +6. Grades +3 and +4 were regarded as normal, grades +5 and +6 as excessive, and grades 0 to +2 as diminished iron stores. In grade 0 no stainable iron was observed; in grade +1 stainable iron was just visible in one or two particles, and in grade +2 stainable iron was just visible in several particles. Only subjects with marrow iron stores in grades 0 to +2 were included in the study.

Results

In comparing the results obtained at the first and final assessments of the patients studied, only paired observations were used. Thus if a particular index was not available in a patient at the first assessment—for technical reasons, for example—it was excluded from the second assessment, and vice versa.

The mean values for haemoglobin, haematocrit, M.C.H.C., serum iron, U.I.B.C., serum folate, and vitamin B_{12} before and after therapy in patients receiving Imferon without added folic acid are shown in Table I. The iron stores are shown in Fig. 1, and the incidence of right shift, megaloblasts, and giant myeloid cells in Fig. 2. There was a marked rise in the mean haemoglobin, haematocrit, serum iron, and percentage saturation and a fall in U.I.B.C. values; the differences in the mean values were all statistically significant (Table II). In no patient after treatment was the haemoglobin value less than 11 g./100 ml. There was a rise of 0.41% in the mean value for the M.C.H.C., but this difference is not statistically significant. There was also little change in the percentage of subjects showing hypochromia (40% at delivery, 36% six weeks later), but the degree of hypochromia was invariably less at six weeks. There was an increase in iron stores in all patients after Imferon therapy.

The mean serum folate activity after Imferon showed little change to the pretherapy level, the difference in the mean values not being statistically significant (Table II). That folate nutri-

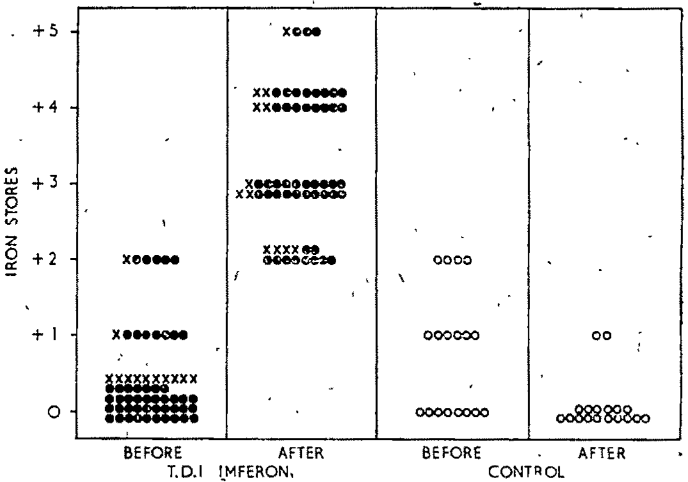


FIG. 1.—Marrow iron stores at delivery and six weeks later. x = Patients who received folic acid as well as Imferon.

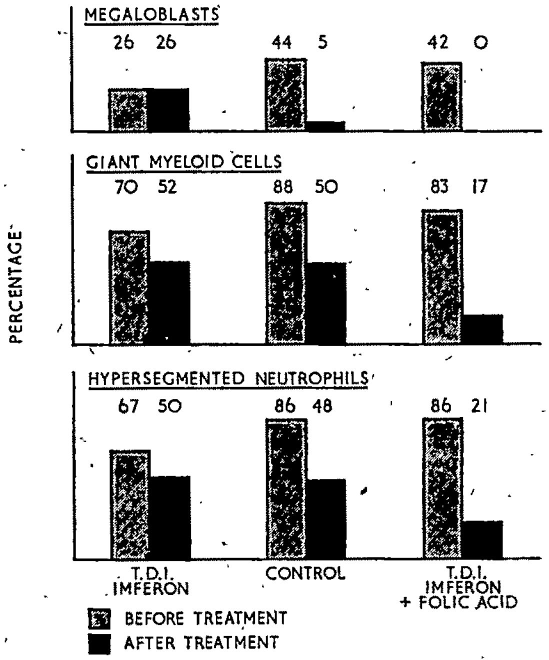


FIG. 2.—Morphological evidence of folate deficiency at delivery and six weeks later.

TABLE I.—*Results at Delivery and Six Weeks Later. Results are Expressed as the Mean Value ± Standard Error*

		Haemoglobin (g./100 ml.)	Haematocrit (%)	M.C.H.C. (%)	Serum Iron (μg./100 ml.)	U.I.B.C. (μg./100 ml.)	Percentage Saturation	Serum Folate (μmg./ml.)	Serum Vitamin B_{12} (μμg./ml.)
T.D.I. Imferon ..	Delivery	8·73±0·17	28·2 ±0·53	31·2±0·24	52·0± 7·01	371·2±14·13	12·5±0·72	3·42±0·21	414·1±27·8
	6 weeks	12·88±0·18	40·6 ±0·46	31·6±0·24	82·6±11·23	198·7± 8·86	30·4±1·52	3·59±0·26	556·2±46·5
T.D.I. Imferon + folic acid	Delivery	8·60±0·34	27·3 ±1·02	31·2±0·58	51·4± 5·32	323·1±26·75	14·4±1·17	2·93±0·32	505·4±66·6
	6 weeks	13·33±0·32	41·46±0·86	32·2±0·51	80·4± 5·77	233·8±19·69	26·9±3·47	23·10±5·32	561·1±56·6
Controls	Delivery	8·78±0·65	28·3 ±0·67	31·0±0·34	50·2± 4·70	273·3±21·55	16·8±2·00	3·40±0·32	539·0±72·0
	6 weeks	11·92±0·27	37·9 ±0·77	31·4±0·44	68·3± 6·17	349·7±10·83	16·3±1·28	6·17±0·57	484·0±61·8

TABLE II.—*Statistical Significance of the Differences in the Mean Values Compared with Six Weeks Later*

		Haemoglobin	Haematocrit	M.C.H.C.	Serum Iron	U.I.B.C.	% Saturation	Serum Folate	Serum Vitamin B_{12}
T.D.I. Imferon	n	98	92	92	100	96	96	104	104
	t	8·68	26·68	1·21	4·47	7·09	8·80	0·60	0·25
	P	<0·001	<0·001	>0·1	<0·001	<0·001	<0·001	>0·1	>0·1
Imferon + folic acid ..	n	28	26	26	28	26	26	26	28
	t	4·73	4·60	1·38	3·03	2·38	2·85	3·05	0·63
	P	<0·001	<0·001	>0·1	<0·01	<0·05	<0·01	<0·01	>0·1
Controls	n	42	40	40	42	42	42	42	40
	t	5·30	5·25	0·63	2·19	2·85	0·20	3·80	0·58
	P	<0·001	<0·001	>0·1	<0·05	<0·01	>0·1	<0·001	>0·1

tion was not obviously improved after Imferon was further reflected in the constant number of subjects who showed megaloblastic change in the marrow before and after therapy. There was, however, a moderate fall in the number of subjects who showed a right shift in the neutrophils and giant myeloid cells in the marrow. The mean serum vitamin-B_{12} concentration after Imferon was higher than the pretreatment level, but the difference is not statistically significant.

The mean values of the various haematological indices and the indices of iron, folate, and vitamin B_{12} nutrition at the first and final assessment in the group who received no therapy are shown in Tables I and II and Figs. 1 and 2. Six weeks after delivery these subjects also showed a marked rise in haemoglobin and haematocrit, the differences in the mean values being statistically significant. In four of the 21 subjects (19%), however, the haemoglobin value was less than 11 g./100 ml. and in two of these it was less than 10 g./100 ml. The mean serum iron level also rose, but in contrast to the patients who received Imferon the U.I.B.C. rose markedly, so that the mean percentage saturation of transferrin showed little change after six weeks. The striking difference in percentage saturation of transferrin between the control and Imferon-treated group was further reflected in the iron stores. In patients who had no stainable iron in the marrow after delivery the particles remained free of demonstrable iron six weeks later. In all but two of the patients with some stainable iron after delivery no iron could be found six weeks later. In these two patients some iron remained in the particles, but a smaller amount than at delivery. There was also a striking increase both in the incidence (10% at delivery and 66% six weeks later) and the degree of hypochromia in this group after six weeks.

In contrast to the group who received Imferon (without folic acid), the control group showed a statistically highly significant rise in mean serum folate levels after six weeks. This improvement in folate nutrition was reflected in the virtual disappearance of megaloblastic change in the marrow. The incidence of giant myeloid cells in the marrow and right shift in the neutrophils also fell, but in many patients these changes were still present six weeks post partum. The mean serum vitamin-B_{12} concentration was slightly lower after six weeks, but the difference is not statistically significant.

The mean values of the various haematological indices and tests of iron, folate, and vitamin B_{12} nutrition in the subjects who received Imferon and folic acid are shown in Tables I and II and Figs. 1 and 2. After treatment with Imferon and folic acid these subjects showed highly significant rises in haemoglobin, haematocrit, serum iron, and percentage saturation, and a fall in U.I.B.C. as observed in the group who received Imferon alone. The mean rise in haemoglobin levels was greater than in the group who received Imferon alone. Iron stores increased in all subjects. The mean serum folate levels showed a marked rise, and morphological evidence of folate deficiency was much less apparent than in the subjects who received only Imferon. The mean serum vitamin-B_{12} concentration was higher after six weeks, but the difference is not statistically significant.

Reactions in Those Having Total Dose Imferon Infusions

Of the 81 patients who received Imferon, five (6.2%) developed thrombophlebitis at the site of the infusion within 48 hours. Two patients also complained of headache during the infusion, but the infusions were completed without further ill-effect. Two patients complained of pain in the arm at the site of the infusion during the administration of the Imferon, but did not develop any evidence of thrombophlebitis. One patient, not included in the series, had an attack of shivering soon after the start of the infusion, but there was no fall in blood pressure or rise in pulse rate. This infusion was immediately discontinued. Major anaphylactic reactions were not encountered.

Compared with the rest of the group there was no obvious difference in the folate nutrition, as determined by serum folate levels and blood and bone-marrow changes, in the patients who showed any form of reaction.

Discussion

The value of intravenous infusion of Imferon has been well substantiated as a rapid means of correcting anaemia in late pregnancy. In a recent study Bonnar (1965) has also demonstrated its effectiveness in correcting anaemia after abortion and in postnatal blood-loss anaemia. In the present study of iron-deficient postpartum anaemia, a mean rise in haemoglobin of 4.15 g./100 ml. was obtained in six weeks in the group receiving Imferon alone. This was greater than the rise obtained in the control group (3.14 g./100 ml.) but not as great as that (4.73 g./100 ml.) in the group receiving folic acid in addition to T.D.I. Imferon. These changes were reflected in the haematocrit values after six weeks. It is thus apparent that iron-deficient postpartum patients can spontaneously correct their haemoglobin levels almost to those found in the subjects given iron therapy. However, the rise in haemoglobin levels in the group of untreated women often failed to reach normal values, and was invariably associated with deterioration in their already precarious iron nutrition. What little iron was present in the marrow particles usually disappeared, hypochromia became more marked, and the percentage saturation of transferrin failed to rise. By way of contrast, in patients who received T.D.I. Imferon therapy iron stores increased markedly, hypochromia decreased, and the percentage saturation of transferrin more than doubled.

The effect of parenteral iron therapy on folate nutrition in pregnancy has been referred to by previous workers. Bonnar (1965) noted that in antenatal patients who received intravenous Imferon, 20% developed signs of an unsuspected folate deficiency which resulted in an impaired response to the iron therapy. Similar findings have been reported by Scott (1963) in a comparable group treated with intramuscular iron. She suggested that the earlier diagnosis of folate deficiency rather than any specific effect of the parenteral iron accounted for this high incidence. However, a recent study by Combrink *et al.* (1966) indicated that parenteral iron therapy itself in antenatal anaemic women may lead to signs of folate deficiency. The administration of folic acid with T.D.I. Imferon therapy will prevent this complication (Varde, 1964 ; Goldthorp *et al.*, 1965).

The results of the present study provide further evidence for a direct effect of parenteral iron therapy on folate nutrition in anaemias associated with pregnancy. In untreated subjects there was marked improvement in the indices of folate nutrition in the six-week period after confinement. This improvement was negligible in patients who received Imferon, the serum folate levels and the incidence of bone marrow megaloblastic change being similar before and after treatment. Addition of folic acid to Imferon therapy resulted in high serum folate levels and disappearance of megaloblasts from the marrow. The mechanism whereby parenteral iron retards improvement in folate nutrition is unknown. It is probably related to increased utilization of haemopoietic factors following on intense stimulation of erythropoiesis due to rapid replenishment of iron stores in the iron-deficient patient. These findings also substantiate the recommendation to administer folic acid routinely with Imferon infusion (Varde, 1964 ; Goldthorp *et al.*, 1965).

The observed changes in serum vitamin-B_{12} concentrations were relatively small. Compared with delivery, the mean values at six weeks were higher in patients who received T.D.I. Imferon and lower in the control group. There was, however, considerable variation in individual levels within the groups, and the observed differences in the mean values are not statistically significant. The results of the present study do not suggest any consistent effect of T.D.I. Imferon therapy on vitamin B_{12} nutrition.

Though most of the subjects in the present study showed evidence of folate deficiency, no major reaction to T.D.I. Imferon therapy was encountered in a total of 81 infusions. This finding does not substantiate the suggestion that major reactions may be related to folate deficiency (Lane and Scott, 1965). Thrombophlebitis at the site of infusion occurred in five patients; it was not related to the use of 5% dextrose water as diluent for the Imferon, as only normal saline was used. The slow rate of infusion may possibly have been a factor in producing thrombophlebitis.

Summary

Iron-dextran by the total dose infusion technique was administered to 81 postpartum anaemic subjects with diminished marrow iron stores. Tests of iron, folate, and vitamin B_{12} nutrition were carried out before therapy and repeated six weeks later.

Iron-dextran therapy was regarded as satisfactory in that anaemia was corrected and tests of iron nutrition returned to normal. In untreated control subjects anaemia was often spontaneously corrected, but this was accompanied by deterioration in iron nutrition.

Iron-dextran therapy retarded the improvement in tests of folate nutrition after confinement which occurred in untreated subjects. This substantiates the recommendation that folic acid be administered routinely to patients receiving Imferon therapy for anaemia associated with pregnancy.

No consistent effect of iron-dextran therapy on vitamin B_{12} nutrition could be shown.

We wish to thank the Director, South African Institute for Medical Research, and the Superintendent, Baragwanath Hospital, Johannesburg, for facilities to carry out this study; Dr. D. Lavery and Dr. R. Cassel for their help; Mrs. J. Oshry and Mrs. G. Bird for technical assistance; Sister M. Johnstone and the nursing staff at Baragwanath Hospital for their enthusiastic co-operation; and Fisons Chemicals (S.A.) (Pty.) Limited for supplies of Imferon. This study was supported in part by a research grant from the World Health Organization.

REFERENCES

Basu, S. K. (1965). *J. Obstet. Gynaec. Brit. Cwlth,* **72,** 253.
Bonnar, J. (1965). *Brit. med. J.,* **2,** 1030.
Bothwell, T. H., and Mallett, B. (1955). *Biochem. J.,* **59,** 599.
Brandt, V., and Metz, J. (1961). *S. Afr. J. med. Sci.,* **26,** 1.
Charlton, R. W., Hardie, N., and Bothwell, T. H. (1965). Ibid., **30,** 71.
Clay, B., Rosenberg, B., Sampson, N., and Samuels, S. I. (1965). *Brit. med. J.,* **1,** 29.
Combrink, P. B., Turchetti, L. C., Pannell, P., and Metz., J. (1966). *S. Afr. med. J.,* **40,** 234.
Goldthorp, W. O., Spencer, D., and Dawson, D. W. (1965). *Brit. med. J.,* **1,** 316.
Herbert, V. (1961). *J. clin. Invest.,* **40,** 81.
Lane, R. S., and Scott, J. M. (1965). *Brit. med. J.,* **1,** 449.
Scott, J. M. (1963). Ibid., **2,** 354.
Varde, K. N. (1964). *J. Obstet. Gynaec. Brit. Cwlth,* **71,** 919.
Waters, A. H., and Mollin, D. L. (1961). *J. clin. Path.,* **14,** 335.

Influenza in the West of Scotland, 1966

J. C. TAYLOR,* M.R.C.P.GLASG.; CONSTANCE A. C. ROSS,† M.D., M.C.PATH.; E. J. STOTT,†‡ B.A.

Brit. med. J., 1967, **3,** 406–408

The west of Scotland experienced concurrent epidemics of influenza type A and type B in the first quarter of 1966. The present study describes virological and clinical findings in 119 cases diagnosed as influenza by the Regional Virus Laboratory, Ruchill Hospital. Four cases of encephalitis associated with one particular age group are also reported.

Materials and Methods

During the epidemics tests for influenza-A and for influenza-B infections were carried out on routine specimens received by the laboratory from patients either in hospital or at home. The patients investigated comprised not only those with influenzal symptoms but also those with infections of the upper and lower respiratory tracts or other pyrexial illnesses for which no other cause could be found. From most of the children only specimens for virus isolation were obtained because of the difficulty of obtaining sera. In contrast, from most of the adults sera only were collected because of limited laboratory resources for isolation of respiratory viruses.

Virus Isolation.—Specimens for virus isolation comprised swabs of throat or throat and nose. Each swab (cotton-wool on wooden shaft) at collection was broken into 2 ml. of transport medium (Grist *et al.*, 1966). Of each extract 0.2 ml. was inoculated into one tube of secondary rhesus monkey kidney tissue culture, which was examined and maintained as described by Grist *et al.* (1966). Growth of either influenza-A (three strains) or influenza-B (23 strains) produced haemadsorption and generally also cytopathogenic effect in three to seven days. The type of influenza was determined by complement-fixation tests against both influenza-A and influenza-B human convalescent sera. Influenza complement-fixing antigen was usually detected at the fifth to eighth day in the primary culture; the remaining strains all fixed complement in the first passage, antigen titres ranging from 2 to 32 for the type B strains and being 32 for all three type A strains. Titres of influenza-B haemagglutinin varied from <4 to 128 in the primary culture and from 8 to 256 in the first pass; titres of influenza-A haemagglutinin were lower, being <4 in the primary culture and not above 8 after two passes. Representative type A and type B strains from children and adults were sent to Dr. H. G. Pereira, W.H.O. Influenza Centre, London, who reported that they were antigenically similar to recently isolated type A and B strains.

Serology.—Paired sera were examined for complement-fixing antibodies against influenza-A and influenza-B soluble antigens and against other relevant viral antigens as described by Grist *et al.* (1966). As the optimal concentrations of both influenza antigens were generally twofold to eightfold greater for young children than for older children or adults, two doses of each antigen were used: the higher concentration for testing sera from children under 6 years of age, and a four times lower concentration for sera from older children and adults. All titres in this paper are expressed as reciprocals.

---

* University Department of Infectious Diseases, Ruchill Hospital, Glasgow N.W.
† Regional Virus Laboratory, Ruchill Hospital, Glasgow N.W.
‡ Present address: Common Cold Research Unit, Harvard Hospital, Salisbury, Wilts.

Virological Findings

The criteria accepted as evidence of infection with influenza-A or influenza-B were virus isolation and/or positive serological findings comprising a fourfold or greater rise in titre, a high but not rising titre ($\geqslant 256$), or a fourfold or greater fall in titre.

Infection with influenza type A or type B was detected in 119 cases—61 due to type A and 58 to type B (Table I). A surprising finding was the complete absence of type A infections in the children aged 6 to 15 years, contrasting with the large number of type B infections. This suggested that children aged 6 to 15 had a high level of immunity against type A_2, the current infecting type A strain in Britain since 1957, but were susceptible to type B infection. In patients under 6 and over 15 years type A was diagnosed more frequently than type B infection.

TABLE I.—*Number of Cases with Influenza in Relation to Age*

Influenza	Age Group (Years)						Total Cases
	0–5	6–10	11–15	16–20	21–50	50+	
Type A ..	9	0	0	7	12	33	61
„ B ..	7	18	9	2	10	12	58
Total cases ..	16	18	9	9	22	45	119

Comparison of Virus Isolation and Serology.—Specimens for both virus isolation and serology were received from only 18 of the 119 influenza patients. Though the numbers are small the results shown in Table II suggest that at ages of over 5 years serological diagnosis by complement fixation was more reliable than virus isolation. In contrast, of the three children under 3 years of age from whom virus was isolated, only one showed a complement-fixing antibody response.

TABLE II.—*Comparison of Virus Isolation and Serology*

Age in Years	No. of Cases	Virology		
		VI+. S+	VI+. S−	S+. VI−
Under 3 ..	3 (1)	1 (1)	2	0
6–15	6	3	0	3
Over 15 ..	9 (4)	7 (2)	0	2 (2)
Total ..	18 (5)	11 (3)	2	5 (2)

Figures in parentheses indicate number of type A cases; others were type B. VI+ = Influenza virus isolation positive. VI− = Influenza virus isolation negative. S+ = Influenza serology position. S− = Influenza serology negative.

Complement-fixing Antibody Response and Age.—Previous workers have shown that the complement-fixing antibody response to soluble antigen is poor in young children with influenza (Grist, 1957; Henle and Lief, 1960). This was confirmed in the present study. Thus, of 60 patients in whom a rise in antibody titre and/or positive virus isolation had been demonstrated, titres greater than 32 were obtained in 36 out of 41 over 15 years of age, in three out of five aged 6 to 15 years, but in none of 14 children under 6 years old.

Clinical Features

The presenting clinical diagnoses in the 88 patients admitted to hospitals are listed in Table III in order of frequency. These patients probably represent the most severe clinical illnesses and complications in the various age groups. Pneumonia was found in all four age groups but was less common in children under 6 years than in the other groups. Influenza was not diagnosed in any of the children under 6 years. The diagnoses which were particularly associated with specific age groups were: croup in the children under 6 years (four of the five cases being under 3 years), encephalitis in those aged 6 to 15 (all four cases being from 6 to 10 years), and acute exacerbations of chronic bronchitis in those over 50.

TABLE III.—*Presenting Clinical Diagnosis in* 88 *Hospital Patients with Influenza*

Diagnosis	Age Group (Years)				Total Diagnoses
	Under 6	6–15	16–50	Over 50	
Pneumonia	3	6	8	14	31
Influenza	0	4	4	7	15
Acute exacerbations of chronic bronchitis	0	0	0	12	12
Acute bronchitis	2	1	4	2	9
Croup	5	0	0	0	5
Encephalitis	0	4	0	0	4
Upper respiratory infection ..	2	1	1	0	4
Myocarditis	0	1	2	1	4
Convulsions	2	0	0	0	2
Gastroenteritis	1	0	0	0	1
Thrombocytopenic purpura ..	1	0	0	0	1
Total patients	16	17	19	36	88

Encephalitis

As the children with encephalitis showed severe neurological involvement their case histories are given below.

Case 1.—A girl aged 6 years had a fatal illness. On 21 February 1966 she developed sore throat, fever, and cough. Three days later her behaviour became abnormal. On admission to another hospital she was semiconscious, reflexes were brisk, and the plantar reflexes were extensor. Over the next two days she became unconscious. On admission to Ruchill her temperature was 101.6° F. (38.7° C.). The tendon reflexes were now absent and the plantar reflexes were extensor. The pupils did not react to light. She was cyanosed and had bulbar paralysis. She died on 28 February, the eighth day of illness. At necropsy the striking feature was marked swelling of the brain due to oedema, but there was no coning. Microscopical examination showed no demyelinization.

Case 2.—A girl of 6 years developed coryza and cough on 19 January 1966. Four days later she was found unconscious. On admission to Ruchill on the sixth day of illness she was in coma. There was nuchal rigidity; the tendon reflexes were present, the plantar reflexes were flexor, and the pupils reacted normally. There were occasional purposeless movements of the arms and trunk but no true convulsions. The temperature was 100.6° F. (38.1° C.). Improvement was apparent four days after onset of coma. Recovery was complete when discharged on 12 February.

Case 3.—A girl of 8 years developed coryza, cough, and vomiting on 25 January 1966. She improved, but after seven days vomiting and cough returned and she talked nonsense. On the ninth day she became unresponsive to stimuli. There were no convulsions. On admission to Ruchill on 4 February her temperature was 101° F. (38.3° C.). Consciousness varied from stupor to coma; reflexes were depressed, muscle tone was low, but the plantars were flexor. The pupils reacted normally and meningism was absent. There were occasional purposeless movements of the upper limbs. Recovery took place very slowly: she began to respond to orders six days from loss of consciousness, but it was another 10 days before her mentality appeared normal. Ultimately recovery was complete.

Case 4.—A boy of 9 years was admitted to hospital on 15 January 1966 after five days' coryza and cough and one day's twitching and incontinence of urine. On admission his temperature was 100.4° F. (38° C.). The tonsils and pharynx were inflamed and the lips were blistered. He had several convulsions in which his gaze deviated to the right, but the convulsive movements were mainly of the left side of his body. Next day he was found to have a left monoparesis of the arm, his left plantar reflex was extensor, and he was in coma. He was transferred to a neurological unit for further investigations. Convulsions ceased 48 hours after onset of nervous symptoms. Right carotid angiography was negative and his left monoparesis was improving when he was returned to Ruchill on the 12th day of illness. Recovery was complete when discharged on 28 March.

Laboratory Findings.—The relevant laboratory findings in the four cases of encephalitis are shown in Table IV. Cerebrospinal fluid showed an increase in cells and/or protein in Case 2 only;

this was the only patient with clinical evidence of meningeal irritation. Evidence of active or recent infection with influenza-B virus was obtained in all cases. The isolation of influenza-B from Cases 1 and 4 and absence of detectable antibody in their "acute" sera indicated that in these two cases the onset of encephalitis occurred early in the illness. However, it was of interest that Case 1 also showed evidence of recent infection with respiratory syncytial virus (high but not rising titres) and Case 4 had an active concurrent infection with herpes simplex (virus isolation and a rising titre). In contrast, failure to isolate influenza virus from Cases 2 and 3 along with high but not rising titres to this virus indicated onset of encephalitis late in the illness.

TABLE IV.—*Laboratory Findings in Encephalitis Cases*

Case	Age in Years	Cerebrospinal Fluid (per ml.)			Virus Isolations (Throat and Nose Swabs)	Serum	
		Cells	Protein	Sugar		Day of Illness Acute/conv.	Influenza-B C.F. Titres Acute/conv.
1	6	5	15	65	Influenza-B	7/ND	[*] <8/ND
2	6	30	60	68	Negative	6/21	256/256
3	8	1	20	71	Negative	11/22	512/128
4	9	1	20	79	Influenza-B. Herpes simplex	5/17	<8/16[†]

[*] Also high titre (512) for respiratory syncytial virus.
[†] Rising titre for herpes simplex (64/256) also obtained.
ND = Not done as patient died.

Discussion

Previous studies, such as those described in the Report of the M.R.C. Working Party on Acute Respiratory Virus Infections (1965), have shown that the clinical picture of influenza and its complications may be very variable, being more frequently atypical at the extremes of life. In young children influenza is generally a mild illness and respiratory complications are rare. The present study has confirmed the variability of the clinical picture, particularly as seen in young children. Though croup was the commonest presenting diagnosis in those under 6 years of age in hospital, none required tracheostomy. In the hospital patients over 50 years old respiratory complications were frequent, the majority presenting with pneumonia or an acute exacerbation of chronic bronchitis; these are well-recognized complications of influenza in older patients (Stuart-Harris, 1966).

Development of encephalitis early and late in the influenzal illness has been described by Hoult and Flewett (1960), who suggested that in the early type of encephalitis in which histological lesions were minimal the damage might be caused by toxin or by actual virus multiplication, and that the late type showing perivascular demyelination might be produced by anti-brain antibodies. In the four cases described in the present study virological findings suggested that encephalitis developed early in the influenzal illness in two and late in the other two. Of the two early cases the patient who died (Case 1) showed serological evidence of recent infection with respiratory syncytial virus; this may have accounted for the severity of the ensuing influenzal infection. The other patient (Case 4) had a concurrent infection with herpes simplex, so it is uncertain whether influenza-B or herpes simplex or a synergic effect of both viruses caused the encephalitis.

All four patients with encephalitis in the present series were aged 6 to 10 years; the absence of this complication in the younger and older age groups is surprising. A possible explanation is that the patients aged 6 to 10 years had the greatest number of type B infections, many of which were probably primary. However, the absence of encephalitis in those under 6 years, in whom there would be an even higher proportion of both type A and type B primary infections, suggests that some other factor relevant to age was related to the onset of encephalitis. In this connexion the poor antibody response of young children to influenza might be relevant, as development of the late type of encephalitis might require both a primary infection and a good antibody response. The poor antibody response of young children might protect them against the type of encephalitis which Webb and Smith (1966) have suggested may be associated with an antigen-antibody reaction. If this type of reaction is concerned in the late type of influenza encephalitis then the age incidence of this complication might depend on the peak age incidence (excluding very young children) of primary infection with influenza; this would vary from epidemic to epidemic, depending on the community's previous experience of the infecting influenza strain or antigenically related strains. To establish a correlation between encephalitis and primary infection detailed serological surveys of influenza antibodies in different age groups of the community would be required. As such surveys had not been done in this area before the present epidemics, further investigations along these lines are indicated.

Summary

During the first quarter of 1966 there were concurrent epidemics of influenza type A and type B in the Glasgow area. Virological diagnosis of active infection with type A was made in 61 patients and of type B in 58. Type A infections were more frequent than type B in patients under 6 years and in those over 15 years. In children aged 6 to 15 years no type A but a large number of type B infections were detected. This suggested that children aged 6 to 15 years had high immunity against type A_2, the current infecting type A strain in Britain since 1957, but were susceptible to type B infections.

In 88 patients admitted to hospital the clinical diagnoses particularly associated with specific age groups were: croup in children under 6 years old, encephalitis in those aged 6 to 10, and acute exacerbations of chronic bronchitis in patients over 50. The four encephalitis cases are described and possible reasons for development of this complication are discussed.

We are grateful to the many doctors in hospital, public health, and general practice (particularly Drs. W. Blair and A. Clarke) who sent us specimens; and to Professor T. Anderson and Dr. I. W. Pinkerton for permission to publish details of the encephalitis cases. We thank Dr. H. G. Pereira, W.H.O. Influenza Centre, Mill Hill, London, for antigenic analysis of influenza strains, Dr. J. F. Boyd for necropsy findings, and Mr. S. McMichael, A.I.M.L.T., and Miss M. Walker for valuable technical assistance.

References

Grist, N. R. (1957). *Scot. med. J.*, 2, 249.
—— Ross, C. A. C., Bell, E. J., and Stott, E. J. (1966). *Diagnostic Methods in Clinical Virology.* Oxford.
Henle, W., and Lief, F. S. (1960). *J. Immunol.*, 84, 491.
Hoult, J. G., and Flewett, T. H. (1960). *Brit. med. J.*, 1, 1847.
Medical Research Council (1965). Ibid., 2, 319.
Stuart-Harris, C. H. (1966). Ibid., 1, 149.
Webb, H. E., and Smith, C. E. G. (1966). Ibid., 2, 1179.

Comparison of Duration of Activity of Corticotrophin-Gelatin and Corticotrophin-Carboxymethylcellulose

M. FRIEDMAN,* M.D., M.R.C.P.ED.

Brit. med. J., 1967, 3, 409–410

Corticotrophin is rapidly destroyed in the blood stream. Several substances have been added to corticotrophin in order to prolong its duration of action. These substances act at the site of injection and delay the release or destruction of corticotrophin. In the United Kingdom gelatin and zinc preparations of corticotrophin have been in use for many years. Recently a preparation of corticotrophin with the addition of carboxymethylcellulose (Crooks A.C.T.H./c.m.c.) has been introduced in this country. The manufacturers have claimed that this preparation "lasts like" the gelatin preparation. An investigation has been undertaken in normal healthy volunteers to test the validity of this claim.

Methods

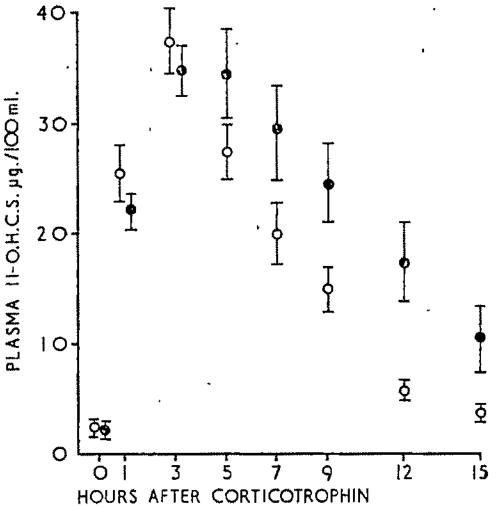
The investigation was carried out on 10 normal healthy volunteer subjects (two women and eight men) aged 22 to 35 years. They continued with their normal activities; there were no restrictions on diet or activity during investigation. Each subject was given 2 mg. of dexamethasone daily in four divided doses on the two days preceding the test and on the day of the test to suppress endogenous corticotrophin release. At 09.00 hours on the day of the test each subject was given either 40 international units of a gelatin-corticotrophin preparation (Acthar Gel Armour Batch No. KG. 2802) or 40 international units of corticotrophin-carboxymethylcellulose preparation (Crooks A.C.T.H./c.m.c. Batch No. 65091) by deep intramuscular injection. After an interval of seven days a second test was carried out under identical conditions administering the corticotrophin preparation not received in the first test. The initial preparation used in each subject was randomly selected. Blood samples were taken before and at 1, 3, 5, 7, 9, 12, and 15 hours after the injection of corticotrophin for the measurement of plasma 11-hydroxycorticosteroid concentration by the method of Mattingly (1962). Urine was collected in two six-hour periods after the corticotrophin injection for measurement of the urine 11-hydroxycorticosteroid concentration by the method of Mattingly *et al.* (1964).

Results

The plasma 11-hydroxycorticosteroid levels after the corticotrophin carboxymethylcellulose and gelatin preparations are given in Table I. Table II shows the urinary 11-hydroxycorticosteroid levels. The Chart shows the mean of the results obtained in the 10 subjects with the standard error of the mean.

A *t* test on means of the paired differences in plasma 11-hydroxycorticosteroid levels of all subjects at each time after the administration of corticotrophin showed that the gelatin preparation produced a greater rise of plasma 11-hydroxycorticosteroids than the carboxymethylcellulose preparation at 5, 7, 9, and 12 hours (5 hours $P<0.05$, 7 hours $P<0.05$, 9 hours $P<0.01$, 12 hours $P<0.02$). At 1, 3, and 15 hours the differences were not significant (1 hour $P<0.1$, 3 hours $P<0.1$, 15 hours $P<0.1$).

A *t* test performed on means of the paired differences in urinary 11-hydroxycorticosteroid excretion in 9 of the 10 subjects showed that there was not a significant difference in the urinary excretion of free 11-hydroxycorticosteroids during the first six hours after administration of the two types of corticotrophin ($P<0.1$). During the second six hours the gelatin preparation produced a greater excretion of 11-hydroxycorticosteroids than the carboxymethylcellulose preparation ($P<0.05$).



Means and standard error of means for each type of corticotrophin. The open circles represent the values obtained with carboxymethylcellulose and the closed circles the values with the gelatin preparation.

Discussion

Intramuscular injection of corticotrophin in saline produces a maximal adrenal-stimulating effect in two hours with a fall in plasma steroids to control levels in four to six hours (Bayliss and Steinbeck, 1954). The short duration of effect is due to enzymatic destruction of the corticotrophin at the site of injection or in the blood stream. The instability of the saline preparations has stimulated the search for long-acting preparations. The addition of a number of substances to corticotrophin has been shown to increase the duration of activity either by delaying the release of corticotrophin or by inhibiting enzymatic destruction of the corticotrophin at the site of injection. Aluminium phosphate in polyvinyl pyrrolidine (Wolfson *et al.*, 1951), procaine (Holbrook, 1951), cellulose and carboxymethylcellulose (Payne *et al.*, 1951; Nordström and Jensen, 1954), oils (Raben *et al.*, 1952), and gelatin (Raben *et al.*, 1952) have all been shown to enhance corticotrophin activity, probably by delaying release at the site of injection. The addition of zinc compounds to corticotrophin is thought to inhibit enzymatic destruction at the site of injection (Ferriman *et al.*, 1954; Homan *et al.*, 1954). The therapeutic efficiency of any individual preparation of corticotrophin is related to the con-

---

* Paediatric Department, University College Hospital, London W.C.1, and Whittington Hospital, London N.19.

TABLE I.—*Plasma* 11-*hydroxycorticosteroid Levels Expressed as µg./*100 *ml. Plasma, at Intervals after Intramuscular Injection of* 40 *i.u. Corticotrophin-carboxymethylcellulose and Gelatin in* 10 *Normal Healthy Subjects*

Type of Corticotrophin	Hours after Injection	Subject										Mean	±1 S.E. of Mean
		1 M	2 M	3 M	4 M	5 M	6 M	7 M	8 F	9 F	10 M		
Carboxymethyl cellulose	0	1·8	2·2	3·4	4·0	2·0	3·4	3·6	2·2	2·2	3·8	2·9	0·3
	1	31·4	21·4	34·8	34·6	18·6	29·8	29·8	25·8	20·4	13·2	25·7	2·3
	3	37·4	29·6	52·6	49·2	32·0	48·6	36·0	27·6	40·6	20·8	37·4	3·3
	5	34·0	26·4	33·6	30·6	20·6	33·8	20·2	29·2	32·4	14·2	27·5	2·2
	7	23·6	24·4	20·0	23·6	20·0	31·6	9·6	20·6	23·8	8·6	20·6	2·2
	9	12·2	19·2	14·8	18·8	10·6	26·8	6·4	14·2	19·8	6·6	14·9	2·0
	12	7·2	10·0	7·0	6·8	5·8	8·4	3·0	6·0	6·8	4·6	6·5	0·6
	15	4·2	6·6	5·0	3·6	3·6	4·6	2·8	3·8	4·2	2·2	4·0	0·3
Gelatin	0	2·4	2·0	4·0	1·8	1·6	1·4	3·4	2·0	3·2	2·4	2·4	0·2
	1	24·0	20·4	22·0	29·6	17·0	21·4	18·6	19·4	31·8	17·2	22·1	1·6
	3	34·0	30·2	41·0	48·2	23·4	28·6	42·8	34·2	43·6	27·2	35·3	2·6
	5	41·8	33·0	45·2	27·0	13·2	30·8	40·2	41·2	56·2	16·0	34·5	4·1
	7	33·2	32·4	36·4	29·2	8·0	33·0	29·6	42·4	44·4	7·2	29·5	4·0
	9	29·8	31·8	24·8	30·0	5·4	28·2	18·4	36·2	35·4	4·4	24·4	3·6
	12	15·0	21·2	10·6	25·4	4·0	17·0	13·2	40·4	26·4	2·2	17·5	3·6
	15	8·4	9·4	8·4	14·2	3·6	6·2	6·8	36·2	13·2	2·0	10·8	3·0

TABLE II.—*Urinary Free* 11-*hydroxycorticosteroids Expressed as µg. per Hour. Each Value Represents the Mean Excretion Over a Six-hour Period*

Type of Corticotrophin	Hours after Injection	Subject										Mean	±1 S.E. of Mean
		1	2	3	4	5	6	7	8	9	10		
Carboxymethyl cellulose	0–6	44·2	12·4	29·4	39·4	12·6	53·4	18·9	—	14·0	12·5	26·3	5·3
	6–12	12·0	20·7	8·5	16·9	8·6	32·6	4·6	—	14·0	15·2	14·8	2·8
Gelatin	0–6	43·6	14·9	28·2	18·6	5·7	36·8	15·0	25·7	13·8	10·2	21·3	3·8
	6–12	23·7	34·0	34·2	25·2	5·0	54·5	16·0	74·4	34·3	3·9	30·0	6·8

centration of corticotrophin and duration of activity, the latter being determined by the carrier vehicle.

A number of factors must be taken into account when comparing the corticotrophin preparations. Considerable variation in individual response to corticotrophin occurs (Bayliss and Steinbeck, 1954). In the present study this is shown by Subject 5 (Table I), who reacted differently from all the other subjects with respect to his response to the gelatin and carboxymethylcellulose preparation. The standardization of different preparations of corticotrophin may vary from batch to batch and from manufacturer to manufacturer. However, the carrier vehicle for corticotrophin is comparably much more important than minor variations in concentration. DiRaimondo and Forsham (1958) have shown that doubling the corticotrophin dose of a gelatin preparation prolongs the increase in steroidogenesis by approximately one hour. In the present study the gelatin preparation appears to be superior to the carboxymethylcellulose preparation at 5, 7, 9, and 12 hours. This difference suggests that gelatin is superior to carboxymethylcellulose in delaying release of corticotrophin from the site of injection and prolonging corticotrophin activity.

Hangård *et al.* (1960), investigating the effect of response of different types of repository corticotrophin preparations, including gelatin and carboxymethylcellulose, were unable to draw definite conclusions from their study. They suggest that individual variations in response and unequal potency of different preparations make comparative studies difficult. In their study they did not inhibit endogenous corticotrophin by pituitary suppression, which introduced a further variable. Hedner (1963) found that a corticotrophin-gelatin preparation had a significantly longer duration of action compared with a preparation of carboxymethylcellulose in equivalent dosage.

Because of its low viscosity, carboxymethylcellulose can be drawn up into a syringe and injected with ease. No prior warming of the preparation is required. This is an advantage. The gelatin preparation, however, has a high viscosity and requires warming before administration. Furthermore, the gelatin may solidify in the syringe, and if not injected soon after warming this may lead to some of the preparation being lost from the joint between the needle and the syringe if excessive force is used during the injection.

The present investigation and the published data available suggest that corticotrophin-carboxymethylcellulose does not have the same duration of activity as the gelatin preparation and is likely to be inferior therapeutically if used in equivalent dosage. Caution should be exercised when changing from one preparation to another in equivalent doses. At present carboxymethylcellulose does not seem to offer any therapeutic advantage over the gelatin preparation. The claim that carboxymethylcellulose "lasts like gel" is not substantiated.

Summary

A comparison has been made of the potency and duration of activity of two preparations of corticotrophin, one combined with gelatin and the other with carboxymethylcellulose. The plasma and urinary 11-hydroxycorticosteroid levels were measured in 10 normal subjects after an intramuscular injection of 40 international units of each preparation. The duration of activity of the carboxymethylcellulose preparation was less than that of the gelatin preparation in 9 out of the 10 subjects. Caution should be exercised when changing from one preparation to another in equivalent doses.

I am grateful to Crooks Laboratories Limited for supplies of carboxymethylcellulose preparation (Crooks A.C.T.H./c.m.c.) used in this study.

REFERENCES

Bayliss, R. I. S., and Steinbeck, A. W. (1954). *Brit. med. J.*, **1**, 486.

DiRaimondo, V. C., and Forsham, P. H. (1958). *Metabolism*, **7**, 5.

Ferriman, D. G., Anderson, A. B., and Turner, P. P. (1954). *Lancet*, **1**, 545.

Hangård, G., Kirkeby, K., and Lingjærde, P. (1960). *Acta med. scand.*, **168**, 205.

Hedner, P. (1963). *Acta endocr. (Kbh.)*, **43**, 499.

Holbrook, W. P. (1951). *Proceedings of the 2nd Clinical A.C.T.H. Conference*, **11**, 24. Philadelphia.

Homan, J. D. H., Overbeek, G. A., Neutelings, J. P. J., Booij, C. J., and van der Vies, J. (1954). *Lancet*, **1**, 541

Mattingly, D. (1952). *J. clin. Path.*, **15**, 374.

—— Dennis, P. M., Pearson, J., and Cope, C. L. (1964). *Lancet*, **2**, 1046.

Nordström, S., and Jensen, C. C. (1954). *Svenska Läk.-Tidn.*, **51**, 2196.

Payne, R. W., Rosenberg, I. N., Raben, M. S., Cleroux, A. P., and Astwood, E. B. (1951). *J. clin. Invest.*, **30**, 665.

Raben, M. S., Rosenberg, I. N., Westermeyer, V. W., and Astwood, E. B. (1952). *J. Amer. med. Ass.*, **148**, 844.

Wolfson, W. Q., Thompson, R. E., Robinson, W. D., Duff, I. E., Cohn, C., Lewis, L., and Hunt, H. D. (1951). *Proceedings of the 2nd Clinical A.C.T.H. Conference*, **11**, 2. Philadelphia.

Cystic Adventitial Disease of the Popliteal Artery

G. J. T. LEWIS,* M.B., F.R.C.S.ED.; D. M. DOUGLAS,† M.B.E., CH.M., F.R.C.S., F.R.C.S.ED.
W. REID,‡ M.B., F.R.C.S.GLASG., F.R.C.S.ED.; J. KENNEDY WATT,§ CH.M., B.SC., F.R.C.S., F.R.C.S.GLASG.

Brit. med. J., 1967, **3**, 411–415

In 1954 Ejrup and Hiertonn recorded a case of stenosis of the popliteal artery caused by a cyst arising from the adventitia, and this case and three similar ones were described by Hiertonn, Lindberg, and Rob (1957) as "cystic degeneration of the popliteal artery." The cardinal features they described were those of a localized arterial disease of young adult males causing intermittent claudication of sudden onset, which was successfully treated by resection of the affected arterial segment with autogenous vein graft or arterial homograft replacement.

This condtion is rare, and of the 32 cases described in the literature 24 have involved the popliteal artery (Sutton, 1962; Hamming and Vink, 1965; and others). It has also been described in the external iliac artery (Atkins and Key, 1946; Jacquet and Meyer-Burgdorff, 1960), the radial artery (Parkes, 1961; Bäckström, Linell, and Ostberg, 1965), and the ulnar artery (Parkes, 1961), and Hiertonn (1966) mentions a case in which the lesion arose from a small branch of the popliteal artery.

This paper presents three additional cases affecting the popliteal artery and reviews the literature on the condition.

Case 1

A boy aged 13 presented at the peripheral vascular unit, Glasgow Royal Infirmary, in March 1964. The previous month, during a gym period at school, he felt a sudden cramping pain in the left calf, and subsequently experienced pain in the left calf and popliteal fossa which stopped him walking at 100 yards (90 metres), and which was relieved by rest. He also complained that the left foot was colder than normal and often became white.

On examination there was wasting of the left calf. The left common femoral pulse was normal, but the left popliteal, posterior tibial, and dorsalis pedis pulses were absent and there was pallor of the left foot on elevation. Oscillometry showed an absence of pulsation in the left calf but normal pulsation in the left thigh. The right leg was normal. A femoral arteriogram showed a smooth stenosis of the popliteal artery, 2 cm. long, at the level of the femoral epiphysial line. The sural arteries arose from the stenosed area and the remaining vessels were normal.

In June the left popliteal artery was explored and found to be dilated immediately above the level of the knee joint, and though dissection caused marked proximal spasm the artery was otherwise normal. On incising the adventitia of the "dilatation," gelatinous material extruded from between the adventitia and media. The media and intima were normal and the arteriotomy was repaired with a vein patch. At the completion of operation normal pulses had returned to the leg.

In August 1966, 27 months postoperatively, he was symptom-free and there was no clinical abnormality of the leg.

Case 2

A man aged 42 presented at the peripheral vascular unit, Glasgow Royal Infirmary, in April 1964 with an 18-month history of claudication in the left calf, discomfort behind the left knee, and numbness of the left foot on walking half a mile (800 metres). There was no other relevant history.

On examination the femoral, popliteal, and posterior tibial pulses were normal but the dorsalis pedis pulse was absent. In the left popliteal fossa there was a visible swelling which was poorly defined, non-pulsatile, and of rubbery consistency. He was admitted for arteriography in July, by which time his claudication was forcing him to stop at a quarter of a mile (400 metres) and the left popliteal and posterior tibial pulses were diminished. A left femoral arteriogram on two occasions failed to demonstrate the superficial femoral artery but a right femoral arteriogram was normal. Left phenol lumbar sympathectomy was performed and his claudication distance increased to more than one mile (1,600 metres) at a normal pace.

The popliteal cyst was thought to be a semimembranosus bursa, but at exploration in October it was found to arise from the anterior wall of the popliteal artery and there was no communication with the knee joint. On incising the cyst a quantity of thick "jelly" extruded. The cyst wall was partially excised, after which the popliteal artery pulsated normally. Postoperatively the popliteal and posterior tibial pulses were normal, and he was asymptomatic for about one year.

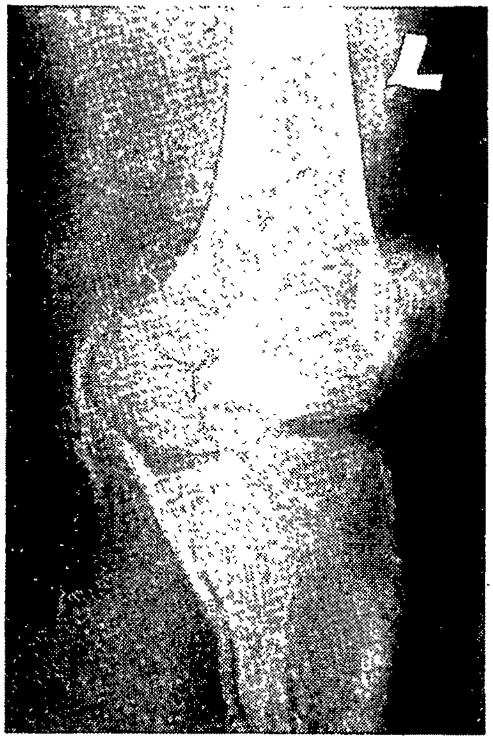


FIG. 1.—Case 2. Arteriogram showing posterior displacement of the popliteal artery due to the cyst.

He then had recurrence of claudication at 400 yards (365 metres), and on examination it was found that the popliteal cyst had recurred and was pushing the popliteal artery posteriorly so that the popliteal pulse was more easily palpable than normal and there was an audible bruit. Arteriography showed postero-medial displacement of the artery (Fig. 1). Ten millilitres of viscous homogeneous gel with a pinkish hue was aspirated from the cyst and he again became asymptomatic.

---

* McIntyre Research Scholar, Glasgow Royal Infirmary. Present address, The Medical Centre, Ararat, Victoria.
† Professor of Surgery, St. Andrews University.
‡ Peripheral Vascular Unit, Glasgow Royal Infirmary and Belvidere Hospital, Glasgow.
§ Peripheral Vascular Unit, Glasgow Royal Infirmary and Belvidere Hospital, Glasgow.

When readmitted in August 1966 he was symptom-free, but a systolic bruit was audible over the easily palpable popliteal artery. At exploration the cyst lay anterior to the popliteal vessels at the level of the knee joint, being bound to the artery and vein by a tough outer sheath of fibrous tissue, which when divided revealed a translucent thin-walled mutilocular cyst. A plane of cleavage existed between the artery and cyst at all but one point where a stalk was present about 2 mm. in diameter and length (Fig. 2), and here the cyst had to be cut off the artery. Histology of the specimen showed several cysts with fibrous connective-tissue walls which peripherally incorporated a very small amount of elastic fibres and with a lining of flattened fibroblast-like cells. Gradations from fully formed cysts to regions of myxomatous degeneration were present (Fig. 3). There was no evidence of neoplasm or inflammation.

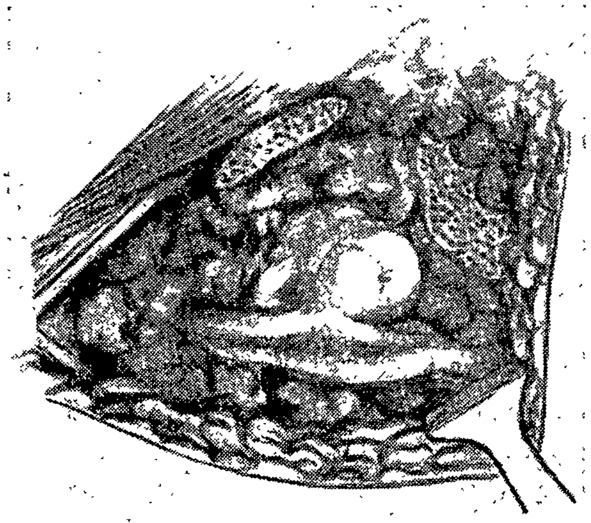


FIG. 2.—Case 2. Findings at operation. The medial head of gastrocnemius has been divided. The lobulated cyst arises from the anterior wall of the artery and the vein is crossing the artery at this level.

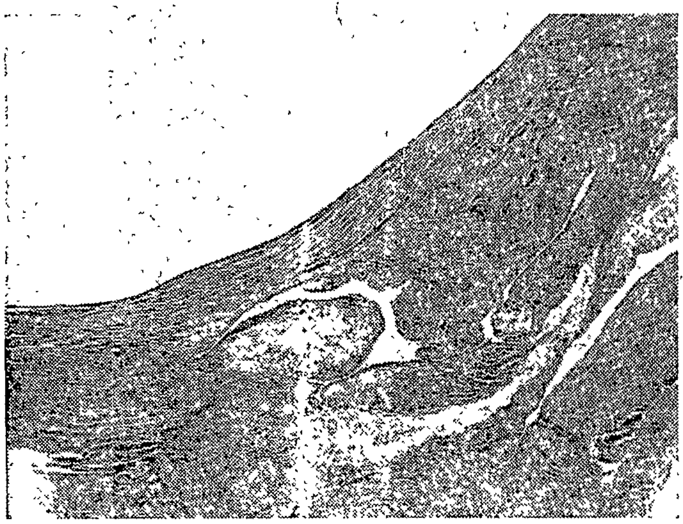


FIG. 3.—Case 2. Photomicrograph of cyst showing the connective-tissue wall and gradations from regions of myxomatous degeneration to fully formed cysts. (Haematoxylin and eosin. ×33.)

Case 3

A man aged 55 attended the vascular clinic at Dundee Royal Infirmary on 20 July 1964 complaining of pain in the right calf on walking 100 yards (90 metres). The onset was gradual over a period of two to three months.

Examination of the right leg showed that all peripheral pulses beyond the femoral artery were absent whereas the pulses in the left leg were normal. Arteriography showed a stenosis of the popliteal artery, and a provisional diagnosis of early atheromatous change was made (Fig. 4).

On 24 July the popliteal artery was explored and a curious cystic mass of tissue involving the adventitia was disclosed. It measured 3 cm. in length and 2 cm. in width, and when it was dissected clear of the vessel the latter took on a normal appearance.

Postoperatively pulsation returned to his pedal vessels, his claudication disappeared, and arteriography showed a return of the vessel to a normal appearance (Fig. 4).

He returned to the vascular clinic on 26 April 1965, 10 months after operation, with a complaint of pain on walking. Arteriography on 9 July showed slight narrowing and irregularity of the proximal part of the popliteal artery. However, his distal pulses were normal, and when seen again on 17 September he was symptom-free.

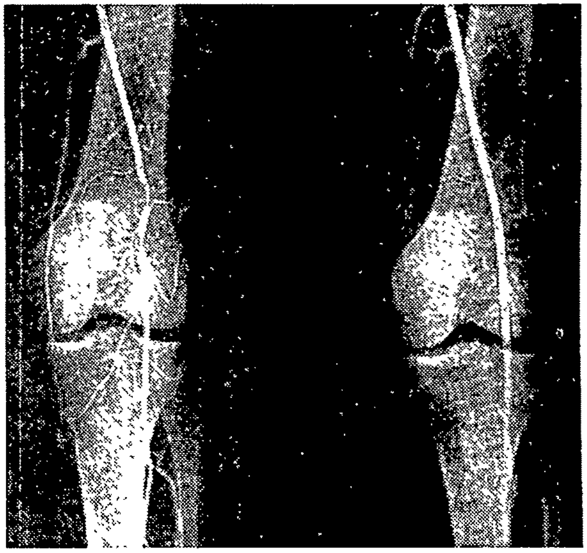


FIG. 4.—Case 3. Preoperative and postoperative arteriograms. In the preoperative picture there is striking demonstration of the development of the geniculate anastomosis around the knee joint. Postoperatively the arteriographic appearance is normal.

The histology of the lesion (Fig. 5) was reported as: "The specimen was a ragged piece of tissue, 12 by 8 by 6 mm., of firm consistency and yellowish-white cut surface. Sections show it to consist of varying cellular fibrous tissue in which there are many fairly sharply circumscribed areas of mucinous degeneration. Various stages in the process leading up to the end-stage of formation of "lakes" of metachromatic mucin can be seen. There would appear to be an initial overgrowth of the fibroblasts, then their gradual conversion to swollen cells with finely granular or foamy cytoplasm; and finally a bursting of the cells with release of the now mucinous contents. The process is akin to that which produces the 'ganglion' in association with the tendon or tendon sheath, but it appears, clinically, that the association was wholly

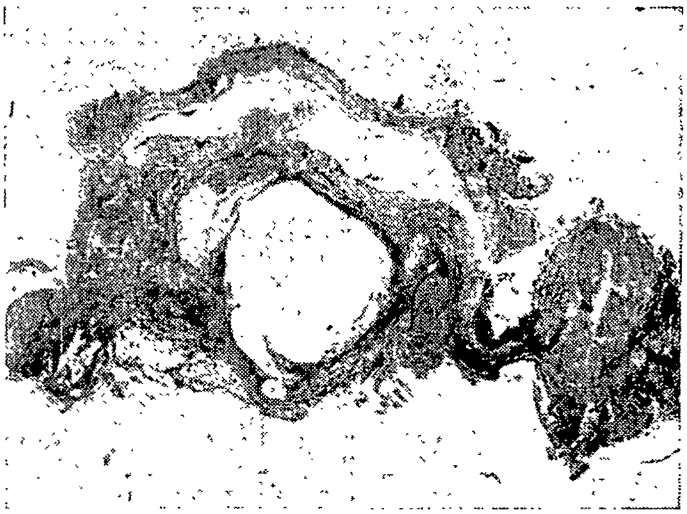


FIG. 5.—The whole section of the lesion removed at operation, showing the cystic spaces which were filled with gelatinous material.

with the wall of the popliteal artery. It is thus difficult to go further than to classify this as ' myxoma of arterial adventitia.' "

Discussion

Cystic degeneration of the political artery is a rare condition the cause of which is unknown. The incidence in the peripheral vascular unit, Glasgow Royal Infirmary, is approximately 1 in 1,200 of those patients presenting with claudication or 1 in 1,000 of those undergoing arteriography, an incidence similar to that reported by Hamming and Vink (1965). The sex incidence in the literature is eight males to one female, which approximates to the sex incidence of occlusion in the lower limb due to atherosclerosis. The three cases reported in females have all involved the popliteal artery. The average age of affected males is 36 years and of females 49 years.

The aetiology of the lesion is obscure. It seems unreasonable to ascribe its development to degenerative changes in an atherosclerotic or otherwise abnormal arterial wall, as our first patient (Case 1) was 13 years of age and Harris and Jepson (1965) described its occurrence in a boy of 11 years, and for this reason the title " cystic degeneration " appears to be a misnomer. Histology shows no evidence of haemorrhage, inflammation, or neoplasia, and the appearance is similar to that found in ganglia elsewhere. On the other hand, ganglia are most commonly found in the late teens and twenties (McEvedy, 1962), whereas this condition has its greatest incidence in the late thirties, a time when atherosclerosis is often developing.

The media and intima are usually intact and any damage to them is probably secondary (Hiertonn *et al.*, 1957 ; Andersson, Gothman, and Lindberg, 1959). Harris and Jepson (1965) reported a significant amount of hydroxyproline present in the

Nature of Lesion and Results of Treatment in 24 Cases of Cystic Adventitial Disease of the Popliteal Artery

Case No.	Year Reported	Author	Age	Sex	Onset	Arteriogram	Year	Operation Findings	Operation	Histology	Condition at Follow-up
1	1957	Hiertonn *et al.*	32	M	Gradual	Stenosis	1953	Walnut-sized swelling, bluish in colour	Resection and autogenous vein graft	Unilocular adventitial cyst. Normal media and intima	Patent 11 years (1964)
2	1957	"	25	M	Sudden	Occlusion, 3 cm.	1955	Fusiform thickening 6 cm. long	Resection and arterial homograft	Adventitial cyst. Partial media necrosis	Patent 11 years (1966)
3	1957	"	24	M	"	Occlusion	1954	Fusiform thickening 9 cm. long, bluish in colour. Periarteritis	Resection and autogenous vein graft	Adventitial cyst communicating with lumen and a double lumen had developed distally. Medial calcification	Patent 10 years (1964)
4	1957	"	32	M		Occlusion, 6 cm.	1956	Fusiform swelling 7 cm. long, light pink in colour	Resection and autogenous vein graft	Adventitial cyst. Normal media	Patent 8 years (1964)
5	1958	Tytgat *et al.*	47	M	"	Stenosis	1957	Pulsatile swelling 5 cm. long with periarteritis	Resection and nylon graft	Multilocular cyst in media and adventitia communicating with lumen in two places	Occluded 4 months later
6	1958	Patel *et al.*	50	F	Gradual	"	1952	Fusiform swelling	Arteriotomy and extrusion of gel		Patent 8 years (1960)
7	1959	Andersson *et al.*	48	M	Unknown	Occlusion, 8 cm.	1959	Fusiform swelling 8 cm. long	Resection and arterial homograft	Cyst between media and adventitia with a tiny communication with the lumen (thought to be secondary). Degenerative changes in media and intima	Patent 7 years (1966)
8	1960	Holmes	42	M	Sudden	Stenosis, 4 cm.	1957	Fusiform swelling 3 cm. long	Excision of cyst with outer part of arterial wall	Cyst lined by degenerated fibrous tissue and covered by fibrin and fibrinoid material	Patent 8 years later
9	1960	Delannoy, Martinot	38	M	Unknown	Stenosis, 2 cm.	1958	Fusiform swelling 5 cm. long	Incision of cyst and extrusion of gel		Patent 2 years later
10	1960	Robb	39	M	Sudden	Stenosis, 3 cm.	1959	Transparent almond-shaped cyst 5 cm. long with periarteritis	Resection and autogenous vein graft	Adventitial cyst with flattened endothelial cell lining	Unknown (1966)
11	1961	Ishikawa *et al.*	32	M	"	Stenosis	1959	" Sausage-like tumour " 3 cm. long	Excision of cyst. (Lumbar ganglionectomy 1 year earlier)	Multilocular cyst lined by lamellar fibrous tissue	Patent 5 years (1964)
12	1962	Chevrier	26	M	"	Stenosis with posterior displacement	1961	Swelling 2 cm. long	Excision of cysts	Adventitial cyst	Patent 6 months later (1961)
13	1963	Simon	52	M	"	Stenosis	1962	" No thickening or hardening "	Resection and Dacron graft		Patent 16 months later (1963)
14	1963	Patel, Cormier	23	M	"	"	1962	Fusiform bluish swelling	Resection of cyst and periarterial sympathectomy	Adventitial cyst with endothelial lining	Not seen since operation
15	1963	Bliss *et al.*	40	F	"		1962	Fusiform swelling 5 cm. long with periarteritis	Incision of cyst with extrusion of gel and biopsy	Dense fibrous tissue with a few elastic fibres	Return of slight claudication 1966
16	1963	Lambley	47	M	"		1962	Fusiform bluish pulsating swelling 5 cm. long	Resection and Teflon graft	Adventitial cyst with endothelial celllining. Patchy medial fibrosis and intimal thickening	Occluded 9 months but symptom-free 3 years later (1966) following lumbar ganglionectomy
17	1964	Barnett, Morris	56	F	Gradual	Occlusion	1963	Fusiform bluish swelling 5 cm. long	Arteriotomy with extrusion of gel and Dacron patch	Subintimal mucinous degeneration	Patent 2 years (1965) but narrowed
18	1965	Harris, Jepson	11	M	Unknown	Severe stenosis	1964	Swelling in two parts. Upper part tense, bluish, 2·5 cm. long	Partial cyst excision with gel extrusion		Unknown (1966)
19	1965	Mentha	33	M	Sudden	Stenosis	1960	Diagnosis made by aspiration of gel	Lumbar ganglionectomy and cyst aspiration		Patent 6 years (1966)
20	1966	Hansen	56	M	Gradual	Occlusion	1963	Fusiform pulsating swelling 5 cm. long	Partial cyst excision with extrusion of gel	Multilocular cyst	Patent 3 years (1966)
21	1966	Barnett *et al.*	61	M	Sudden	Stenosis on lateral view only	1965	Fusiform swelling 3·5 cm. long	Resection and autogenous vein graft		
22	1967	Case 1	13	M	"	Stenosis	1964	Fusiform swelling 3 cm. long	Arteriotomy with extrusion of gel	Nil	Patent 2 years (1966)
23	1967	" 2	42	M	Gradual	Stenosis with displacement	1964	Lobulated translucent cyst on one side of artery	Incomplete excision (1964)		Recurrence 1 year
							1966	" " "	Excision of cyst in toto	Multilocular cyst	Patent 6 months (1966)
24	1967	" 3	55	M	"	Stenosis	1964	Gelatinous cystic mass 3 by 2 cm.	Excision of cyst in toto	" "	Patent 1 year (1965)

Note: Cases reported by Hamming and Vink (1965), Grepe (1963), Sutton (1962), and Bartos (1966) are not reviewed above.

gel and suggested that this indicated its origin from collagen tissue, but quantitative analysis of the protein of the gel from Case 2 does not support this view (see Addendum). Most authors—for example, Ishikawa, Mishima, and Kobayashi (1961)—have suggested that repeated minor trauma to the popliteal artery plays a significant part. The fact that the lesion is almost always in close association with the back of the knee joint and that gelatinous degeneration of the tendon sheaths in this region is common raises the possibility that regional factors may be concerned—for example, the range of movement of the knee joint and of the adjacent artery and tendons. But a more attractive theory might be the incorporation, during development, of mucin-secreting cells from the endothelium of the knee joint in the adventitia of the artery. These cells secreting small amounts of mucin over many years might eventually give rise to tense adventitial cysts which encroach on the lumen of the vessel.

The usual presenting symptom is intermittent claudication, which may be of gradual or sudden onset and may be accompanied by a cold white foot and pain. Sometimes the initial symptoms are episodic and the pain is atypical of claudication (Barnet and Morris, 1964 ; Hiertonn *et al.*, 1957). The pulse pattern is variable, and in the two cases with "ischaemic rest pain" the lower-limb pulses were normal (Chevrier, 1962 ; Mentha, 1965), suggesting a neuritis from pressure on the popliteal nerves. Exercise or knee flexion may cause the disappearance of distal pulses (Ishikawa *et al.*, 1961). A visible and palpable swelling (Case 2) has not previously been reported, though Lambley (1963) noted the affected popliteal artery to be more easily palpable than normal and Mentha (1965) recorded a bruit at the level of the stenosis.

The condition can usually be recognized by the typical arteriographic appearances, which show a localized lesion at or above the level of the knee joint in an otherwise normal popliteal artery. The lesion may cause stenosis, occlusion, or displacement of the artery. The stenosis is a smooth indentation of the arterial wall which may be one-sided or hour-glass in appearance, and which may vary in severity with the pulse wave (Jacquet and Meyer-Burgdorff, 1960) or posture (Bliss, Rhodes, and Rains, 1963). Similar stenotic appearances may be caused by a local atheromatous plaque, but post-stenotic dilatation has not been noted with cystic degeneration and in doubtful cases a lateral arteriogram may show irregularity. With adventitial cysts, lateral views may also show posterior displacement of the artery (Case 2) or a rigid arterial segment causing kinking of the artery when the knee is flexed (Ishikawa *et al.*, 1961). Occlusion may be due to contact between the intimal surfaces of the artery (Hiertonn *et al.*, 1957 ; Harris and Jepson, 1965), but more often it is due to thrombosis after severe stenosis. Once thrombosis has occurred, the arteriographic appearances resemble those of arteriosclerosis, though a smooth tapering-off at the limits of the occlusion (Andersson *et al.*, 1959)—aply termed the "scimitar" effect by Harris and Jepson (1965)—may suggest cystic pressure.

At operation the lesion most commonly appears as a well-defined lump, bluish in colour, non-pulsatile, elastic in consistency, and of variable length (2–9 cm.), and it may lie to one side of, or partially or completely invest, the artery. It has also been described as a dilatation of the artery (Simon, 1963) as yellowish brown in colour (Ishikawa *et al.*, 1961) and as a pulsatile lump (Lambley, 1963 ; Tytgat, Derom, and Galinsky, 1958). Dense periarterial adhesions similar to those found in Case 2 have been reported by other authors (Hiertonn *et al.*, 1957 ; Robb, 1960 ; Tytgat *et al.*, 1958 ; Ishikawa *et al.*, 1961 ; Bliss *et al.*, 1963).

The type and outcome of surgical treatment in 24 cases are summarized in the Table ; all the cases appear to have had excellent initial results. The late results in 13 of them have been obtained by correspondence with previous authors. When a stenosis is present, incision of the cyst with extrusion of the gel or excision of the cyst in toto (with or without arteriotomy) may give a satisfactory long-term result, but when occlusion is present arterial resection with autogenous vein graft should be performed, as synthetic grafts at this level are prone to occlusion. Case 2 supports the view that recurrence may follow partial excision of the cyst (Bäckström *et al.*, 1965), and Rains (1966) writes of the recurrence of claudication four years after incision alone. In contrast, in one case the arteriogram returned to normal after lumbar ganglionectomy and cyst aspiration and the patient was symptom-free six years later (Mentha, 1966).

Summary

Cystic adventitial disease of the arteries is a rare and only recently recognized entity which most commonly occurs in the popliteal artery, causing intermittent claudication. Three further cases affecting the popliteal artery are presented.

The aetiology of the condition is obscure. The cyst containing gel may be unilocular or multilocular, and appears to arise from the arterial adventitia. Histology shows no evidence of haemorrhage, inflammation, or neoplasia. The absence of hydroxyproline in the gel is against an origin from collagen or elastin, and its occurrence in children is against degenerative changes in the arterial wall.

The typical clinical picture is of intermittent claudication of sudden onset in a young adult male. The pulse pattern is variable and the popliteal pulse may be absent or more easily palpable than normal, or an audible bruit may be present over it. Exercise or knee flexion may cause the disappearance of pedal pulses.

The arteriographic appearance is of stenosis, displacement, or occlusion at or above the level of the knee joint in an otherwise normal popliteal artery.

A review of the results of treatment indicates that after complete excision of the cyst (with or without arteriotomy) or arterial resection with autogenous vein-graft replacement the prognosis is excellent.

We wish to thank Mrs. J. Lewis for the operative illustration in Case 2 ; Dr. D. Raeside and Dr. George Howie for the excellent arteriograms ; Dr. E. Walker and Dr. W. W. Park for the histological studies ; and Mr. P. Kelly for some of the photographic reproductions. Finally, we thank all those previous authors who so kindly provided us with their long-term follow-up findings.

REFERENCES

Andersson, T., Gotham, B., and Lindberg, K. (1959). *Acta radiol. (Stockh.)*, **52**, 455
Atkins, H. J. B., and Key, J. A. (1947). *Brit. J. Surg.*, **34**, 426.
Bäckström, C. G., Linell, F., and Ostberg, G. (1965). *Acta chir. scand.*, **129**, 447.
Barnett, A. J. (1966). Personal communication.
—— Dugdale, L., and Ferguson, I. (1966). *Med. J. Aust.*, **2**, 355.
—— and Morris, K. N. (1964). Ibid., **2**, 793.
Bartos, J. (1966). *Langenbecks Arch. klin. Chir.*, **314**, 177.
Bliss, B. P., Rhodes, J., and Rains, A. J. Harding (1963). *Brit. med. J.*, **2**, 847.
Chevrier, J. L. (1962). *Mém. Acad. Chir.*, **88**, 261.
Delannoy, E., and Martinot, M. (1960). Ibid., **86**, 824.
Evans, G. (1966). Personal communication.
Gothman, B. (1966). Personal communication.
Gripe, K. (1963). *Nord. Med.*, **70**, 1381.
Hamming, J. J., and Vink, M. (1965). *J. cardiovasc. Surg.*, **6**, 516.
Hansen, J. P. (1966). *Acta chir. scand.*, **131**, 171.
Harris, J. D., and Jepson, R. P. (1965). *Aust. N.Z. J. Surg.*, **34**, 265.
Hiertonn, T. (1966). Personal communication.
—— and Lindberg, K. (1957). *Acta chir. scand.*, **113**, 72.
—— —— Rob, C. (1957). *Brit. J. Surg.*, **44**, 348.
Holmes, J. G. (1960). *J. Amer. med. Ass.*, **173**, 654.
—— (1966). Personal communication.
Ishikawa, K. (1966). Personal communication.
—— Mishima, Y., and Kobayashi, S. (1961). *Angiology*, **12**, 357.
Jacquet, G. H., and Meyer-Burgdorff, G. (1960). *Chirurg.*, **31**, 481.
Lambley, D. G. (1963). *Brit. med. J.*, **2**, 849.
—— (1966). Personal communication.
McEvedy, B. V. (1962). *Brit. J. Surg.*, **49**, 585.
Mentha, C. (1965). *J. Chir. (Paris)*, 89, 173.
—— (1966). Personal communication.

Parkes, A. (1961). *J. Bone Jt Surg.*, **43B**, 784.
Patel, J. (1966). Personal communication.
—— and Cormier, J. M. (1963). *Presse méd.*, **71**, 244.
—— Facquet, J., and Piwnica, A. (1958). Ibid., **66**, 1164.
Rains, A. J. Harding (1966). Personal communication.
Robb, D. (1960). *Brit. J. Surg.*, **48**, 221.
Simon, R. (1963). *Mém. Acad. Chir.*, **89**, 849.
Sutton, D. (1962). *Arteriography*, p. 84. Edinburgh and London.
Tytgat, H., Derom, F., and Galinsky, A. (1958). *Acta chir. belg.*, **57**, 188.

Addendum: Amino-acid Analysis of Protein Present in a Popliteal Artery Cyst

G. LEAF,* M.SC., PH.D.

The gel obtained from the cyst in Case 2 was stored frozen at −20° C. A portion was analysed by the microKjeldahl method and found to contain 0.52% nitrogen, corresponding to a protein content of approximately 3%. The remainder of the gel was lyophilized and 3 mg. of the dried material was hydrolysed with 1 ml. 6N HCl in an evacuated sealed tube at 115° C. for 20 hours. Hydrochloric acid was removed from the hydrolysate in a rotary evaporator and the residue analysed for amino-acids by Piez and Morris's (1960) modification of the method of Spackman, Stein, and Moore (1958). The results are shown in the Table, where they are compared with values for collagen from human tendon (Eastoe, 1955) and elastin from bovine aorta (Gotte, Stern, Elsden, and Partridge, 1963). The absence of hydroxyproline and hydroxylysine from the hydrolysate was confirmed by paper chromatography with the use of butanol/acetic acid/water (4:1:5) and water-saturated phenol as solvents and both ninhydrin and isatin as staining reagents. The paper chromatograms confirmed the presence of substantial amounts of glucosamine.

It will be noted that the amino-acid composition of the protein differs markedly from that of a representative collagen, and the failure to detect hydroxyproline suggests that neither collagen nor elastin could be present in more than traces. The presence of glucosamine and the fact that the amino-acids recovered account for only 53.6% of the dry matter suggest that the main constituent may be a mucoprotein. There was insufficient material to investigate this matter further.

Amino-acid Composition of Protein from Popliteal Cyst Compared with Those of Collagen and Elastin

	Cyst Protein	Collagen	Elastin
Aspartic acid	38·4	50·5	15·6
Threonine	24·4	19·3	13·4
Serine	23·2	38·5	10·5
Glutamic acid	52·9	75·5	23·1
Proline	23·6	127·2	117·3
Hydroxyproline	0	96·2	11·4
Glycine	87·0	338·0	318·7
Alanine	41·0	115·6	223·6
Cystine	19·0	0	0
Valine	29·0	26·5	136·7
Methionine	4·3	6·0	2·0
Isoleucine..	6·4	9·5	30·5
Leucine	32·3	27·2	67·2
Tyrosine	11·2	3·8	12·7
Phenylalanine	18·8	14·8	36·4
Lysine	42·3	22·5	8·2
Histidine	9·5	5·6	1·9
Arginine	19·9	51·2	9·8
Glucosamine	29·2	—	—
Hydroxylysine	0	9·3	—

Values are expressed as μmoles amino-acid per 10^5 g. dry matter for the unknown protein and μmoles per 10^5 g. protein for collagen (human tendon, Eastoe, 1955) and elastin (bovine aorta, Gotte *et al.*, 1963).

REFERENCES

Eastoe, J. E. (1955). *Biochem. J.*, **61**, 589.
Gotte, L., Stern, P., Elsden, D. F., and Partridge, S. M. (1963). Ibid., **87**, 344.
Piez, K. A., and Morris, L. (1960). *Analyt. Biochem.*, **1**, 187.
Spackman, D. H., Stein, W. H., and Moore, S. (1958). *Analyt. Chem.*, **30**, 1190.

---

* Institute of Biochemistry, University of Glasgow.

Medical Memoranda

Chronic Thyrotoxic Myopathy with Involvement of Respiratory and Bulbar Muscles

Brit. med. J., 1967, **3**, 415–416

Numerous reports of chronic thyrotoxic myopathy have followed Bathurst's (1895) original description. The incidence of respiratory and bulbar muscle weakness in previously reported cases was extremely rare; furthermore, in most of these cases the diagnosis could be challenged because of lack of proper documentation or correct interpretation. In a review of the condition by Whitfield and Hudson (1961) the respiratory and bulbar muscles were not mentioned, and in a reappraisal by Havard (1962) it was stated that these muscles are little if at all affected.

This report describes a case of chronic thyrotoxic myopathy in which weakness of the respiratory and pharyngeal muscles was a prominent feature.

CASE REPORT

An 83-year-old man was admitted to hospital with nine months' history of progressive loss of weight, generalized weakness and lassitude, shortness of breath on exertion, and difficulty in swallowing. During that period he was investigated elsewhere but no definite diagnosis was made. Initially he was described as being thin, but he looked fit and active and no abnormal physical signs were noted. Three months before admission he developed oedema of the ankles and distension of the neck veins; he was treated for congestive cardiac failure but his condition continued to deteriorate.

When first seen in hospital he had lost 3 stones (19 kg.) in weight. He was dyspnoeic at rest and so weak that he had difficulty in rising from the sitting or lying position; he was unable to swallow solid food and had difficulty with liquids.

On examination he looked emaciated and ill. The pulse was regular at 90 a minute, was collapsing in character, and the blood pressure was 160/60. The apex beat was forcible but not displaced. The jugular venous pressure was raised and he had oedema of the ankles. Chest expansion was poor and there were a few scattered rhonchi in both lung fields. The liver and spleen were not palpable. The striking findings were confined to the neuromuscular system, which showed profound weakness and wasting of the proximal and distal muscles of the limbs and of the trunk muscles. There were no fasciculations and the tendon reflexes were normal. The cranial nerves were intact and there was no sensory loss.

The thyroid gland was not enlarged and no thyroid bruit could be heard. There were no eye signs, apart from a slight lid lag. His hands were warm and he had fine tremors of the outstretched fingers.

Investigations.—Hb 14 g./100 ml.; white cell count 5,000/cu. mm.; E.S.R. 22 mm. in one hour (Westergren); blood urea 47 mg./100 ml. Serum electrolytes, liver-function tests, and glucose-tolerance curve were normal. Chest *x*-ray examination showed a normal-sized heart and clear lung fields, and the E.C.G. was normal. Barium studies of the gastrointestinal tract did not reveal any abnormality.

In view of the negative barium studies, the dysphagia was ascribed to weakness of the pharyngeal muscles as part of a generalized myopathy. The diagnosis of chronic thyrotoxic myopathy was confirmed by thyroid function studies which showed protein-bound iodine 12.7 µg./100 ml., radioactive iodine uptake 87.7% at four hours and 70% at 24 hours, and B.M.R. +21% and +24%. Myasthenia gravis was excluded by a negative edrophonium chloride (Tensilon) test.

Respiratory Function Tests

	Before Treatment	After Isoprenaline Inhalation	After Intravenous Edrophonium (10 mg.)	15 Days	3 Months
				After Treatment	
Vital capacity (ml.)	1,550	1,500	1,600	2,500	3,000
Predicted V.C. (ml.)	3,000	3,000	3,000	3,000	3,000
% of predicted V.C.	52	50	53	83	100
% in 0·75 second ..	40	41	43	42	45
M.B.C. (l./min.) ..	25	25	27	42	54
Predicted M.B.C. ..	70	70	70	70	70
% of predicted M.B.C.	36	36	39	60	77
Peak expiratory flow rate (l./min.) ..	185	220	190		270
Arterial blood:					
*p*H	7·404				
CO_2 tension ..	42·5 mm. Hg				
O_2 saturation ..	95·5%				
Po_2	84 mm. Hg				

The respiratory function tests (see Table) showed a moderate degree of airway obstruction with an F.E.V.$_{0.75}$ of 40% but a considerable reduction in vital capacity to 52% of the predicted value, presumably due to respiratory muscle weakness. There was no improvement in the vital capacity after isoprenaline inhalation or intravenous edrophonium.

The patient was treated with carbimazole 20 mg. t.d.s. at first, but the dose had to be increased subsequently to 30 mg. t.d.s. Improvement began on the seventh day, and when he was seen three months later his symptoms had completely subsided. The dysphagia was one of the first symptoms to respond, and after two weeks' treatment swallowing had returned to normal. The response of respiratory function was dramatic, and on the fifteenth day of treatment the vital capacity was 83% of the predicted value.

It is interesting to note that as soon as clinical improvement became manifest the patient developed overt signs of hyperthyroidism with motor hyperactivity and a marked lid retraction and lid lag. These signs were presumably masked by the severe muscle weakness.

DISCUSSION

In many respects the clinical features of this case resemble those in previous reports. Thus the relatively short duration of the illness, the masking of signs of thyrotoxicosis, the distribution of muscle weakness and wasting, and the excellent response to treatment have all been emphasized in the past. In addition, the severity of thyrotoxicosis as shown by thyroid-function tests has been stressed.

The B.M.R. is usually high but, as in the present case, it may be only slightly raised (Millikan and Haines, 1953 ; Collings and Lienhard, 1957 ; Gimlette, 1959).

Electromyographic and histological techniques have been extensively studied and frequently reported in the past but have failed to provide any help in the diagnosis ; the findings have been normal, equivocal, or non-specific (Millikan and Haines, 1953 ; Kite *et al.*, 1954 ; Collings and Lienhard, 1957 ; Hed *et al.*, 1958 ; Melville, 1959). It has also been shown that there is no quantitative difference in creatinine excretion in patients with chronic thyrotoxic myopathy or uncomplicated thyrotoxicosis (Quinn and Worcester, 1951). These tests were not carried out in our patient. It is now generally agreed that the diagnosis should mainly depend on clinical assessment, and an essential requirement is a satisfactory response to treatment.

Weakness of the respiratory and bulbar muscles has been described in cases of "acute thyrotoxic myopathy"; it is doubtful, however, if this condition exists as a distinct entity, and it would appear that such cases were probably examples of myasthenia gravis associated with thyrotoxicosis (Millikan and Haines, 1953).

In chronic thyrotoxic myopathy involvement of these muscles must be exceedingly rare or overlooked in its milder forms. In five previously reported cases there were insufficient data to reliably exclude myasthenia gravis.

Death from respiratory failure has been reported in three cases ; the case reported by McEachern and Ross (1942) was thought to be an example of chronic thyrotoxic myopathy in spite of a myasthenic defect in the electromyogram and a positive response to neostigmine. In the other two cases myasthenia was not excluded (Morgan and Williams, 1940 ; Thorn and Eder, 1946).

Dysphagia was the presenting symptom in the case reported by Leach (1962), but the patient was also suffering from dystrophia myotonica.

Heinrich *et al.* (1962) reported a case of "encephalopathic hyperthyroidism" in a man aged 70 who presented with dysphagia, had most of the features of chronic thyrotoxic myopathy, but, in addition, had a few neurological signs which could well have been due to an associated cerebrovascular disease.

I am grateful to Dr. C. E. Davies for allowing me to report this case.

D. GAAN, M.B., B.CH., M.R.C.P., M.R.C.P.ED.,
United Sheffield Hospitals. Now at the Manchester Royal Infirmary.

REFERENCES

Bathurst, L. W. (1895). *Lancet*, **2**, 529.
Collings, H., and Lienhard, W. F. (1957). *Neurology (Minneap.)*, **7**, 667.
Gimlette, T. M. D. (1959). *Brit. med. J.*, **2**, 1143.
Havard, C. W. H. (1962). Ibid., **1**, 440.
Hed, R., Kirstein, L., and Lundmark, C. (1958). *J. Neurol. Neurosurg. Psychiat.*, **21**, 270.
Heinrich, W. D., McCabe, E. B., Nicely, D. A., and Elder, J. C. (1962). *Amer. J. Roentgenol.*, **88**, 336.
Kite, W. C., McLintock, J. C., and Graves, R. W. (1954). *N.Y. St. J. Med.*, **54**, 1613.
Leach, W. (1962). *J. Laryng.*, **76**, 237.
McEachern, D., and Ross, W. D. (1942). *Brain*, **65**, 181.
Melville, I. D. (1959). *Scot. med. J.*, **4**, 318.
Millikan, C. H., and Haines, S. F. (1953). *Arch. intern. Med.*, **92**, 5.
Morgan, H. J., and Williams, R. H. (1940). *Sth. med. J. (Bgham, Ala.)*, **33**, 261.
Quinn, E. L., and Worcester, R. L. (1951). *J. clin. Endocr.*, **11**, 1564.
Thorn, G. W., and Eder, H. A. (1946). *Amer. J. Med.*, **1**, 583.
Whitfield, A. G. W., and Hudson, W. A. (1961). *Quart. J. Med.*, **30**, 257.

Current Practice

GROWING POINTS

Autoimmune Disease—I

G. L. ASHERSON,* D.M., M.R.C.P.

In some human diseases antibodies react with human tissue *in vitro*. These antibodies are called *autoantibodies*, and are found in rheumatic fever, Hashimoto's thyroiditis, systemic lupus erythematosus, and other diseases. The presence of autoantibodies is compatible with the view that tissues are damaged by an autoimmune process directed against components of the patient's own tissues. For this reason Hashimoto's thyroiditis and systemic lupus erythematosus are called *putative* autoimmune diseases.

For readers wishing to learn more about autoimmunity the recent books by Humphrey and White (1964) and Glynn and Holborow (1965) are recommended. The bibliography for the statements made in this article is given by Asherson (1965).

Tissue Damage due to Immune Reactions

The tissue damage caused by autoimmune reactions to the components of an animal's own tissue is a special example of tissue damage due to immune reactions. There are two main types of immunological tissue damage: that due to humoral factors (antibodies) and that due to cellular factors. The former is called *immediate hypersensitivity* ; the lesions characteristically appear within minutes or hours of exposure to antigen, and histological examination shows exudation of plasma and infiltration with polymorphs in some cases. The latter is called *delayed hypersensitivity* ; the lesions reach a maximum 24 to 48 hours after exposure to antigen, and histology shows infiltration with chronic inflammatory cells such as histiocytes and lymphocytes.

Immediate hypersensitivity reactions can be transferred passively from one person to another with serum (passive transfer). In the Prausnitz-Kustner reaction intradermal injection of serum from an allergic person causes local weal and flare when antigen is injected into the same area. In contrast the delayed hypersensitivity reaction—for example, the tuberculin reaction—cannot be transferred by serum alone, and cells such as peripheral white cells, or lymph-node, spleen or peritoneal exudate cells are required for its passive transfer from one animal to another.

Immediate Hypersensitivity

Patients injected with penicillin sometimes produce antibodies against the drug, so that when they meet penicillin again anaphylactic shock or urticaria develops. Other antibodies cause vascular damage with polymorph infiltration of arteriolar walls, where they react with their corresponding antigen. This is known as the *Arthus reaction*, and may be important in the pathogenesis of certain types of arteritis.

Antibodies may also be directed against components of the animal's own tissue. Patients with Hashimoto's thyroiditis have a cytotoxic antibody which, in the presence of complement, kills thyroid cells in tissue culture. Yet other antibodies are unable to cause tissue damage, either because they have the wrong biological properties or because they are directed against an inappropriate or inaccessible antigen. Many apparently healthy people have autoantibodies against thyroglobulin which are not thought to cause tissue damage. Babies of mothers with systemic lupus erythematosus have circulating antibodies against nuclei (*antinuclear factor*) which has crossed the placenta: these do not cause tissue damage and cannot penetrate the nuclei of intact cells. (See Fig. 1.)

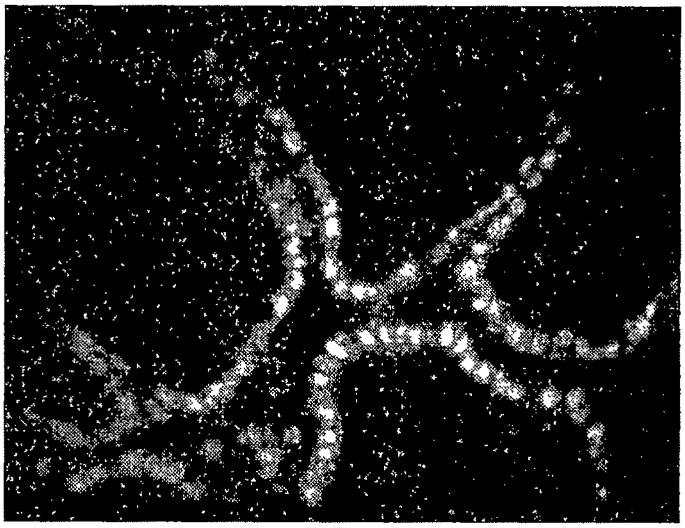


FIG. 1.—Antinuclear factor demonstrated in the serum of a patient with systemic lupus erythematosus by immunofluorescence using calf thyroid (by courtesy of Dr. E. J. Holborow).

At the other extreme certain antibodies are protective. After they have recovered from experimental allergic (autoimmune) encephalomyelitis rats have an antibody which protects other rats from the encephalomyelitis which would otherwise follow injection of brain in Freund's adjuvant. The antibody acts by blocking the induction or the damaging effect of immune responses, and this protective effect is called *immune enhancement*.

Complement

Complement is the name given to a group of factors in normal serum which are necessary for the haemolytic, cytotoxic, and certain other damaging actions of antibody. Thus red cells are agglutinated *in vitro* by certain physicochemical types of antibody, but they are lysed only in the presence of complement. Indeed, red cells coated with antibody (sensitized red cells) are used to detect complement.

---

* Reader in Immunology, Department of Bacteriology, the London Hospital Medical College, London E.1.

At suitable concentrations many antibodies will form precipitates with soluble antigens. When the concentration of antigen is high, however, these complexes are soluble, and soluble antigen–antibody complexes are thus formed. These complexes often fix—that is, combine with—the components of complement, and so cause glomerular and vascular damage. They may be responsible for renal damage in systemic lupus erythematosus.

In the presence of complement antigen–antibody complexes release a soluble factor which promotes the migration of polymorphs. This may be important in causing the polymorph infiltrate in the Arthus reaction and the damaging effect of soluble antigen–antibody complexes.

Delayed Hypersensitivity

The Mantoux reaction is the classical example of delayed hypersensitivity. The site of injection of tuberculin becomes infiltrated with lymphocytes and histiocytes, and the maximal reaction occurs after 24 to 48 hours. In animals this lesion can be transferred by cells but not by serum alone. This indicates that delayed hypersensitivity is not due to a conventional circulating antibody. It is sometimes explained by postulating a hypothetical antibody which is bound to the cells.

Despite the development of certain *in-vitro* tests in man delayed hypersensitivity has only been detected by skin tests.

In autoimmune disease it is customary to attribute tissue damage to delayed hypersensitivity, partly because of its importance in experimental autoimmune disease, and partly because there is a poor correlation between the presence of circulating antibody and tissue damage in diseases such as Hashimoto's thyroiditis. Though serum alone will not transfer delayed hypersensitivity in animals, cells and serum are synergic in transferring delayed hypersensitivity to several protein antigens. The implication is that in autoimmune disease tissue damage may be due to both cellular and humoral factors rather than to either singly.

Mode of Production of Autoimmune Responses

Autoimmune responses are a special example of immune responses. They are those responses in which the antibody will combine with the animal's own tissue components *in vitro,* or in which delayed hypersensitivity can be produced with the animal's own tissue components. Tissue damage is not a constant feature of the autoimmune response, either because the type of response is inappropriate or because the antigen is inaccessible. By definition it is not necessary that the production of an autoantibody should be stimulated by the animal's own tissue components. Indeed, tissue from other species (*heterologous* tissue) is usually better than tissue from the same species (*homologous* tissue) in causing the production of autoantibodies. Autoimmune responses should be distinguished from *isoimmune* responses[1] —for example, the blood-group antibodies, which react with the red cells of some but not all humans and which do not react with the subject's own red cells.

Immune Tolerance

The first exposure to an antigen may alter the effect of the second exposure to it in several different ways. The classical effect of the first injection of antigen is to increase the magnitude and speed of the response to the second injection: this is known as the *secondary response.* When soluble antigen is given in neonatal life, however, the response to the second injection is depressed. For instance, the injection of bovine serum albumin into newborn rabbits prevents the production of antibody which otherwise follows the injection of bovine serum-albumin in later life: this is known as *immune tolerance.* Some antigens are also able to suppress immune responses in adult animals in long-continued low dosage or very high single doses, while intermediate doses favour antibody production: this is known as *immune paralysis,* and it is thought to be the same type of phenomenon as immune tolerance.

The conditions for suppressing delayed hypersensitivity are less exacting than the conditions for suppressing the production of antibody. This selective diminution of delayed hypersensitivity is called *immune deviation,* and it may be important in limiting tissue damage even when autoantibodies are formed.

Normally animals do not produce antibodies against their own tissue components because of immune tolerance, though there are three situations in which autoantibodies are characteristically produced.

Antigens Similar to but not Identical with Self

When animals are injected with tissue similar to but not identical with their own tissue components autoantibodies are formed and sometimes tissue damage occurs. This is a general and important mechanism. Weigle showed that rabbits injected with rabbit thyroglobulin failed to produce autoantibodies or tissue damage. On the other hand, injection of chemically *altered* thyroglobulin (without adjuvant) led to the formation of autoantibodies against rabbit thyroglobulin and to the production of thyroiditis. This provides direct evidence that *altered* self components can cause tissue damage. Another possible example is the formation of autoantibody which occurs in rats whose livers are damaged by the injection of carbon tetrachloride.

Certain bacteria have antigens similar to those in mammalian tissue. The group A beta-haemolytic streptococcus has antigens similar to human heart, and the nephritogenic type 12-streptococcus has antigens similar to human kidney. *Escherichia coli* has antigen similar to human colon. These bacteria will cause antoantibody formation against heart and colon in animals, and it is thought that the antibodies against heart and colon found in rheumatic fever and ulcerative colitis may arise through this mechanism.

Immunization with Adjuvant–Antigen Mixtures

Certain materials (*adjuvants*) increase the intensity and change the nature of the immune response. The best-known example is Freund's complete adjuvant, which consists of a creamy emulsion of an aqueous solution of antigen, paraffin oil, and detergent, to which dead tubercle bacilli are added. Freund's *complete* adjuvant—i.e., with tubercle bacilli—has four distinctive actions, which do not occur when Freund's *incomplete* adjuvant—i.e., without tubercle bacilli—is used. These are:

(1) Increased delayed hypersensitivity.

(2) Increased production of cytotoxic antibody.

(3) Increased production of antibody which adheres to macrophages (cytophilic antibody).

(4) Increased production of autoimmune disease and autoantibodies when antigens such as brain, testis, peripheral nerve, thyroid, adrenal, kidney, labyrinth, uvea, and muscle are injected.

The role of Freund's complete adjuvant in producing experimental autoimmune disease has been used as evidence that delayed hypersensitivity is important in the pathogenesis of autoimmune disease. It is not clear whether Freund's complete adjuvant favours autoantibody formation by altering the immune system, or whether it also causes the antigen to be altered so that it becomes similar but not identical with self.

---

[1] The nomenclature used in transplantation work is different. Antigens identical with those of an animal are called *isologous*, while those differing are called *homologous*. The new terms *syngeneic* and *allogeneic*, respectively, avoid this confusion.

Familial Factors

New Zealand black mice (NZ/B mice) spontaneously develop haemolytic anaemia and glomerulonephritis associated with antibodies against red cells and antinuclear antibodies. Germinal centres which appear in the thymus resemble those seen in systemic lupus erythematosus and myasthenia gravis. The disease provides a useful model of systemic lupus erythematosus. Recent evidence shows that these mice carry a leukaemia virus which may be important in their disease.

Classification of Human Autoimmune Disease

Three major groups of autoimmune disease may correspond to the three groups which can be produced in animals:

(1) Diseases in which micro-organisms cause an autoimmune process. Possible examples are rheumatic fever, acute glomerulonephritis, and primary atypical pneumonia.

(1*a*) Diseases (or autoantibody production) due to exposure to altered or secluded tissue components. Examples are the production of antibody to heart, spermatozoa, and pancreas after damage to the corresponding organ.

(2) Hashimoto's thyroiditis and diseases such as pernicious anaemia and Addison's disease (non-tuberculous adrenalitis), which show clinical, serological, and familial overlap with it. The autoantibodies found characteristically react with *organ-specific* antigens in the thyroid, stomach, and adrenal. Autoantibodies reacting with widely distributed antigens (*non-organ-specific* autoantibodies) are rarely found.

(3) Systemic lupus erythematosus and other diseases, apparently affecting many systems, which sometimes merge clinically with systemic lupus erythematosus. These diseases usually show a high incidence of antinuclear factor and other autoantibodies against widely distributed antigen. Organ-specific antigens of the type seen in the Hashimoto group of diseases have a normal or only slightly raised incidence.

Detection of Autoantibodies

The finding of autoantibodies is important in the diagnosis of putative autoimmune diseases. There are three main classes of immunoglobulins: IgM (macroglobulin), IgG (7*S* gammaglobulin—the common type of antibody), and IgA (7*S* gammaglobulin, which appears in secretions). Different types of antibody have different biological properties and are detected by different means.

Gel Precipitation.—Many antibodies precipitate with their corresponding antigen when they are mixed in the right proportions. When serum containing antibody diffuses towards antigen in an agar plate precipitin lines may form where the antibody and antigen meet. This method will detect antibodies against antigen occurring in the liver and many other organs in Sjögren's disease. Large amounts of antibody against thyroglobulin can sometimes be found with this method in Hashimoto's thyroiditis.

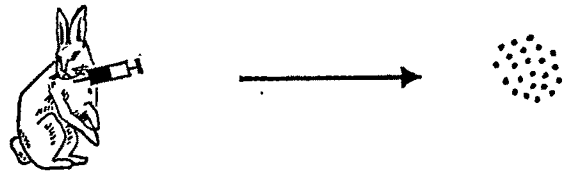
Tanned-red-cell Haemagglutination.—The precipitation test can be made very sensitive if the antigen is attached to an inert carrier such as a red blood cell. An important example is the tanned-red-cell technique for measuring autoantibodies to thyroglobulin. When sheep red cells are treated with tannic acid their surface is altered so that thyroglobulin will adhere. The tanned red cells coated with thyroglobulin are agglutinated by autoantibodies to thyroglobulin. These antibodies may show titres up to several million in Hashimoto's thyroiditis. This technique can be used to detect antibody against heart in the post-cardiotomy syndrome, and against muscle in myasthenia gravis.

Latex-fixation Test.—Antigen can also be attached to latex (rubber) particles, which are then agglutinated by antibody. Latex particles coated with human gammaglobulin are agglutinated by the rheumatoid factor (commonly found in the serum of patients with rheumatoid arthritis), which behaves like an antibody to altered human gammaglobulin.

In the *Rose-Waaler reaction,* sheep red cells are coated with rabbit gammaglobulin by mixing them with a subagglutinating amount of rabbit anti-sheep-red-cell serum. These cells are agglutinated by those rheumatoid factors which react with animal gammaglobulin. (See Fig. 2.)

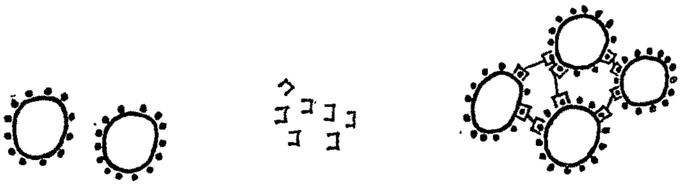
Complement Fixation.—When certain antibodies combine with antigen the resultant complex will react with a group of factors in fresh mammalian serum which are collectively known as complement. Sheep red cells coated with antibody are lysed by complement and are used as a detector system to show whether complement fixation has occurred. The complement-fixation test is used to detect autoantibody against thyroid cytoplasm, stomach, and adrenal gland in Hashimoto's thyroiditis, pernicious anaemia, and Addison's disease. These are examples of organ-specific autoantibodies.

FIG. 2.—Mechanism of the Rose-Waaler reaction for rheumatoid factor.



Rabbit is given injection of sheep red cells.

Antibody is produced against sheep red cells.



Sheep red cells are coated with a subagglutinating amount of rabbit antibody (7S, IgG) to sheep red cells. The antibody is altered by the act of combining with the sheep red cells.

Rheumatoid factor in patient's serum.

The coated sheep red cells are agglutinated by the rheumatoid factor present in the serum of many patients with rheumatoid arthritis. This is usually a macroglobulin antibody, and reacts with altered gammaglobulin.

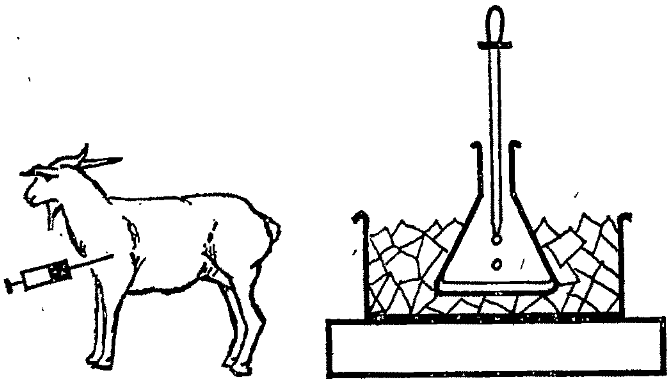
The Rose-Waaler reaction is sometimes called the sheep cell agglutination test (S.C.A.T.) or the differential agglutination test (D.A.T.).

Complement-fixing autoantibodies can also be demonstrated against a widely distributed antigen which occurs in liver, kidney, and many other organs. This is called the *autoimmune complement-fixation test* and it is an example of a non-organ-specific autoantibody. These autoantibodies are found in many patients with systemic lupus erythematosus, primary biliary cirrhosis, lupoid hepatitis, and Sjögren's disease, and in a few patients with rheumatoid arthritis and idiopathic pulmonary fibrosis.

Autoantibodies which react with the Wassermann antigen (alcoholic extract of beef heart) in some patients without syphilis are responsible for the biologically false-positive reaction. Transient biologically false-positive reactions are sometimes due to infection, such as glandular fever or infectious hepatitis, but about a sixth of all patients with chronic biologically false-positive reactions (positive reactions for over six months, with a negative treponema-immobilization test for syphilis) develop serious disease resembling rheumatoid arthritis or systemic lupus erythematosus.

FIG. 3.—Immunofluorescence.

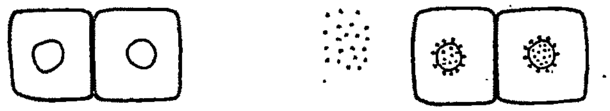
I. Preparation of Fluorescent Antihuman Gammaglobulin.



Antihuman gammaglobulin is prepared by injecting purified human gammaglobulin into a goat or rabbit.

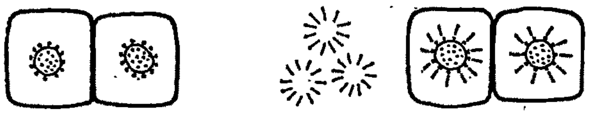
The serum is conjugated with fluorescein isothiocyanate.

II. Immunofluorescent Test for Antibody to Nuclei.



Tissue sectioned in cryostat to prevent damage to antigen. In some cases specially prepared paraffin sections can be used.

Serum containing antinuclear factor is applied to the section. Antibody (human gammaglobulin) adheres to the nuclei. The section is then washed.



The section is treated with fluorescent rabbit or goat anti-human gammaglobulin. This adheres to the sites where human gammaglobulin has combined with the nuclei. The section is examined under ultraviolet light. The nuclei give an apple-green fluorescence.

NOTE:

(1) Immunofluorescence may also be used to detect the site of binding of complement. The section is treated with human serum and complement (fresh human or guinea-pig serum) and the adherence of complement is detected by a fluorescent anticomplement serum. This is a microscopic complement-fixation test.

(2) Bound gammaglobulin refers to gammaglobulin found in sections which have not been treated with human serum in vitro. Immunoglobulins can be shown in antibody-producing cells. In other sites the finding of bound immunoglobulin provides some evidence of an in vivo antibody-antigen reaction if the gammaglobulin is unaccompanied by other serum proteins.

(3) Specific antisera can be prepared against different human immunoglobulins—such as IgG, IgA, and IgM—and these can be used to distinguish between different types of antibodies by immunofluorescence.

Immunofluorescence.—Immunofluorescence (Coons technique) is based on the fact that antibodies are gammaglobulins and are good antigens (see Fig. 3). Rabbits immunized with human gammaglobulin produce antibodies which react specifically with human gammaglobulin. These rabbit antisera can be conjugated with fluorescent dye, such as fluorescein, and used to detect human gammaglobulin.

Many autoantigens survive freezing of tissue and being cut into histological sections in a specially refrigerated cabinet or *cryostat* (at −20° C.). The sections are treated with serum being tested and then with the fluorescein-conjugated antihuman gammaglobulin. Microscopic examination in ultraviolet light shows fluorescence wherever the autoantibodies adhere.

Immunofluorescence is used to detect antibodies against nuclei—antinuclear factor. These are found in nearly all patients with systemic lupus erythematosus, and in many patients with lupoid hepatitis and Sjögren's disease, and in a variable number of patients with rheumatoid arthritis, polyarteritis nodosa, scleroderma, and dermatomyositis. Antibodies against the cytoplasmic constituents of thyroid, stomach, and adrenal can be demonstrated in diseases of the Hashimoto group. Antibodies occur against salivary-duct cells in Sjögren's disease, against heart and muscle in myasthenia gravis, and against mitochondria in primary biliary cirrhosis.

Immunofluorescence can be adapted to recognize the three types of immunoglobulin (IgM, IgG, and IgA) and complement-fixing antibodies. It can be used to detect gammaglobulin and complement which has become bound to human tissue *in vivo.* This uncommon occurrence provides some evidence of *in-vivo* antibody-antigen reactions. Bound gammaglobulin is found in the auricle of the heart in some cases of rheumatic fever, and in the kidney in systemic lupus erythematosus and many cases of nephritis.

Coombs Consumption Test.—Antibody against human gammaglobulin is known as *Coombs reagent.* The *Coombs consumption test* is an ingenious method of measuring antibody. Particulate antigen is mixed with the test serum and then washed repeatedly. It is assumed that antibody will adhere despite repeated washing, while non-specifically adhering gammaglobulin will be washed off. The ability of the treated particulate antigen to reduce the titre of an antihuman-gammaglobulin serum (Coombs reagent) is then measured. Some workers have found antibody against joint tissue in rheumatoid arthritis by this means.

(Part II of this article, with References, will appear in next week's issue.)

TODAY'S DRUGS

With the help of expert contributors we publish below notes on a selection of drugs in current use.

Prevention of Motion Sickness

Many factors are concerned in the production of motion sickness. Travel by sea or air may not affect those in whom a car journey induces violent symptoms, and the same stimulus may not cause motion sickness in a given individual on successive occasions. Visual and olfactory stimuli may precipitate nausea and vomiting, and without doubt psychological factors are often involved and may be "trigger" mechanisms in susceptible people. The final common pathway seems to involve a labyrinthine response, as patients whose vestibular function has been abolished by disease or surgical procedures are not subject to motion sickness.[1] This view is also supported by the observation that simultaneous movement in two planes can be used as an experimental tool in the production and study of this disorder.[2]

Controlled Trials

With so many variables the design of controlled trials of drugs in the prophylaxis of motion sickness has proved extremely difficult. Many of the available reports are of little value, as adequate controls have not been employed or the exposure of subjects to test conditions has not been matched to the period of maximum effect of the drug used. In a detailed and critical review of the methods available for the study of this problem Brand and Perry[3] concluded that "there is only one valid way of determining whether a compound is effective as a treatment for motion sickness and that is to test it in a properly designed field study in man." It is unfortunate that the failure to perform "properly designed" field studies has so often vitiated the conclusions of long and laborious exercises in clinical pharmacology.

Recent developments in intercontinental and space travel have given an urgency to the quest for effective prophylaxis, and several groups of American workers are engaged in studying this problem. The need for standardized test conditions has led to the development of new techniques. Of these the human centrifuge, a slowly rotating room in which subjects perform stereotyped head movements in a plane at right angles to that of rotation, has recently been described, and it has been claimed that this produces adequate and reproducible stimuli comparable to those existing in the natural situation.[4] Other attempts to produce standard conditions have led to the use of different types of swing, and in Great Britain to the testing of subjects exposed to artificial waves.[5] In all of these designs, where motion is orderly and predictable, some measure of habituation may occur, and care must be taken to ensure that the drugs tested are administered in a random sequence and compared with a placebo and no treatment at all.

Drugs With Proved Efficacy in Prevention of Motion Sickness

Drug (Group and Approved Name)	Adult Dose	Duration (hours)	Some Proprietary Preparations and Presentations
Phenothiazine antihistamines			
Promethazine	25–50 mg.	4–6	Phenergan tabs. 10, 25 mg.
Promethazine chlorotheophyllinate	25 mg.	4–6	Avomine tabs. 25 mg.
Ethanolamine antihistamines			
Diphenhydramine	50 mg.	4–6	Benadryl caps. 25 mg.
Dimenhydrinate (Diphenhydramine chlorotheophyllinate)	50 mg.	4–6	Dramamine tabs. 50 mg.
Piperazine antihistamines			
Cyclizine	50 mg.	6–8	Marzine tabs. 50 mg. Sereen tabs. 50 mg.* Valoid tabs. 50 mg.
Meclozine	50 mg.	12–24	Ancolan tabs. 25 mg. Sea-legs tabs. 12·5 mg.
Hyoscine	0·6 mg.	1½–3	Kwells tabs. 0·3 mg. Travel tabs. 0·3 mg.

* "Sereen" was formerly Boots' proprietary preparation of hyoscine 0·3 mg. Since 1958 the name has been given to the tablet form of cyclizine 50 mg.

Despite all these difficulties certain facts have been established, and a few drugs have demonstrated their efficacy consistently in controlled trials. The most important are considered individually below.

However, it should be emphasized that the essence of therapy in motion sickness lies in prophylaxis. Once nausea and vomiting are established no single drug is completely effective in relieving the symptoms. Vomiting may cause the rejection of swallowed tablets, and drugs may have to be given by injection to control symptoms at this stage.

Moreover, much can be achieved by attention to general measures and by avoiding precipitating situations. Car sickness in children is probably the most prevalent form of motion sickness and can often be reduced by frequent stops, adequate ventilation, and the avoidance of travel immediately after a meal. There is a tendency for children to "grow out" of a predisposition to motion sickness, but even in those who do not these common-sense precautions and the use of appropriate doses of prophylactic drugs will usually reduce the problem to manageable proportions.

Specific Drugs

Antihistamines

Promethazine.—This compound is a phenothiazine derivative with antihistamine properties. An oral dose of 25–50 mg. commonly produces drowsiness, which precludes use of the drug when activity and alertness are required. Its duration of action lies between four and six hours, the effect appearing after about 30 minutes. For prolonged prophylaxis it may be given twice or thrice daily.

A closely related compound, *promethazine chlorotheophyllinate,* is also available in 25-mg. doses, but appears to offer no specific advantage over promethazine in controlling symptoms. Neither of these drugs provides completely reliable prophylaxis, but both have been shown to be of value on prolonged journeys, where some degree of sedation is an acceptable side-effect.

Diphenhydramine and its Chlorotheophyllinate Derivative, Dimenhydrinate.—These are ethanolamines with antihistamine properties. Their duration of effect is similar to that of promethazine, and both have proved highly effective in preventing motion sickness. Side-effects may limit their use in some cases, as both produce drowsiness and occasionally vertigo.

Cyclizine and Meclozine.—These are antihistamines of the piperazine group. Of the more recent drugs available for the prevention of motion sickness these are the most effective. Cyclizine in a dose of 50 mg. has proved of value in car, air, and sea travel, is effective for up to six or eight hours, and has a low incidence of side-effects. The most prominent is sedation, but this is less frequent and intense than with many other antihistamines.

Meclozine, in a dose of 50 mg., has the longest duration of effect of the drugs considered here, and has been shown to act for at least 12 and sometimes up to 24 hours. Although it may cause slight sedation, it provides prolonged prophylaxis, and is probably the drug of choice when this is required.

Some years ago it was suggested that cyclizine and meclozine, which have been employed in pregnancy sickness, might be responsible for foetal abnormalities. A prolonged investigation, both by the manufacturers concerned and by independent medical research workers, has not established any definite hazard. However, the decision to use antiemetic or any other drugs in pregnancy should be taken only after careful consideration leads the prescriber to conclude that their use is essential to the patient's well-being.

All the above drugs are antihistamine compounds and may be bought freely. Some of the proprietary preparations and their doses are shown in the Table. Drugs in this group may all give rise to symptoms of parasympathetic blockade. The results are seldom severe enough to be unpleasant, but dryness of the mouth, blurred vision, and urinary difficulties have all been reported and presumably result from this atropine-like action. Gastrointestinal side-effects are occasionally seen but are unlikely to be troublesome with the relatively small total doses used in preventing motion sickness.

Hyoscine

This drug has emerged with a clear advantage from every controlled trial that has been designed to test the efficacy of drugs in the *short-term* prevention of motion sickness. The desired protection is achieved rapidly, in some cases within 20 minutes of administration, and lasts for up to three hours, but the actions of hyoscine on the parasympathetic nervous system are such that its side-effects are often more prominent than those of the antihistamines. Drowsiness, difficulty in accommodation, and dryness of the mouth may all occur, and in the elderly this compound may cause mental confusion.

In an attempt to reduce the sedative effects to a minimum hyoscine has been given with amphetamine, and it is claimed that this combination is highly effective. These claims are at present unsupported, and any drug combination containing amphetamine is of itself open to objection.

Other Preparations

Many other compounds have been advocated for the prophylaxis of motion sickness. Barbiturates have little specific effect, but produce sedation, and may allay anxiety. The phenothiazines, including chlorpromazine, which are of considerable use in the management of nausea and vomiting from other causes, have virtually no effect in motion sickness, and other drugs with tranquillizing actions are of no proved value, although they may possibly be useful in reducing anxiety. Although often included in proprietary mixtures, vitamins of any group have no effect in the prevention of motion sickness.

Undesirable Effects of Drugs

The possible consequences of taking effective drugs must always be remembered and should be stressed to the patient. Alcohol consumed on the cross-channel ferry may potentiate the effects of drugs taken to combat motion sickness. Sedation and impaired visual accommodation may render a driver unfit for Continental roads. Individual susceptibility to side-effects, however, might be established by a test dose of the chosen drug taken some days before the projected journey.

The inevitable conclusion from a survey of the published trials of drugs in motion sickness is that for short-term prophylaxis hyoscine is superior to all other compounds despite its side-effects, while for longer journeys there is a clear place for the antihistamines. No single drug will guarantee protection in all cases, but appreciable benefit can usually be obtained.

Those who prefer older remedies which have not been subjected to controlled clinical trial are referred to an index of treatment for 1910, which advocates "tight clothing around the abdomen," "the prone position," and "iced champagne."

REFERENCES

[1] Johnson, W. H., and Ireland, P. E., *Aerospace Med.*, 1966, **37**, 181.
[2] —— and Taylor, N. B. G., *Acta oto-laryng. (Stockh.)*, 1961, **53**, 211.
[3] Brand, J. J., and Perry, W. L. M., *Pharmacol. Rev.*, 1966, **18**, 895.
[4] Wood, C. D., Graybiel, A., and McDonough, R., *Aerospace Med.*, 1966, **37**, 187.
[5] Glaser, E. M., and McCance, R. A., *Lancet*, 1959, **1**, 853.

ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Shock with Insertion of I.U.D.

Q.—*What is the mechanism of the shock that can occur with the insertion of an intra-uterine contraceptive device, and what is the appropriate treatment?*

A.—It has been known for a long time that some women will faint when the cervix is stimulated, as being grasped by a vulsellum forceps or by the passage of a sound through the cervical canal. Why it should happen with some but not all women is not known, but it may be that it is more likely in those who are apprehensive, even though the apprehension is not overt.

The stimulus to the cervix presumably sets up afferent stimuli, and on the efferent side the vagus slows, and may temporarily stop, the heart, with consequent cerebral anaemia. Prevention might be by reassurance and full explanation of what is to be done, and by avoiding the use of the device in those who are obviously anxious.

When "shock" occurs it is treated on the lines usual in a faint—e.g., laying the patient down, elevating her legs, injecting analeptics, and possibly external cardiac massage, though these more heroic measures should not usually be needed. Though the device once through the cervical canal is unlikely to be a continuing cause of the shock, it would seem sensible in such a patient to try some other form of contraception.

Blood Groups and Rhesus Immunization

Q.—*Is there any known association between rhesus negativity and one of the ABO blood groups?*

A.—There is no known association between these blood-group systems. On the other hand, there are some interesting observations on the influence of the ABO groups on immunization to the Rh antigen in rhesus-negative mothers.

Rhesus-negative subjects receiving Rh-positive blood are far less likely to form Rh antibodies when there is incompatibility in the ABO system than when they are given blood of the same ABO group. Further, immunization to the Rh antigen by Rh-negative mothers is less common when the infant is ABO incompatible with the mother. To put it another way, an ABO-compatible, rhesus-positive foetus is much more likely to immunize its Rh-negative mother than a foetus of different ABO blood group.

The explanation probably lies in the rapid removal of ABO-incompatible cells from the recipient's circulation by either anti-A or anti-B present in serum, in much the same way that rhesus sensitization is prevented by clearing Rh-positive cells from the circulation by administering a serum containing anti-D.

REFERENCES

[1] Stern, K., Goodman, H. S., and Berger, M., *J. Immunol.*, 1961, **87**, 189.
[2] Nevanlinna, H. R., and Vainio, T., *Vox Sang. (Basel)*, 1956, **1**, 26.

Virus Infections

Q.—*Is there any evidence to suggest that virus infections are more common and more severe because antibiotic suppression of the bacterial infections has left the viruses a clearer field?*

A.—There is no evidence to support a belief that virus infections are more common than they were before antibiotics became available for therapy. It is true that some virus infections have become more prominent, but that is because more attention has been focused on them and their recognition and investigation have become possible as the result of great advances in the laboratory.

Book Reviews

Dangers in Food

Toxicants Occurring Naturally in Foods. Food Protection Committee, Food and Nutrition Board, National Academy of Sciences, National Research Council. (Pp. 301. $6.00.) Washington: National Research Council. 1966.

To control food production so that no known toxic additives or contaminants enter human food is difficult, but it would seem impossible at the present time to prevent consumption of toxic materials that occur naturally in food. The widespread occurrence of toxic materials is illustrated by the book under review, which is a compilation of 27 chapters by different experts commissioned by the Food Protection Committee of the U.S. National Academy of Sciences.

The many subjects discussed include goitrogens, oestrogens, carcinogens, lathyrogens, favism, haemagglutinins, cyanogenetic glycosides, stimulants and depressants, antigens and allergens, pressor amines, antivitamins, antienzymes, cholinesterase inhibitors, natural radioactivity, fungal toxins, seafood toxins, spices and flavours, unusual foods (including quail and ackee), vitamins, excesses of amino-acids, essential minerals, food fats, gossypol, nitrates and nitrites, oxalates, and the effects of sodium chloride in relation to the protective action of potassium. Although this list of subjects is long it cannot be considered as complete as bacterial toxins, narcotics, hallucinatory agents, and the possible effects of cholesterol on circulation are not discussed. This list of chapters illustrates the wide range of potentially harmful materials occurring in food. Many diseases in man, including cancer and mental diseases, could be due to natural foods. The difficulties of attributing a particular disease to any special food are great because people in developed and sometimes even in developing countries consume many different foods. The identification of toxic principles in food is a field of preventive medicine that requires more thought and investigation.

Most of the contributors in the volume are objective and cautious and stress the need for more information that can be gained only by research and epidemiological studies. Dr. M. Stob, however, writing about natural oestrogens, concludes that "consumption of any food product in quantity sufficient to cause a physiologic effect due to oestrogens it contains seems remote." Few studies of oestrogenic activity of human foods, however, have been made and the dose causing a "physiologic effect" in women is difficult to assess. The growth of hormone-dependent cancers may require minute quantities of hormone.

The book provides valuable accounts of toxic materials that occur in foods of many different countries. In addition to the scientific descriptions there are some legends, such as a charming account of the discovery of coffee by the "prior of an Arabian convent." The food protection committee and the many contributors are to be congratulated on producing an interesting and stimulating compilation at a reasonable price.

E. BOYLAND.

Common Skin Diseases

Treatment of Common Skin Diseases. Articles originally published in the Current Practice section of the *British Medical Journal.* (Pp. 116; illustrated. 10s.) London: British Medical Association. 1967.

Diseases of the skin account for some 10% of consultations in general practice. At least 80% of these patients are suffering from eczema, warts, acne, pruritus, psoriasis, tinea, or too much or too little hair. The therapeutic repertory of some practitioners is sadly limited; corticosteroids, often unnecessarily associated with the potentially sensitizing neomycin, tend to be prescribed indiscriminately as a panacea.

In this very modestly priced but attractively produced book the Editor of the *B.M.J.* has republished 14 articles which have recently appeared in its pages. All are sound and practical. Twelve chapters are concerned with common diseases, and experienced dermatologists provide clear guidance on their management based on long personal experience. Contact dermatitis deserved a longer chapter, and the material that has been competently but illogically and misleadingly compressed into a single chapter on "infectious eczemas" could have been more appropriately classified.

Two chapters are concerned with less common conditions, ichthyosis and lupus erythematosus. Both are excellent, and one can appreciate the Editor's reluctance to discard them in favour of chapters on scabies and pyogenic infections which, on account of the continued and increasing prevalence of these disorders, should have been included. These are the only important omissions.

The general practitioner will find this book authoritative, readable, and helpful. It can be recommended as excellent value for money.

A. J. ROOK.

Scientific Exploration of Development

Human Development. Edited by Frank Falkner, M.D., M.R.C.P. (Pp. 644 + xx; illustrated. £7.) Philadelphia and London: W. B. Saunders. 1966.

In a delightfully lucid foreword which needs no translating Professor Robert Debré introduces *"le livre sur le développement de l'homme, où le Professeur Frank Falkner a réuni tant de savants."* The subject and the savants cross international boundaries. The editor, with a background of research and long experience in co-ordination at the Centre International de l'Enfance, has welded the savants into an admirable team.

In this one book basic sciences and medicine are brought together and skilfully deployed. The title might well have been "Human Biology." As it is, from the twin-words "growth and development" the editor has dropped one because the accepted distinction between growth (the multiplication of cells and changes in size) and development (the maturation of structures and functions) is no longer tenable. "In other words," he writes, "the twins were in reality uni-ovular." "The subject of human development is in a rapid state of change. Some of its students cry forward to fewer data on more subjects and others cry back to more data on fewer subjects. This well-known state, if lucky, results in a fertile oscillatory tandem." After this quotation, from Tanner, Professor Falkner remarks "it is our responsibility as human biologists to remove the element of luck," and he and his colleagues show how it is being done.

I imagine that most clinicians, as I did, will find it difficult to stop nibbling from such an impressive selection of skilfully interrelated topics, but will continue to use the book as an essential source for reference. The basic early chapters deal with biological principles of growth, general considerations in human development, statistics, and developmental genetics. Subsequent chapters describe physiological growth and biochemical, hormonal, sexual, and nutritional influences. Informative sections on the development of the nervous system (before and after birth), of vision, bones and skeleton, face and teeth, are complemented by others, equally stimulating, on speech, language and hearing, psychology, cultural patterning (a fascinating description), and even immunology. The influence of family and social factors on intellectual development is one example of the good editing and synthesis throughout the book.

In scope and range, in erudition and readability, this forward-looking compilation will surely prove essential for both bedside paediatricians and back-room research workers. It will give enjoyment, too, to any doctor who is interested in the scientific exploration of the strange ways in which we humans grow.

JOHN APLEY.

An Old Friend—Unchanged

Hamilton Bailey's Demonstrations of Physical Signs in Clinical Surgery. 14th edition. Edited by Allan Clain, M.B.(Cape), F.R.C.S.(Eng.) (Pp. 627+x; illustrated. 75s.) Bristol: John Wright. 1967.

Hamilton Bailey's *Physical Signs* is well established as a pillar of clinical teaching. In its fourteenth edition, with 247,000 copies sold, it no longer needs a reviewer's commendatory pat on the back. Rather it impels one to be critical, to ask whether the book continues to maintain its own high standard, and how it should be judged as an instrument of teaching in the context of the present day.

The value of this book lies in its illustrations. Bailey, as a good clinical teacher, preferred pictures to words, but sometimes his zeal as a collector carried him away; he judged a picture by its attractiveness rather than its message, he retained old friends when they had ceased to be relevant, and he could not bring himself to dispose of duplicates. Consequently, some of his illustrations are out of place in a student's book, some are out of date, and many are out of proportion to the importance of their subject. Moreover, most teachers will now agree that the needs of clinical teaching have changed, and that, however important the spot diagnosis of lumps and bumps, it is at least as important to avoid emphasizing rarities.

Thus, Hutchinson's teeth, Clutton's joints, syphilitic dactylitis, empyema necessitatis, and osteomyelitis of the sternum should all go overboard. So too should go the monstrosities of surgical museums, the turban tumour, the puffy and peculiar tumours of Pott and Cock respectively, the cystosarcoma phylloides, and the dermatofibrosarcoma protuberans. So too such delineations of the obvious as the cauliflower ear, the bat ears, the genu recurvatum, and some of the nine pictures of exophthalmos. And it is debatable if even the photograph of a tape measure, a pleasing whim when introduced by the maestro, should be perpetuated.

Mr. Allan Clain, who has been responsible for this edition, acknowledges that devotion to a former chief has led him to initiate few changes, and his piety will be respected. But some radical amendments will be needed next time.

CHARLES ILLINGWORTH.

Psychiatric Campaigner

The Unquiet Mind. The Autobiography of a Physician in Psychological Medicine. By William Sargant. (Pp. 240+xvi; illustrated. 30s.) London: William Heinemann. 1967.

The main purpose of this book, the author says, is to describe the fascinating progress of medical and surgical treatments of mental disorders during the last three decades. The autobiographical method of presentation has always appealed to some clinical teachers, especially to those who experience their work as an unending personal battle against two monsters—disease and the ignorance of their colleagues. The successful ones among those campaigners are, like generals, apt to publish autobiographies.

The physical treatments of mental disorders about which Dr. Sargant writes with such fervour are used all over the world and have transformed the psychiatric scene. However, Dr. Sargant paints too rosy a picture of their effects. So enthusiastic is he about them that lay readers may be led to assume, mistakenly, that a therapeutic breakthrough comparable to the introduction of the antibiotics into the treatment of infectious diseases had taken place in psychiatry. Many of them will feel very angry about the psychiatrists who do not share the author's approach and whom he castigates so severely. In evaluating those methods he relies largely on his own clinical experience, because he "distrusts statistical reports on treatments by any writer for whose judgement and lack of bias he cannot personally vouch." He does, however, accept such reports if they concern treatments not favoured by him—for example, psychotherapy. There is, of course, more to psychiatric treatment than the use of drugs, shocks, and surgery, valuable though they are.

Among the various good causes the author has espoused and which he discusses in the book are the establishment of psychiatric departments in general hospitals and the reform of the criminal law relating to mental illness. The book is written in a breezy style and reads well. Some of the text might be too technical for the lay reader. The author is at his best when he describes his life and work under the London blitz, but his explanation of the differences between the outcome of neurotic reactions to combat stress in the two world wars is questionable.

Many of his friends, including the present reviewer, will feel that the author has not done himself justice. He is not really the intolerant, self-opinionated, and naive man he makes himself out to be in this book. He is, in fact, broadminded, modest, charitable of other people's shortcomings, and he respects all therapeutic approaches in psychiatry. Only when he is in a campaigning mood are those virtues less manifest. But this is the risk of an autobiography written on active service and under the influence of the mass media, when issues and events tend to be presented to the general public as either black or white and always as very simple.

E. STENGEL.

Books Received

Review is not precluded by notice here of books recently received.

Angiologie-Fibel. By Dr. Werner Schoop. (Pp. 154+xii; illustrated. DM. 19.80.) Stuttgart: Georg Thieme. 1967.

Protides of the Biological Fluids. Vol. 14. Edited by H. Peeters. (Pp. 734+xiii; illustrated. £12.) London: Elsevier. 1967.

The Surgical Anatomy of the Temporal Bone and Ear. By Barry J. Anson, Ph.D.(Med.Sc.), and James A. Donaldson, M.D., F.A.C.S. (Pp. 211+x; illustrated. £5 12s.) London: W. B. Saunders. 1967.

Leitfaden der Neurologie. Edited by F. Laubenthal and H. Schliack. (Pp. 301+xi; illustrated. DM. 29.70.) Stuttgart: Georg Thieme. 1967.

Principles of Hospital Planning. Edited by Robert Jefford, B.A., D.S.A., A.H.A. (Pp. 83. 15s.) London: Pitman. 1967.

Scoliosis. A Manual of Concept and Treatment. By Stanley Hoppenfeld, M.D. (Pp. 115+xi; illustrated. 60s.) London: Pitman. 1967.

Cecil-Loeb Textbook of Medicine. 12th edition. Edited by Paul B. Beeson, M.D., and Walsh McDermott, M.D. (Pp. 1738+xxxix+liv; illustrated. Single volume £7 3s. 6d. Two-volume set £8 11s. 6d. De luxe edition £10 10s.) London: W. B. Saunders. 1967.

A History of the International Council of Nurses. 1899–1964. The First Sixty-Five Years. By Daisy Caroline Bridges, C.B.E., R.R.C., S.R.N., S.C.M., F.R.S.H. (Pp. 254+xxi. 40s.) London: Pitman. 1967.

Current Perspectives in Social Psychology. 2nd edition. Edited by Edwin P. Hollander and Raymond G. Hunt. (Pp. 685+xii. 40s.) London: Oxford University Press. 1967.

The Hazards of Immunization. By Sir Graham S. Wilson, M.D., LL.D., F.R.C.P., D.P.H. (Pp. 324+x. 45s.) London: Athlone. 1967.

Law and Psychiatry. Cold War or *Entente Cordiale*? By Sheldon Glueck. (Pp. 181+ix. 38s.) London: Tavistock. 1967.

The Papers of Alfred Blalock. Vols. 1 and 2. Edited by Mark M. Ravitch. (Vol. 1: pp. 1123+lxvi. Vol. 2: pp. 1127–2026+ix; illustrated. £20 per set.) Baltimore: Johns Hopkins Press. London: Oxford University Press. 1967.

Manual of Applied Nutrition. 5th edition. Nutrition Department, the Johns Hopkins Hospital. (Pp. 175. 52s.) Baltimore: The Johns Hopkins Press. 1966.

Negligence in Modern Law. By M. A. Millner, B.A., LL.B., B.C.L. (Pp. 248+xxxviii. 48s. Paper 35s.) London: Butterworth. 1967.

Structure and Habit in Vertebrate Evolution. By G. S. Carter. (Pp. 520+xiv; illustrated. 63s.) London: Sidgwick & Jackson. 1967.

Le Trepanacion en España. Edited by Jose M. Lopez Pinero. (Pp. 480+xii; illustrated. No price given.) Madrid: Third European Congress of Neurosurgery. 1967.

Symposium Report: The Importance and Treatment of Inflammation in Ophthalmology. Edited by Dr. P. D. Fowler and Dr. G. F. B. Birdwood. (Pp. 131; illustrated. Free on demand.) Obtainable from Geigy (U.K.) Ltd., Pharmaceuticals Division, Roundthron Industrial Estate, Wythenshawe, Manchester 23. 1967.

A Synopsis of Children's Diseases. 4th edition. By John Rendle-Short, M.A., M.D., M.R.C.P., D.C.H., and O. P. Gray, M.B., Ch.B., M.R.C.P., D.C.H. (Pp. 681+xii. 52s. 6d.) Bristol: John Wright. 1967.

Middle Articles

CONTEMPORARY THEMES

Relevance of American Experience of Narcotic Addiction to the British Scene

GRIFFITH EDWARDS,* M.A., D.M., D.P.M.

Brit. med. J., 1967, 3, 425–429

The United States has had a large drug addiction problem for a long time. At present there are probably upwards of 60,000 narcotic addicts in the U.S.A. (O'Donnell and Ball, 1966), with New York alone perhaps accounting for half the total. In comparison the problem in Britain seems small, but the concern here must be not so much with the problem's present absolute size as with its rate of growth—from 57 heroin addicts in 1954, 521 in 1965 (Home Office figures), with by now perhaps 2,000 to 3,000, and extrapolation to 10 years hence suggesting a quite frightening figure. In planning our own response to this problem it is natural to turn for guidance to America's much greater experience.

But is American experience relevant to our own country's problem ? The gross disparity, diminishing though that gap may be, between the two prevalence rates immediately suggests that different processes may be at work. One obvious explanation for this disparity in addiction rates is the contrasting general level of social disturbance in the two countries, as shown by the data in the Table.

Some Indices of Social Problems in U.S.A. and England and Wales, 1964

	U.S.A.	England & Wales
Infant mortality (deaths under 1 year of age per thousand live births) ..	44·0	19·9
Illegitimate live births per thousand live births	121	72
Divorces granted during year per thousand population	2·3 (provisional figure)	0·7
Suicide per thousand deaths	12·0	10·4
*Murder per million population ..	48	6
*Robbery per million population ..	582	83·5 (incl. blackmail)

Data gathered from *Vital Statistics—Statistical Abstracts of U.S.A.* and *Annual Abstract of Statistics*, Central Statistical Office, H.M.S.O., London.

* For difficulties of comparison between criminal statistics of different countries, see *Cultural Factors in Delinquency*, edited by T. C. N. Gibbens and R. H. Ahrenfeldt, p. 87. Tavistock Publications, London, 1966.

Thus undoubtedly a large part of America's drug addiction represents one more manifestation of the problems stemming from poverty, city disorganization, and the failure of the United States to integrate into its larger society the Negro, the Puerto Rican, and the Mexican. Narcotic addiction is to a considerable extent overrepresented in ethnic subgroups (Vaillant, 1966). Work by Chein *et al.* (1964) has shown the close relation in New York between addiction rates and the " delinquent subculture " of areas of poverty. Moreover, drug-addiction rates in the Chinese inhabitants of New York are falling, the presumed explanation being that they are gradually becoming assimilated and are advancing their social status (Ball and Lau, 1966).

The differences between the U.S. and British scenes should certainly not be minimized. America, for instance, has an entrenched black market and greatly different legal provisions, while the addict is submitted to pressures towards treatment. Moreover, the absence of a national health service may bear on the ability of society to respond to a problem such as addiction. Nevertheless, to conclude that the explanation of American addiction is simply a matter for the sociologist would be wrong, for even in the very worst areas only a small proportion of those at risk become addicts. The general impression of American workers seems to be that although some fortuitous circumstance, some juxtaposition, may result in " the ordinary kid " becoming an addict, it is necessary to look at personality as well as the surroundings. Not all American narcotic addicts come from the grossly underprivileged sectors of society: America also has its white addicts of relatively privileged background, and Ball (1965) and Bates (1966) have shown how incorrect any description of the American addict would be which generalizes him into one stereotype. The tendency now is toward the delineation in America of several different types of narcotic addiction.

The history of narcotic addiction in the U.S.A. shows the rapidity and unpredictability with which drug-abuse patterns can change ; and here surely is something which comes very close to home. O'Donnell and Ball (1966) have shown that in the earlier part of this century the American addict was thought of usually either as a Chinese " dope-fiend " or quite often as a respectable middle-class citizen from a rural area, while in some parts of the country free prescribing of opiates for gynaecological disorders meant that female were higher than male addiction rates. The Chinese problem has faded out, addiction has become dominantly urban, the Negro and now the Puerto Rican have become heavily involved, and recently there has been growing alarm about the increased use of amphetamine, barbiturates, and tranquillizers, and the cult of using psychedelic drugs among college students and the emancipated. The vital lesson is that patterns of drug usage are not static. Even if some aspects of the American drug problem seem remote from our likely experience today, we must heed the warning that America's problems today may be ours of tomorrow.

Legal Provisions, Punishment, and Compulsory Treatment

In fulfilment of the U.S. Government's obligations as a signatory to the 1912 Hague Opium Convention, which required member countries to introduce legislation to control domestic production, sale, and distribution of opiates and cocaine, Congress in 1914 passed the Harrison Act. Schur

---

* Addiction Research Unit, Institute of Psychiatry, Maudsley Hospital, London S.E.5.

(1963) has argued that the original intention of this Act was not to remove the management of the addict from the doctor. He contends that it was the Narcotics Bureau's misinterpretation of the Act's provisions that led to the bringing into existence of a large "criminal class." In 1951 Federal legislation (the Boggs Act) introduced severe mandatory minimum prison sentences, and with the Boggs–Daniel Act of 1956 penalties were made even heavier—5 to 20 years for a first offence, and 10 to 40 years for a second or subsequent offence of unlawful sale, possession, or importing of narcotic drugs, and the possibility of the death penalty for selling heroin to anyone under 18. Marihuana is for legal purposes generally classed in the U.S.A. as a narcotic.

"Civil Commitment"

An important new trend in legislative policy has recently developed with the introduction, first at State and now at Federal level, of "Civil Commitments." California's Civil Commitment Programme was set up in 1961 after a court ruling that previous provisions which sought to make *criminal* the mere fact of being an addict, as opposed to possession or sale of drugs, was unconstitutional. California has something between 10,000 and 20,000 addicts, and the intention of this legislation was to enable the State to institute an effective policy for the first time.

Previously an obvious addict picked up on some petty offence such as stealing would have been back on the street after a short sentence, for the court could take no cognizance of his addiction. But under the new Act a person found guilty of a misdemeanour or non-violent felony, and identified as an addict, can be committed for up to seven years to the California Rehabilitation Centre programme, which is administered by the Department of Correction. Of this seven-year term, rather more than the first year is on average spent in a closed institution, where the emphasis is on counselling, work rehabilitation, and exploitation of a therapeutic milieu. The addict is then placed on parole with strict supervision and chemical testing. Any breach of parole—a positive urine test or naline test (Way *et al.*, 1963, 1966)—will result in his immediate return to custody. By mid-1968 it is expected that there will in California be an institutional population of just under, and an outpatient load of just over, 2,000 cases (Wood, 1967).

Civil commitment is now also being introduced under the 1966 Federal Narcotic Rehabilitation Act (U.S. Government, 1966), and on 1 April 1967 an ambitious State civil commitment scheme began to operate in New York (State of New York, 1966). But for much of this legislation time is required to determine how the law will work in practice, and to see what interpretations will be made by the courts.

The questions of whether the addict is to be regarded as a patient or as a criminal and of whether narcotics should be legalized or still harsher laws enacted, have produced in the U.S.A. a debate of quite dramatic acerbity, despite a remarkable dearth of evidence on which to base assertions. A publication of the Federal Narcotics Bureau (U.S. Treasury Department, 1966) urges that "much effort needs to be exerted to have both the heavy penalties and compulsory hospitalization extended to every part of the United States." Chein, on the other hand, has argued that the worst consequences of addiction result not from the drug but from public policy towards the user, and it has been pointed out that the addict, risking his life every time he takes heroin, is not in the nature of logic particularly likely to be deterred by harsh penalties (Narcotics Conference Report, 1963).

Though this American debate on compulsion is highly relevant to the British scene, the central issues require clarification. Two separate questions are involved: firstly, whether harsh legal measures can prevent addiction, and, secondly, whether compulsion can be of help in the treatment of the individual.

Effects of Strict Legislation

National figures on the drug addiction rate are not sufficiently accurate or sensitive to reflect time trends or the influence of specific legislative measures. Strict laws in Ohio cut down narcotic convictions by 80%, but, to quote the Narcotics Bureau (U.S. Treasury Department, 1966): "Of course, some of the racketeers moved their dirty trade into more easy-going States." Champions of the punitive approach can argue that the problem in America would have been even worse if the law had been more lenient, but this is no more than speculation. Moreover, legislation there, aimed specifically at "the pedlar" rather than at the addict, seems to have proved relatively unsuccessful, partly because the two are often one and the same person and partly because the really high-level criminal is seldom convicted.

Thus, on reviewing the American experience, vindictive legislation is apparently not a successful method of preventive medicine. The important lesson for Britain is that, despite more than 40 years of punishing the addict, America still has a large drug-addiction rate, a well-established black market, and an addict population which is forced into varieties of criminality.

Compulsion in Treatment

Considering the role of compulsion in assisting in the treatment of the individual patient, one finds that the evidence is perhaps rather disturbing in its bearing on current British policy. Vaillant and Raisor (1966) reported a 12-year follow-up on 100 addicts discharged from the Federal hospital at Lexington. Because many of these patients had over the years undergone, in more or less random sequence, voluntary hospitalization, short- or long-term imprisonment, or imprisonment and parole, the authors were able to identify groups of patients who had as it were acted as their own controls. Patients were usually seen at three-monthly intervals by social workers whose prime aim was to obtain follow-up information, but who also offered social-work help. One-year abstinence rates following the different "treatments" were as follows: hospitalization 4%; short-term imprisonment (less than nine months) 4%; long-term imprisonment (more than nine months) 13%; imprisonment plus subsequent parole supervision 67%. The efficacy of probation is supported by the most recent report on the California Programme (Wood, 1967), which states that 34% of men on probation have not taken drugs for a year.

Does probation backed by effective threat of reimprisonment therefore offer excellent hope while other methods give derisory results? The intepretation of Vaillant and Raisor's important study should be more guarded than this, and it must be emphasized that they were comparing very vigorous probation supervision with community care which must often have been far from intensive.

Nevertheless, there seems to be a strong feeling among experienced workers in the U.S.A. that an element of coercion is necessary (Maurer and Vogel, 1967; Lieberman and Brill, 1967). Here, then, is a dilemma—repressive legislation appears to be an ineffectual and dangerous public health measure, and yet the threat of imprisonment seems to increase the chances that the probated addict will respond to treatment. How is Britain to solve this dilemma?

A Solution in Britain?

The only way of determining whether in Britain treatment can be successful without compulsion is to try intensive-treatment programmes in the setting of present law, and carefully to assess the results which are obtained. For a proper judgement such treatment must be skilled and energetic, and one can predict at the outset that voluntary treatment will *appear* to be ineffective if the treatment under consideration is lackadaisical, carried out by medical staff with too many other commitments, and unsupported by adequate social work and rehabilitative services—in other words, treatment which focuses on detoxification rather than on the needs of a troubled person. In summary, therefore, rather than focusing energies and attention on reshaping the law, the whole lesson of the American scene in this respect would seem to be that we should act now while the problem is still relatively a small one, and set up the very best possible treatment services so that voluntary methods will be given more than a handicapped chance to prove their worth.

Heroin Dispensing and Alternatives to Heroin

In 1919 following a Supreme Court decision which appeared to indicate that the private physician who prescribed maintenance drugs to his addict patient would be risking prosecution, a number of special narcotic dispensaries were set up to cope with the needs of addicts suddenly deprived of their supplies. By 1923, however, the last of these dispensaries was closing down, and the experiment was generally being pronounced a failure.

What really happened ? Though the American Medical Association (1963) has attempted to answer this question, it seems that proper data on the experiment were never gathered. The clinics closed partly because of medical pressure and partly because of opposition from the Narcotics Bureau ; most clinics made no attempt at treatment but simply handed to the addict his drugs. Diversion of narcotics to other than registered addicts occurred and there were complaints that criminal elements were being attracted to the areas of town where the dispensaries were situated.

If the role of the clinics envisaged in the British legislation (House of Commons, Dangerous Drugs Bill, 1967) should degenerate into a mere handout centre, it is likely that the American experience would be repeated. Thus it is vitally important that the staff of the clinics which are being set up under the 1967 Act should be concerned with and involved in the total treatment programme, should have as their aim to woo the addict off drugs, and must have immediately available facilities for detoxification and later rehabilitation, so that, when the addict shows interest in treatment, treatment can be provided. The doctors staffing these clinics cannot be part-time clinical assistants unsupported by psychiatric training.

Even if the new British clinics are adequate for the purpose the policy of heroin prescribing will still face very considerable difficulties, inherent in the properties of the drug itself. The American evidence seems to suggest that its pharmacology weighs heavily against the possibility that most of our addicts will be safely maintained on a fixed dose of heroin, will return to social functioning, and be prevented from diverting their supplies to the black market (Wikler, 1952 ; Fraser *et al.*, 1963).

Maintenance Dosage

American studies also throw some light on what is one of the essential assumptions underlying the new British policy—namely, that an individual, satisfactory, fixed maintenance dose can be determined for any particular addict so that he will receive enough not to be tempted to patronize the black market, while at the same time he has no excess to sell or proselytize. Work by Martin and Fraser (1961) has shown that the patient may be in pharmacological balance—receiving the " correct dose " so far as the doctor is concerned—but may still, in the patient's judgement, be requiring more of the drug. Moreover, under a policy which seeks to stop the addict from turning to the black market, if doctor and addict disagree on " need," then the addict must be the arbiter. One way of preventing over-prescribing might be to rely on chemical assay methods. Urine levels will, however, largely reflect only the time at which the last injection was given, and a person with a considerable drug dependency might some time after the last injection show a near zero blood level. No doubt some technique could be worked out, but it is difficult to believe that such methods could easily be applied to the routine work of a drug maintenance clinic.

Hence research in America suggests that maintenance drugs will have to be given under the strictest supervision. Because heroin is a short-acting drug this will entail injections three or four times a day, and the demands on the staff at the clinic and on the patient in terms of travelling time are going to be considerable. Thus in reality either the drug will have to be given daily into the patient's own hands, or a supply of prescriptions will have to be deposited with a chemist for daily dispensing. In either case the possibility of black-market diversion is opened up again, while the fact that the patient is continuing to give his own probably unsterile injections carries the likelihood of more than occasional tragedy.

Whatever the theoretical arguments, only close observation of the actual running of the new clinics will give the answers—whether patients can be maintained successfully on a fixed dosage schedule, whether for most addicts less than optimal supplies of safely and legally obtained heroin are an acceptable alternative to escalation and seeking drugs on the black market, whether diversion of supplies to illicit distribution continues, whether training in sterile injection techniques can decrease the incidence of infections. But American evidence is not encouraging—heroin for maintenance is a bad choice of drug.

Other Drugs for Maintenance

Could any other drug be used ? Dole and Nyswander (1965, 1966, 1967) have shown that methadone (Physeptone) is sometimes an acceptable alternative to heroin. The obvious advantages of methadone are that it is a long-acting drug and therefore given only once a day, that it can be taken orally, and that in daily doses of 80–120 mg. it blocks the euphoric effect of any other narcotic which is coincidentally taken, but does not in itself produce psychological or motor effects which impair social functioning. This interesting work has been criticized on several grounds, some of which are ill-founded, and there is an obvious need for continuing, careful assessment of the results of treatment.

The development of a series of N-substituted benzo-morphan derivatives may be of particular importance—for example, cyclazocine, which experimentally has been shown to be able to block the effects of morphine in daily doses up to 240 mg. (Martin *et al.*, 1966) and which in clinical practice is also of some value (Jaffe and Brill, 1966). The hope is that drugs can be developed which, unlike methadone, do not subject the addict's system to the continuing experience of narcotic intoxication but which relieve drug hunger and drug-seeking activity—cyclazocine itself, though given orally, is perhaps too short-acting to provide the ideal answer. Patients may find that by taking cyclazocine during the week and stopping it at week-ends they have a way of " chipping " without becoming " hooked."

Two important differences should be noted between the American and British scenes so far as drug substitution is concerned. Firstly, in Britain addicts take a much higher heroin dosage than in America and the efficacy of substituting or blocking drugs is not so certain. Secondly, in America the choice facing the addict is between easily available methadone and expensively, criminally, and dangerously obtained weak heroin, whereas in Britain the choice is between free methadone and free, good quality, safely and legally obtained heroin. Only experience will show how many addicts genuinely want to give up heroin but, despite their intentions, find the task of remaining abstinent too difficult. Any change in the law that sought to make methadone a drug which the doctor could prescribe without the addict's choice being consulted would have sound pharmacological argument on its side, but at present would probably result in a considerable number of addicts turning to the black market.

Hospitals and Alternatives to Hospitals

In the U.S.A. generally there is a mood of disillusionment regarding the role of conventional psychiatric inpatient ward care in the treatment of drug addiction. If there is no compulsion the patient discharges himself, and if there is compulsion then the patient and staff work against each other, or, worse still, the patients learn to "give the right answers." And yet there is the feeling that if the addict is to have any hope of successfully breaking with his habit and with the life pattern of the addict–criminal subculture he requires a period in a controlled environment right away from the street. This argument is supported by evidence that in the rat physiological changes persist for at least six months after heroin withdrawal (Martin *et al.*, 1963) and by Wikler's (1965) theory, which emphasizes the importance of conditioning factors in opiate addiction and relapse.

The way out of this particular dilemma seems to be to provide the initial period of "control and removal" in some sort of therapeutic community, either within the hospital or prison, or in some quite other facility unrelated to conventional institutions. In this both Synanon and Daytop have clearly played a major part in making people think again.

Synanon was started in 1958 (Casriel *et al.*, 1963) and today is a community of 700 former addicts who live without drugs and without locked doors. The community owns a fleet of cars and trucks, threatens to buy an aeroplane, runs businesses, has its own dance band, and bids fair to becoming one of the great American success stories. The brashness and aggressiveness of some of Synanon's claims have drawn criticism, and the critic can rightly point out that records which would allow proper assessment of results are not available, that because no urine testing is allowed validation of all claims is uncertain, and that Synanon may be similar to the methadone programme in that it takes an atypical addict. A visit to Synanon and time spent casually talking to its residents strongly suggests, however, that whatever the ultimate statistics this organization is achieving very remarkable successes. The importance of Synanon is not only in terms of the count of addicts helped, but also lies in what psychiatry has to learn from the methods of treatment which the community has evolved (Holzinger, 1965). Daytop village in New York (Shelly and Bassin, 1965), based on the Synanon model, seems to be achieving similar success ; but in Daytop, unlike Synanon, many of the residents are under the coercion of a probation order.

The most interesting departures which Synanon and Daytop have made from the usual psychiatric approach to drug addiction include their emphasis on the addict not being ill but his being "stupid" and "a baby." Emphasis is on feeling rather than on cognition. The communities make no pretence at democracy, and the confusion regarding role and authority structure which can so easily occur in psychiatrically run models of the therapeutic community has in Synanon and Daytop been avoided. Interreaction in group discussions is often verbally violent and brutally frank, but there is also an emphasis on mutual concern—"you really have to love people, not just want to help them like a social worker."

Could a Synanon or Daytop function in Britain ? There would seem to be no inherent reason why such an experiment should not succeed here, and the influence of the experiment on the whole scene might be important, forcing rethinking and imagination. The idealism, energy, and sheer fun of such communities may be more able to win the interest and loyalty of the young addict than can the "square" world of the mental hospital.

Community Centred Programmes

In the organization of psychiatric care the general American trend is toward provision of community-based services (Glasscote *et al.*, 1964 ; Ozarin and Brown, 1965), and thinking on the services for the narcotic addict follows this direction. Those authorities who advocate the initial period of "control" within a closed institution or Synanon type facility would probably all agree that there is no value in this period of removal from society unless on return to society continued help is given. Nevertheless, Vaillant and Raisor (1966) showed, with the particular group of addicts studied and with the community services of rather heterogeneous and uncertain intensity, that only small success could be expected from community care without coercion.

Though caution is necessary in applying experience to Britain, several U.S. experiments in community treatment of addicts are worth mentioning, particularly that of Dr. Efron Ramirez, in Puerto Rico (Ramirez, 1966). This rather startlingly reverses the usual phases of treatment: community care starts the treatment and only later is inpatient therapy offered. The induction phase—"a training process for future treatment"—lasts two to three months and comprises the street encounter, a sort of day hospital programme, and then detoxification. Ramirez believes that the best person to win the addict into treatment is the recovered addict, and it is the recovered patient who goes out on to the street to look for new clients, and the "training for treatment" then continues "in a store front office in a neighbourhood of high drug incidence." The period of residential treatment which follows is expected to last 10 to 12 months, and this is followed by a year in a "re-entry house," in which control is looser and there is gradual resumption of everyday life in the community. Ramirez has now moved to New York, where he is Co-ordinator of Addiction Programmes.

Several other influential but more orthodox community orientated projects have been based on and linked with hospital outpatient departments: the New York Demonstration Centre (Brill, 1965) ; the programme run by the Metropolitan Hospital Centre (Brotman *et al.*, 1965) ; the Washington Heights Rehabilitation Centre (Brill, 1966). The Greenwich Village Counselling Centre (Osnos and Laskowitz, 1966) and the Special Problems Centre in San Francisco have shown the feasibility of treating narcotic addicts and non-addict clients in the same premises.

Conclusions

The growing rate of drug addiction in Britain (Bewley, 1966) has forced revision of the law, but the underlying philosophy which guides the British approach remains unaltered: the thesis was and is that the interests of treatment and prevention are best served by regarding the addict as a patient, by giving him heroin if he so demands, by wooing him rather than coercing him into treatment, and by keeping addiction above ground rather than by driving it into the criminal underworld. The next few years will show whether this philosophy can be the basis of a viable policy. There is nothing in the American experience which guarantees failure, but much to suggest that we are playing against long odds—heroin is a bad and unpleasant drug for maintenance, and to hope that without any form of coercion the addict can be persuaded to abandon freely available narcotics is ambitious indeed. The whole of American experience would suggest that if our new programme is to be other than foredoomed to failure and a prelude to debacle, it must be conducted with vigour and energy, must be a matter of reaching out rather than of sitting back in hospitals, must focus on human needs and rehabilitation rather than on drug maintenance or detoxification. Saving of money at this stage may prove a costly economy.

As for research, the important focus in Britain as in any other country must be on finding why people become addicts and on discovering how they can be aided to recovery: the most profitable focus is likely to be on the society and the person rather than on the drug. Addiction research is nothing special: it is part medical and psychiatric research, and if the experts become isolated work will suffer. The study of schizophrenia, of the alcoholic, of the recidivist, exploration of the effective elements within psychotherapy, the wide and general field of psychopharmacology—all this is germane.

If there is one final lesson to be learnt from all of those who have been grappling with the problem of drug addiction in America for years, it is that discussion in these highly charged and disturbing matters should remain open—that rationality should prevail.

This paper is based on the experience of an eight-week trip to the U.S.A. and on discussions held with many people who with the greatest generosity and courtesy gave their time. To all of them I would like to express my warm and personal gratitude. My particular thanks are due to Dr. Stanley Yolles, Director of the National Institute of Mental Health, Washington, and to Dr. Sherman Kieffer and Dr. Tom Cassidy. The sponsorship of the National Institute of Mental Health made this trip possible. I would like to thank my secretary, Mrs. Julia Polglaze, and Miss Elsie Hoffmeister.

REFERENCES

American Medical Association (1963). Narcotics Addiction: official actions of the American Medical Association.

Ball, J. C. (1965). *J. Criminal Law, Criminology and Police Science*, **56**, 203.

—— and Lau, M. P. (1966). *Social Forces*, **45**, 60.

Bates, W. B. (1966). Ibid., **45**, 61.

Bewley, T. (1966). *Bull. Narcot.*, 18, No. 4, 1.

Brill, L. (1965). In *Narcotics*, edited by D. M. Wilner and G. G. Kassebaum. New York.

—— (1966). New York City Dept. of Health.

Brotman, R., Meyer, A. S., and Freedman, A. M. (1965). *Comp. Psychiat.*, **6**, 104.

Casriel, D. (1963). *So Fair a House*. Englewood, N.J.

Chein, I., Gerrard, D. L., Lees, R. S., and Rosenfeld, E. (1964). *The Road to H*. New York.

Dole, V. P., and Nyswander, M. (1965). *J. Amer. med. Ass.*, **193**, 646.

—— —— (1966). *N.Y. St. J. Med.*, **66**, 2011.

—— —— (1967). *Arch. environ. Hlth*, **14**, 477.

Fraser, H. F., Jones, B. E., Rosenberg, D. E., and Thompson, A. K. (1963). *Clin. Pharmacol. Ther.*, **4**, 188.

Glasscote, R. M., Sanders, D. S., Forstenzer, H. M., and Foley, A. R. (1964). The Community Mental Health Center, Washington.

Holzinger, R. (1965). *Quart. J. Stud. Alcohol.*, **26**, 304.

Home Office (1966). Report to the United Nations by H.M. Govt. on the Working of the International Treaties on Narcotic Drugs.

House of Commons (1967). Dangerous Drugs Bill. H.M.S.O., London.

Jaffe, J. H., and Brill, L. (1966). *Int. J. Addict.*, **1**, 99.

Lieberman, L., and Brill, L. (1967). Rational Authority in the Treatment of Narcotic Offenders. Awaiting publication.

Martin, W. R., and Fraser, H. F. (1961). *J. Pharmacol. exp. Ther.*, **133**, 388.

—— Gorodetzky, C. W., and McClane, T. K. (1966). *Clin. Pharmacol. Ther.*, **7**, 455.

—— Wikler, A., Eades, C. G., and Pescor, F. T. (1963). *Psychopharmacologia (Berl.)*, **4**, 247.

Maurer, D. W., and Vogel, V. H. (1967). *Narcotics and Narcotic Addiction*, 3rd ed. Springfield, Illinois.

Narcotics Conference Report (1963). *Publ. Hlth Dep. (Wash.)*, 78, 669.

O'Donnell, J. A., and Ball, J. C. (editors) (1966). *Narcotic Addiction*. London.

Osnos, R., and Laskowitz, D. (1966). *Bull. Narcot.*, **18**, No. 4, 31.

Ozarin, L. D., and Brown, B. S. (1965). *Amer. J. Orthopsychiat.*, **35**, 10.

Ramirez, E. (1966). In *Committee on Problems of Drug Dependence*. National Academy of Sciences, National Research Council, Division of Medical Sciences, Washington.

Schur, E. M. (1963). *Narcotic Addiction in Britain and America*. London.

Shelly, J. A., and Bassin, A. (1965). *Corrective Psychiat.*, **11**, 186.

State of New York (1966). Art. 9, Mental Hygiene Law: Narcotic Control Act.

U.S. Government (1966). Public Law 89–793, 89th Congress.

U.S. Treasury Dept. Bureau of Narcotics (1966). Prevention and Control of Narcotic Addiction. Washington.

Vaillant, G. E. (1966). *J. nerv. ment. Dis.*, **142**, 534.

—— and Raisor, R. W. (1966). *Fed. Prob.*, 30, No. 2, 53.

Way, E. L., Elliott, H. W., and Homof, N. (1963). *Bull. Narcot.*, 15, No. 1, 29.

—— Mo, B. P. N., and Quock, C. P. (1966). *Clin. Pharmacol. Ther.*, 7, 300.

Wikler, A. (1952). *Psychiat. Quart.*, **26**, 270.

—— (1965). In *Narcotics*, edited by D. M. Wilner and G. G. Kassebaum. New York.

Wood, R. W. (1967). *Lincoln Law Review*.

MEDICAL ETHICS

Supervision of the Ethics of Clinical Investigations in Institutions

Report of the Committee Appointed by the Royal College of Physicians of London[*]

Following the receipt of a letter on 5 September 1966 on this subject from certain Fellows, the College appointed a committee to consider how far supervision of clinical investigation was required, and, if it was required, how best it might be effected.

The term "clinical investigation" is regarded by the Committee as covering all forms of experiment on man. There are broadly two kinds of clinical investigation or research. The first is that which has direct diagnostic or therapeutic relevance to the individual patient and which therefore seldom poses serious ethical problems. Indeed the doctor could sometimes be said to have failed in his duty to his patient if he did not perform such an experiment.

The second kind of investigation or research is that which is carried out to advance knowledge, and from which the subject, be he a patient or a normal person, cannot expect direct personal benefit. This kind of clinical investigation benefits the community, but may present difficult ethical problems in relation to the individual.

The design and conduct of clinical investigation should be guided by a code of ethical practice, and the Code of Ethics of the World Medical Association (Declaration of Helsinki) is accepted throughout the civilized world. The Medical Research Council has also issued a statement on "Responsibility in Investigations on Human Subjects" (M.R.C. Annual Report, 1962–3. Cmnd. 2382, H.M.S.O.). This has been reprinted, together with the Declaration of Helsinki, in the *British Medical Journal* (1964, 2, 177, 178).

The Committee accepts that these statements define the ethical situation and considers that all clinical investigators should be familiar with their recommendations. However, because of the wide varieties of research, formal codes can provide only general guidance, and their application to specific problems must often remain a matter of opinion.

The Committee considers that it is of great importance that clinical investigation should be free to proceed without unnecessary interference and delay. Imposition of rigid or central bureaucratic controls would be likely to deter doctors from undertaking investigations, and if this were to happen the rate of growth of medical knowledge would inevitably diminish, with resultant delay in advances in medical care.

The Committee is satisfied that in the great majority of cases a very high ethical standard has been maintained in clinical investigations in this country.

The number of doctors involved in clinical investigation at the present time is large and is likely to increase, and the types of investigation are tending to become more complex. The Committee considers that it has now become necessary for a procedure to be available for the ethical guidance of clinical investigators. The provision of such guidance would not only serve to allay understandable anxiety in the public, but would be appreciated by clinical investigators themselves when faced with ethical problems.

---

[*] Members of the Committee: Sir Max Rosenheim (*chairman*), Dr. F. Avery Jones, Dr. G. M. Bull, Professor D. V. Hubble, Professor A. C. Dornhorst, Dr. J. D. N. Nabarro, Professor D. R. Laurence, Dr. J. P. P. Stock, Dr. K. Robson, and Dr. P. A. Emerson.

The Committee's conclusions and recommendations are as follows:

(1) The planning and conducting of clinical investigations demand skill, experience, and judgement. Difficult ethical problems occasionally arise and even the most experienced workers would often welcome the opinion and advice of their peers.

(2) The competent authority—for example, Board of Governors, Medical School Council, Hospital Management Committee, or equivalent body in non-medical institutions—has a responsibility to ensure that all clinical investigations carried out within its hospital or institution are ethical and conducted with the optimum technical skill and precautions for safety. This responsibility would be discharged if, in *medical institutions* where clinical investigation is carried out, it were ensured that all projects were approved by a group of doctors, including those experienced in clinical investigation. This group should satisfy itself of the ethics of all proposed investigations. In *non-medical institutions* or wherever clinical investigation—that is, any form of experiment on man—is conducted by investigators with qualifications other than medical, the supervisory group should always include at least one medically qualified person with experience in clinical investigation.

(3) The Committee deliberately refrains from formulating precise rules for supervision because the way in which this could best be organized must vary with different institutions. The variety of investigations and the importance of not discouraging the proper acquisition of knowledge that may prove useful in caring for the sick makes it necessary for each project to be considered separately.

(4) Procedures involving interference with normal function in volunteers carried out for purposes of education rather than investigation—for example, the use of drugs in student practical classes—pose special problems because of the student–teacher relationship and should be subject to the same supervision.

M. L. ROSENHEIM,
President.

COMPUTERS IN MEDICINE

Bibliography on Cannabis: a Medlars Search

The list of references below has been selected by computer at the United Kingdom Medlars Information Retrieval Service in Newcastle from a file of 500,000 references. This file was begun in 1963 by the U.S. National Library of Medicine in Washington, where the articles in over 2,000 medical journals are indexed. The index entries are then processed by computer. Outputs of the system include "Index Medicus" (published monthly; each article is listed under about three of the most important headings), and computer retrieval tapes (on which each article carries about 10 headings). The printed "Index Medicus" is available in about 200 libraries in Britain, and copies of the tapes have been made available to the U.K. Medlars service.

For a simple search, such as this one on cannabis, "Index Medicus" is quicker and cheaper, but for more complex literature problems computer searching may be economic. Inquiries should be addressed to the National Lending Library for Science and Technology, Boston Spa, Yorkshire.

Evaluation of Dependence-Producing Drugs: Report of a W.H.O. Scientific Group, W.H.O. Tech. Rep. Ser., 1964, **287**, 1.

Drugs of Addiction, *Brit. med. J.*, 1964, **2**, 1119.

Toxicologic Report, *Brit. med. J.*, 1964, **2**, 1348.

Bartholomew, A. A., and Reynolds, W. S., Four Cases of Progressive Drug Abuse, *Med. J. Aust.*, 1967, **1**, 653.

Bennett, A E., Compulsive, Addictive Personality Problems, *Med. Tms (Lond.)*, 1964, **92**, 433.

Berner, P., Hoff, H., and Kryspin-Exner, K., Zur Psychopathologie der Sucht, *Wien. med. Wschr.*, 1963, **113**, 759.

Christozov, C., L'aspect Marocain de l'intoxication Cannabique d'après des Études sur des Malades Mentaux Chroniques, *Maroc méd.*, 1965, **44**, 866.

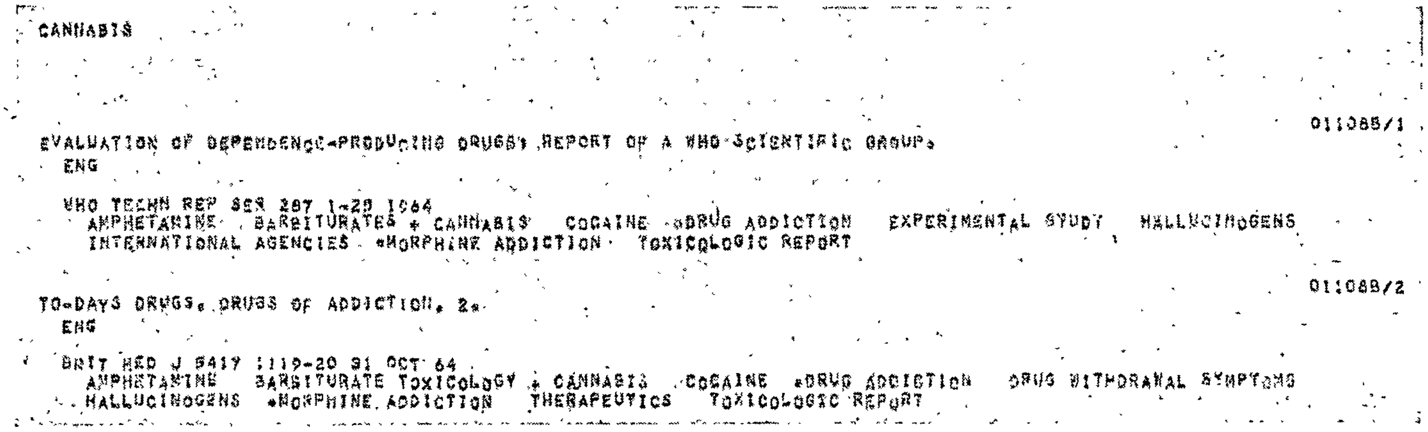
Freedman, A. M., and Wilson, E. A., Childhood and Adolescent Addictive Disorders, *Pediatrics*, 1964, **34**, 283.

Gaulden, E. C., Littlefield, D. C., Putoff, O. E., and Seivert, A. L., Menstrual Abnormalities Associated with Heroin Addiction, *Amer. J. Obstet. Gynec.*, 1964, **90**, 155.

Ludwig, A. M., and Levine, J., Patterns of Hallucinogenic Drug Abuse, *J. Amer. med. Ass.*, 1965, **191**, 92.

McMorris, S. C., What Price Euphoria, The Case against Marijuana, *Med.-leg. J. (Camb.)*, 1966, **34**, 74.

Martin, W. R., Fraser, H. F., Gorodetzky, C. W., and Rosenberg, D. E., Studies of the Dependence-Producing Potential of the Narcotic Antagonist 2-Cyclopropylmethyl-2-Hydroxy - 5,9 - Dimethyl - 6,7 - Benzo - morphan (Cyclazocine, Win-20, 740, Arc 11-C-3), *J. Pharmacol. exp. Ther.*, 1965, **150**, 426.



```
CANNABIS

EVALUATION OF DEPENDENCE-PRODUCING DRUGS, REPORT OF A WHO SCIENTIFIC GROUP.        011085/1
  ENG

  WHO TECHN REP SER 287 1-29 1964
   AMPHETAMINE  BARBITURATES *CANNABIS  COCAINE *DRUG ADDICTION  EXPERIMENTAL STUDY  HALLUCINOGENS
    INTERNATIONAL AGENCIES *MORPHINE ADDICTION  TOXICOLOGIC REPORT

TO-DAYS DRUGS. DRUGS OF ADDICTION. 2.                                              011088/2
  ENG

  BRIT MED J 5417 1119-20 31 OCT 64
   AMPHETAMINE  BARBITURATE TOXICOLOGY *CANNABIS  COCAINE *DRUG ADDICTION  DRUG WITHDRAWAL SYMPTOMS
   HALLUCINOGENS *MORPHINE ADDICTION  THERAPEUTICS  TOXICOLOGIC REPORT
```

Part of the print-out of the search on cannabis. All the index terms are given, and each article was listed in *Index Medicus* under the terms prefixed *.

Mendes, J. F., Toxicofilias Medicamentosas, *J. med. (Porto)*, 1964, **54**, 625.

Meyerstein, A. N., Drug Addiction: A Review, *J. Sch. Hlth*, 1964, **34**, 77.

Runk, B., and Zinn, U., Haschich—Inhaltsstoffe, Synthese und Wirkungen, *Med. Mschr.*, 1965, **19**, 165.

Sussman, S., Narcotic and Methamphetamine use during Pregnancy. Effect on Newborn Infants, *Amer. J. Dis. Child.*, 1963, **106**, 325.

Tadros, C., Le Paradis Artificiel, *Praxis*, 1964, **53**, 665.

Varenne, G., Het Begrip Toxicomanie, *Belg. T. Geneesk.*, 1964, **20**, 1236.

Pop Pot, *Lancet*, 1963, **2**, 989.

Beliaev, N. V., Universalnaia Toksikodermiia Posle Ostrogo Otrav'eniia pri Kurenii Indiiskoi Konopli, *Vestn. Derm. Vener.*, 1964, **38**, 77.

Bose, B. C., Saifi, A. Q., and Bhagwat, A. W., Effect of Cannabis Indica on Hexobarbital Sleeping Time and Tissue Respiration of Rat Brain, *Arch. int. Pharmacodyn.*, 1963, **141**, 520.

Bose, B. C., Saifi, A. Q., and Bhagwat, A. W., Observations on the Pharmacological Actions of Cannabis Indica. II., *Arch. int. Pharmacodyn.*, 1964, **147**, 285.

Bose, B. C., Saifi, A. Q., and Bhagwat, A. W., Studies on Pharmacological Actions of Cannabis Indica (Linn). III., *Arch. int. Pharmacodyn.*, 1964, **147**, 291.

Bose, B. C., Vajayvargiya, R., Saifi, A. Q., and Bhagwat, A. W., Chemical and Pharmacological Investigations of Cannabis Indica (Linn). I., *Arch. int. Pharmacodyn.*, 1963, **146**, 99.

Boyd, E. S., and Meritt, D. A., Effects of Barbiturates and a Tetrahydrocannabinol Derivative on Recovery Cycles of Medial Lemniscus, Thalamus and Reticular Formation in the Cat, *J. Pharmacol. exp. Ther.*, 1966, **151**, 376.

Boyd, E. S., and Meritt, D. A., Effects of Thiopental and a Tetrahydrocannabinol Derivative on Arousal and Recruiting in the Cat, *J. Pharmacol. exp. Ther.*, 1965, **149**, 138.

Carlini, E. A., and Kramer, C., Effects of Cannabis Sativa (Marihuana) on Maze Performance of the Rat, *Psychopharmacologia (Berl.)*, 1965, **7**, 175.

Carlini, G. R., and Carlini, E. A., Effects of Strychnine and Cannabis Sativa (Marihuana) on the Nucleic Acid Content in Brain of the Rat, *Med. Pharmacol. exp. (Basel)*, 1965, **12**, 21.

Christozov, C. L'aspect Marocain de l'intoxication Cannabique d'après des Études faites dans les conditions d'un hôpital Psychiatrique de Malades Chroniques, *Maroc méd.*, 1965, **44**, 630.

Farmilo, C. G., and Genest, K., Narcotics and Related Bases, *Progr. Chem. Toxicol.*, 1963, **1**, 199.

Grlic, L., A Study of Infra-red Spectra of Cannabis Resin, *Planta med. (Stuttg.)*, 1965, **13**, 291.

Grlic, L., and Tomic, N., Examination of Cannabis Resin by Means of Ferric Chloride Test, *Experientia (Basel)*, 1963, **19**, 267.

Hay, R. K., The Management of Intractable Pain due to Advanced Malignant Disease, *Winnipeg clin. Quart.*, 1963, **16**, 24.

Herisset, A., Besson, P., and Autin, C., Aperçu Toxicologique sur les Variétés de Chanvre Cultivées en Anjou, *Ann. pharm. franç.*, 1965, **23**, 631.

Heslop-Harrison, J., Ultrastructural Aspects of Differentiation in Sporogenous Tissue, *Symp. Soc. exp. Biol.*, 1963, **17**, 315.

Hively, R. L., Mosher, W. A., and Hoffmann, F. W., Isolation of Trans-delta-tetrahydrocannabinol from Marijuana, *J. Amer. chem. Soc.*, 1966, **88**, 1832.

Hollister, L. E., Chemical Psychoses, *Ann. Rev. Med.*, 1964, **15**, 203.

Forte, F., Haag, M., and Claussen, U., Tetrahydrocannabinocarboxylic Acid, A Component of Hashish. I, *Angew. chem. Eng.*, 1965, **4**, 872.

Forte, F., and Sieper, H., Zur Chemischen Klassifizierung von Pflanzen. XXV. Quantitative Bestimmung von Haschischinhaltsstoffen nach Dunnschichtchromatographie, *J. Chromatogr.*, 1964, **14**, 178.

Mechoulam, R., and Gaoni, Y., A Total Synthesis of DL-Delta-1-Tetrahydrocannabinol, the Active Constituent of Hashish, *J. Amer. chem. Soc.*, 1965, **87**, 3273.

Mohan, H., and Sood, G. C., Conjugate Deviation of the Eyes after Cannabis Indica Intoxication, *Brit. J. Ophthal.*, 1964, **48**, 160.

Noirfalise, A., Considérations sur le Cannabis Sativa, *Arch. belges Méd. soc.*, 1965, **23**, 373.

Salustiano, J., Hoshino, K., and Carlini, E. A., Effects of Cannabis Sativa and Chlorpromazine on Mice as Measured by Two Methods used for Evaluation of Tranquilizing Agents, *Med. Pharmacol. exp. (Basel)*, 1966, **15**, 153.

Santos, M., Sampaio, M. R., Fernandes, N. S., and Carlini, E. A., Effects of Cannabis Sativa (Marihuana) on the Fighting Behavior of Mice, *Psychopharmacologia (Berl.)*, 1966, **8**, 437.

Stuart, K. L., Ganja (Cannabis Sativa, L.). A Review, *W. Indian med. J.*, 1963, **12**, 156.

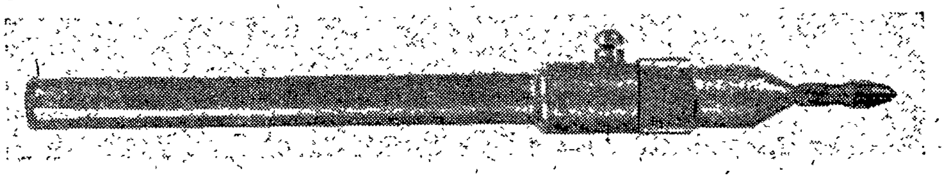
Usdin, E., and Amai, R. L., Psychotropic and Related Compounds, *Psychopharmacol. Serv. Cent. Bull.*, 1963, **2**, 17.

NEW APPLIANCES

Miniature Electric Drill

MR. RICHARD HARRISON, department of orthopaedic and accident surgery, North Lonsdale Hospital, Barrow-in-Furness, writes: A majority of the drills produced for orthopaedic use are easily recognized as modifications of ordinary workshop tools. As such they serve well enough for the making of large-calibre holes in, for example, the femur, but are quite unsuitable for the precise drilling of small bones which is entailed in hand surgery and maxillofacial operations. The instrument shown here was specifically designed for single-handed manipulation, and the following advantages are claimed for it: (1) Its weight and size enable it to be held in the same manner as a fountain-pen. The operator's other hand is free to manipulate the tissues being drilled. His increased sense of the direction the drill is taking facilitates to a remarkable degree such procedures as the insertion of a Kirschner wire. (2) No air-hoses or electric leads are involved. (3) The drill is sterilized as a single unit. The elimination of connexions which might become loose enhances its reliability.

The instrument is 9½ in. (25 cm.) long and has an anodized case enclosing three 1.5-v. pen-torch batteries. These are connected through a push-button switch with a motor which drives a miniature chuck through gears having a ratio of 141:1. With the batteries it weighs 5 oz. (140 g.).



The instrument is ordinarily sterilized by immersion in a 1% alcoholic solution of chlorhexidine for 15 minutes, and can with advantage be kept in a tubular plastic container filled with the same fluid. Treatment with formalin vapour, or ethylene oxide, and dry storage would also be appropriate. In the two prototype drills the batteries required renewal only after being being used for several operations, unless these followed each other in rapid succession.

The drill was designed by Mr. John Collins, of Hugh Steeper Ltd., London S.W.15, who are now undertaking its manufacture.

Correspondence

Letters to the Editor should not exceed 500 words.

Changed Character of Osteomyelitis

SIR,—Your leading article (29 July, p. 255) the "Changed Character of Osteomyelitis" provokes us to make certain comments in the hope of correcting a dangerous over-simplification of the problems involved.

We agree that the disease has changed from the fulminating type seen 25 years ago to a more benign type, but the local lesion may still prove disastrous to limb if not to life. In our experience the disease presents more commonly in young children and infants than in adolescents, and it is the metaphysis rather than the epiphysis which is initially involved.

Broad-spectrum antibiotics exhibited in the first 24 hours may cure the disease, but when the physical signs of local tenderness and oedema are present there is tension in the underlying bone. This calls for immediate decompression by incision and bone drilling, except in neonates, when aspiration of the abscess is often sufficient. In particular we are opposed to the observation that "when subperiosteal pus is found there is no need to drill the underlying bone." Such a finding serves to prove that the surgical intervention is already too late and that only decompression will avert years of ill-health. Delay may lead to massive sequestration, or destruction of epiphysis or joint. Without decompression pyrexia and generalized systemic disturbance may not resolve in spite of antibiotics.

The treatment of acute osteitis is based on the fact that bone cannot swell and surgical decompression is the one rational treatment to prevent ischaemic necrosis. "Better an occasional dry operation than an undrained abscess."—We are, etc.,

H. L.-C. WOOD.
R. C. F. CATTERALL.
R. Q. CRELLIN.

Accident and Emergency Service,
King's College Hospital,
London S.E.5.

Thyrocalcitonin

SIR,—Your leading article on calcitonin (29 July, p. 256), accompanied as it is by the report of the Clinicopathological Conference (p. 293), is very interesting. If calcitonin is a hormone that lowers the concentration of calcium in the plasma, it will reduce the activity of the sympathetic system. When the impulse passing down the postganglionic fibre releases noradrenaline the amount released depends on the calcium concentration, and if the calcium is low very little is released.[1]

If an unusual amount of calcitonin is released, and the plasma calcium is therefore low, two symptoms may be expected owing to the ineffective sympathetic activity. The first is diarrhoea and the second is a falling blood pressure. Both these were present in the patient who was discussed at the Conference. His blood pressure was 130/80 in 1963, and was finally 95/60.

It is conceivable that the slow rise of blood pressure with age in ordinary people may be due to a declining release of calcitonin.—I am, etc.,

Oxford. J. H. BURN.

REFERENCE

[1] Burn, J. H., and Gibbons, W. R., *J. Physiol. (Lond.)*, 1965, 181, 214.

SIR,—I read your leader on thyrocalcitonin (29 July, p. 256) with interest. The references to primary sources seem occasionally arbitrary, but there is one glaring omission. No mention is made of the pioneer work and continuing important contributions of Professor D. H. Copp, who was responsible for the name "calcitonin."[1] The major part of his original work, although later modified, has proved to be correct and should be given pride of place in any review of the development of this expanding subject.—I am, etc.,

IAIN MACINTYRE.

Department of Chemical
Pathology,
Royal Postgraduate Medical School,
London W.12.

REFERENCE

[1] Copp, D. H., Cameron, E. C., Cheney, B. A., Davidson, A. G. F., and Henze, K. G., *Endocrinology*, 1962, 70, 638.

*** We regret this omission. In our issue of 5 August, p. 364, will be found a full report on the contribution Professor Copp gave on calcium homoeostasis at the Centenary Meeting of the Canadian Medical Association.—ED., *B.M.J.*

On Withholding Antibiotics

SIR,—I note from your report on the discussion concerning antibiotics at the Annual Meeting (22 July, p. 235) that it was the general practitioner's view that "antibiotics should not be withheld." This is, in a way, indicative of the present trend to misuse and plain abuse of antibiotics in general practice. Many of us seem to miss the point that the true value of antibiotics is that they have the power to reduce mortality in cases of severe infection, and that the promotion of resistant organisms by careless misuse will seriously curtail this function. Cases of fulminating pneumonia still occur, and deaths from many varieties of bacterial infection are still common. The frequency of such tragedies will increase if we disregard or minimize the risks of resistance.

The reasons for this therapeutic folly are probably several, but perhaps the major one is inadequate "antibiotic education." Whatever the answer, we may soon find that antibiotics, currently our most powerful therapeutic weapons, are becoming impotent.—I am, etc.,

St. Helens, Lancs. ALAN RUSSELL.

Clinician's Approach to Respiratory Viruses

SIR,—I should like to express my agreement with the views of Dr. Neville C. Oswald in his article "Clinician's Approach to Respiratory Viruses" (1 July, p. 35); it is certainly time for "some bridges [to] be erected between the hospitals and the virologists' strongholds." I like to think that in this area we have constructed, or are constructing, such bridges, and the clinicians do not find difficulty in having virological specimens examined. Certainly I receive a high degree of co-operation from the clinicians, and I sincerely hope this is a reciprocal arrangement. I feel the following analysis of the specimens examined supports my statement that the clinicians here can get suitable virological specimens examined without difficulty.

During the period January 1965 to June 1967 we received a total number of 11,065 specimens of which more than 80% were from hospital patients. During the 12-month period October 1965 to September 1966 we examined 2,525 serum samples and 1,616 specimens for virus isolation from hospitals. These hospital specimens were received from as many as 30 different hospitals, and the overall positive result rate was 13% and 11% respectively. These figures include specimens from the infectious disease unit, from which we examined 1,514 serum samples and 862 specimens for virus isolation; of these 18% of the serum samples were positive, and agents were isolated from 16% of the virus isolation specimens. I think these figures illustrate that, provided satisfactory specimens are sent to the laboratory, assistance can be given to the clinicians in a fair number of cases.

Clinical virology can be practised, but to be successful there must be co-operation between the clinician and the virologist. The former should appreciate that the virology department is often overworked and understaffed, that the tests are laborious and expensive, and that both quick and accurate results are only occasionally possible (accuracy must not be sacrificed for speed no matter how great the pressure of work); whereas the virologist is dependent on the clinician for collection of worthwhile specimens, without which his laboratory tests are of little value, and he must endeavour to supply results (within a reasonable time) which have some meaning to the clinician. Contact and co-operation between the clinician and the virologist should be encouraged in preparation for the day when rapid diagnostic methods and antiviral agents are available.—I am, etc.,

M. H. Hambling.

Virus Laboratory,
Public Health Laboratory,
Leeds 15.

Sir,—Dr. N. C. Oswald in his valuable article on the clinician's approach to respiratory viruses (1 July, p. 35) suggested "token laboratories under the general supervision of virologists, the day-to-day work being carried out by senior technicians."

An arrangement of this kind has proved successful in Birmingham, where such laboratories have been set up in the Children's and Dudley Road Hospitals. A well-trained technician, provided with suitable tissue cultures and media, can achieve from specimens hot from the patient an excellent rate of isolation, especially of respiratory viruses. The most skilled virologist several miles away will not do nearly so well with specimens taken by an unskilled hand and transported across several miles of heavy traffic, at some later hour when the hospital van happens to be making the journey. Sera, on the other hand, are best sent to the main laboratory for investigation. It is both tedious and expensive to set up complement fixation tests for virus infections just for a few sera.—We are, etc.,

T. H. Flewett.
East Birmingham Hospital.

K. B. Rogers.
Children's Hospital,
Birmingham.

J. D. Williams.
Dudley Road Hospital,
Birmingham.

Ten-year Recovery from Chronic Lymphocytic Leukaemia—Twelve Years Later

Sir,—One often reads reports of patients whose illness does not conform to the ordinary run, but rarely does one hear of the subsequent fate of these patients. In 1955 I described a patient with chronic lymphocytic leukaemia who had recovered so far as to present for 10 years a completely normal picture both clinically and haematologically.[1] She died, nearly 84 years old, in November 1966. The course of her illness during her last 12 years is interesting enough to warrant reporting.

She was born in 1882. In 1943, after not feeling well for about one year, she was found to be suffering from chronic lymphocytic leukaemia with a lymphocyte count of 219,520/cu. mm. She was treated with *x* rays, her peripheral blood picture became and remained normal for 10 years, and the spleen and lymph nodes were not palpable. She had, however, recurrent respiratory infections, which responded to treatment with tetracycline. In 1961 the white cell count began slowly but steadily to rise, and continued to do so until her death in 1966. The spleen was palpable three fingerbreadths below the costal margin. Respiratory infections became more frequent and she had to be put on a maintenance dose of tetracycline in April 1965, on which she remained until her death. Respiratory infections were now less frequent and responded to ampicillin. The spleen reached the umbilicus in October 1965, and the serial blood pictures can be seen from the Table. Her final illness began in September 1966, with a lower respiratory infection mainly of the right lower zone, which at first responded to ampicillin. However, she did not recover, the lung became consolidated, the spleen had nearly reached the iliac crest, the haemoglobin fell to 38%, and she died on 7 November 1966, almost 84 years old.

The duration of the illness, if a duration of one year before diagnosis is assumed, would amount to 24 years. The longest known survival seems still to be the patient described by Marlow and Bartlett,[2] who died at 74, his leukaemia having lasted 29 years. He had always a raised white cell count and had various treatments throughout his illness. McGavran[3] described a case of 25 years' duration, also with a raised white cell count all the time. He died at 78. I have been unable to find any other cases of equally long duration in the literature.

The next point of interest is the remission of 16 years. There are several reports of long remissions in the literature, but none of them amounts to 16 years. Durant and Finkbeiner[4] report one patient with a remission of 10 years with normal clinical findings and normal blood count and bone marrow. Another of their patients had a normal blood count and bone marrow for five years, but still had "leukaemic" skin lesions. Geller[5] reports a clinical and haematological remission of nine years. Walter, Szur, and Lewis[6] report a prolonged remission with no clinical signs for more than eight years, but two marrow punctures during this time were consistent with chronic lymphocytic leukaemia in remission. Reich[7] reports a patient with normal blood count, bone marrow, and clinical findings for five years.

The ultimate fate of all these patients with remission is not known, but Wintrobe[8] seems to be right when he says that "in many instances, and perhaps always, there is a phase of long duration in which there are signs of the disease and no symptoms; very occasionally, a long period may ensue in the course of this phase when even signs are minimal or absent."

I wish to thank Dr. R. L. Turner, consultant pathologist, Bradford Royal Infirmary, for his advice and his kindness in going through the manuscript.

—I am, etc.,

Bradford 3. Max Schott.

References

[1] Schott, M., *Brit. med. J.*, 1955, **1**, 877.
[2] Marlow, A. A., and Bartlett, G. R., *J. Amer. med. Ass.*, 1953, **152**, 1033.
[3] McGavran, C. W., *Ann. intern. Med.*, 1938, **12**, 396.
[4] Durant, J. R., and Finkbeiner, J. A., *Cancer (Philad.)*, 1964, **17**, 105.
[5] Geller, W., *Arch. intern. Med.*, 1964, **114**, 444.
[6] Walter, L. H., Szur, L., and Lewis, S. M., *Brit. med J.*, 1958, **1**, 859.
[7] Reich, C., *J. Amer. med. Ass.*, 1959, **170**, 169.
[8] Wintrobe, M. M., *Clinical Haematology*, 1961, 6th ed., p. 951. London.

Date	Hb %	RBC (m./cu.mm)	C.I.	Leucocytes	Polymorphs	Lymphocytes	Monocytes	Eosinophils	Basophils	Remarks
7/7/43	70	3·48	1·00	224,000	3,360	219,520	1,120	0	0	
2/1/56	90	5·60	0·80	5,500	3,025	2,310	165	0	0	
2/1/57	95	5·45	0·87	5,600	1,505	2,408	172	215	0	
30/12/57	80	4·75	0·84	4,300	3,472	1,960	56	56	56	
29/12/58	80	5·40	0·74	6,500	2,015	4,160	260	65	0	
30/12/59	80	4·78	0·84	10,700	4,387	5,992	214	107	0	
19/12/60	92	4·57	1·00	8,000	2,560	5,040	160	160	80	
8/12/61	85	5·41	0·79	17,000	4,080	12,750	0	170	0	
22/6/62	75	4·18	0·90	18,700	2,057	16,082	187	374	0	
4/12/62	80	4·66	0·86	31,100	4,354	26,435	0	311	0	
30/10/63	70	4·10	0·85	39,700	3,176	36,127	0	0	397	
15/5/64	75	5·18	0·72	45,600	1,824	43,776	0	0	0	
3/11/65	63			44,000	2,200	40,480	880	440	0	
14/10/66	38			29,000	1,160	26,970	580	290	0	P.C.V. 22% M.C.H.C. 25·4%

per cu.mm.

Amoebic Pericarditis

Sir,—Slight errors are unavoidable in any general article as concise and comprehensive as that on pericarditis by Dr. K. Somers (13 May, p. 423). We feel, however, that the treatment outlined for amoebic pericarditis requires correction.

Emetine hydrochloride and dehydroemetine are extremely effective in hepatic amoebiasis, and indeed are superior to chloroquine. At present their use in amoebic pericarditis is mandatory. Chloroquine may with advantage be combined with emetine preparations, but in the dosage recommended in the article it is liable to produce vomiting. The correct dosage of chloroquine sulphate in adults would be 600 mg. of the base initially, followed by 300 mg. six hours later and then 150 mg. twice or thrice daily for 28 days.

Metronidazole has recently proved outstandingly effective in hepatic amoebiasis and may have a valuable place in the treatment of amoebic pericarditis.—We are, etc.,

S. J. Powell.
A. J. Wilmot.
R. Elsdon-Dew.

Amoebiasis Research Unit,
Durban, South Africa.

Management of Breast Cancer

Sir,—At Bristol Sir Stanford Cade (22 July, p. 227), in discussing relative values of different forms of treatment, is reported as saying that "chemotherapy was the treatment of last resort. It had never cured patients with this condition."

As initiators of systemic therapy[1] in this country we proffer some remarks on this dogmatic statement. Is it implied that there is a cure for breast cancer, or are results still to be assessed by the five-yearly, etc., yardstick? We would agree that chemotherapy, if used only as a treatment of last resort, must undoubtedly give disappointing results. It is in these circumstances that most surgeons and radiotherapists have employed such therapy. Has Sir Stanford used chemotherapy as a primary treatment for apparently early patients, and if so has he considered this facet in his judgement? Our five-year results[2] in apparently early patients, employing systemic assessment and treatment in an admittedly small series, are sufficiently encouraging to warrant continuation.

The arguments will continue anent a condition in which the deaths, using contemporary measures, have increased by 4% from 1963 to 1964,[3] but the long-repeated exercises in surgery and radiation which have hitherto shown little reward are still being pursued. The way ahead would seem to lie in improved systemic treatment for what is potentially a systemic condition even in the most apparently early patient.

Minimal controlled surgery should only be permissible when a satisfactory systemic picture is present or obtained, and should certainly be delayed in the advanced patient. In the meantime, to catch the patient in apparent (with a negative systemic assessment) true Stage 1 should be our aim, since the results of treatment by any method are relatively good.

We note that early detection at well-women clinics and self examination was not discussed at the symposium—the early detection of what is usually a symptomless condition is surely a prime necessity.—We are, etc.,

G. WHYTE WATSON.
ROBERT L. TURNER.

Department of Chemotherapy,
Bradford Royal Infirmary,
Bradford, Yorks.

REFERENCES

[1] Watson, G. W., and Turner, R. L., *Brit. med. J.*, 1959, 1, 1315.
[2] —— —— *Chemotherapia (Basel)*, 1966, 11, 261.
[3] Adams, M. J. T., and Spicer, C. C., *Lancet*, 1965, 2, 732.

Wassermann Reaction and Vaccination

SIR,—The percentage of the normal population in which positive Wassermann reactions may be detected depends on the sensitivity of the lipoidal antigen used. This explains Lynch's[1] high figure of 27% acute positive biologically false-positive reactions following vaccination, cited in your leading article (13 May, p. 394). This is borne out by a detailed examination of Lynch's results:

Type of Antigen Used	Type of Response to Vaccination	
	Primary	Accelerated
Very sensitive lipoidal antigen Hinton test	35/96 positive*	7/114 positive*
V.D.R.L. test (quantitative)	4/97 positive*	1/115 positive

* Doubtful results excluded.

Similar results have been suggested by Salo *et al.*,[2] who gave an overall figure of 6.6% acute positive biologically false-positive reactions using the V.D.R.L. antigen, following vaccination.

Thus the commonly used V.D.R.L. test yields a result of nearer 6% positive acute biologically false-positive reactions rather than 27%, so presenting far less of a problem than represented. Although almost all subjects (with the exception of those, in theory only, without any reagins) will produce a rise in reagin titre, only 6% will have a sufficient rise to be detected by the less sensitive V.D.R.L. test.

It would be of great advantage if the lipoidal antigens were not only standardized with respect to other laboratories but also to "biological phenomena."—I am, etc.,

D. J. M. WRIGHT.

King's College Hospital,
London S.E.5.

REFERENCES

[1] Lynch, F. W., Kimball, A. C., and Kernan, P. D., *J. invest. Derm.*, 1960, 34, 219.
[2] Salo, O. P., Somer, T., Aho, K., and Cantell, K., *Ann. Med. exp. Fenn.*, 1966, 44, 304.

Diet and Diverticulitis

SIR,—My views on the importance of diet in the causation of diverticulosis coli have been misrepresented in your correspondence columns by Dr. E. H. Goulston (6 May, p. 378), when he commented on a letter by Drs. T. L. Cleave and G. D. Campbell (2 July, 1966, p. 50).

They pointed out that African natives living on a tribal diet do not develop diverticulosis, but they do so when they become urbanized and change to a Westernized diet. Also, thirty years ago their coloured cousins in the U.S.A. were less affected by the disease than their white compatriots, whereas nowadays both racial groups are equally prone to develop diverticula. Concurrently the amount of maize eaten in America has decreased dramatically. Drs. Cleave and Campbell blame the increased use of refined carbohydrates in the form of white flour and sugar in our so-called civilized diet for these changes, and have submitted evidence for this conclusion elsewhere.[1]

Dr. Goulston dismissed their theory, saying that, "The time-honoured label of colonic stasis and diet as regards aetiology (of diverticulosis) is wearing thin, especially when one reads the studies by N. S. Painter *et al.* . . ." This implies that I disagree with Drs. Cleave and Campbell and that I consider that our diet does not cause diverticulosis. Nothing could be further from the truth.

My studies on the pressures in the human colon in health and diverticulosis did not reveal the aetiology of the disease but its pathogenesis. The pulsion force that drives the colonic mucosa through the muscle coat is generated by segmentation of the colon, which can produce high localized intracolonic pressures. Segmentation occurs spontaneously or can be caused by emotion, mechanical stimuli, or by certain drugs, of which morphine is one. I have suggested that segmentation, and hence high intracolonic pressures, may be caused by our diet or by substances that we inhale. I have argued that a colon of small diameter can segment more readily than a colon that has a large lumen, and hence that a narrow colon is more prone to develop diverticula.[2-4] This would explain why rats, which have a narrow colon, owing to being fed on a low residue diet, develop diverticula,[5] while Africans, who eat a high residue diet and have a wide colon, remain free from the disease. It is my belief that a high residue diet may be contraindicated in the treatment of the established disease.

It would be ridiculous to attribute the rapid increase in the incidence of diverticulosis in Western society to a genetic change, so, if the human body has not changed, the disease must be caused by external factors affecting the body. Drs. Cleave and Campbell have presented evidence that our "civilized" diet is responsible not only for diverticulosis but also for other diseases. Only when the factors in our diet that cause increased segmentation and pressure production have been identified will both the pathogenesis and the aetiology of diverticulosis be known. Meanwhile the simple theory advanced by Drs. Cleave and Campbell—namely, that our diet is abnormal and responsible for many of the ills that affect civilized man—deserves consideration and immediate investigation.—I am, etc.,

NEIL STAMFORD PAINTER.

The Manor House Hospital,
London N.W.11.

REFERENCES

[1] Cleave, T. L., and Campbell, G. D., *Diabetes, Coronary Thrombosis, and the Saccharine Disease*, 1966. Bristol.
[2] Painter, N. S., *Ann. roy. Coll. Surg. Engl.*, 1964, 34, 98.
[3] —— Truelove, S. C., Ardran, G. M., and Tuckey, M., *Gastroenterology*, 1965, 49, 169.
[4] —— *Amer. J. dig. Dis.*, 1967, 12, 222.
[5] Carlson, A., J., and Hoelzel, F., *Gastroenterology*, 1949, 12, 108.

Treatment of Radiation Sickness

SIR,—The communication on this subject by Drs. H. Mattie, E. W. Emery, and I. D. Hill, and Professor D. R. Laurence (22 July, p. 215) does little to clarify the longstanding confusion about the value of drugs in the treatment of radiation sickness. They carried out in 82 patients a double-blind trial comparing the effect of 3 mg. pyridoxine hydrochloride daily with 150 mg. daily, and established no significant difference. No attempt was made to demonstrate that pyridoxine administration at *any* dose level is more effective than a placebo, and in fact they quote two reported controlled trials as showing no difference between the two.[1 2]

Their series of cases is of course too small to provide significant information on this problem when analysed according to criteria emphasized by me 10 years ago[3]:

(*a*) Radiation sickness comprises a complex of symptoms, of which each symptom must be considered separately for response. Vomiting is the easiest of all to control, nausea rather less so, while anorexia and lassitude are the most resistant to treatment.

(*b*) The degree of relief of each symptom, partial or complete, must be specified. Whereas abolition of vomiting can be measured quantitatively, the complete abolition of lassitude and anorexia is in my experience almost impossible for a patient to admit.

(*c*) In view of the variation of degree of radiation sickness with the site of irradiation, size of field, and daily dose, drugs are best compared on the basis of their efficacy in relation to one specific technique. Postoperative breast irradiation is well suited to this purpose.[2 4]

(*d*) Placebo tablets give a surprisingly high proportion of relief of symptoms. They relieve vomiting in over 50% of cases as a whole, although the proportion relieved is much smaller when the abdomen or pelvis is being irradiated. Thus the proportion of patients receiving treatment to this area must be equated to compare any two series.[5]

I have published an analysis of over 1,000 controlled drug trials in radiation sickness based upon these criteria.[5] Included were 201 patients receiving 40 mg. daily of pyridoxine hydrochloride and 60 patients receiving a placebo (30 mg. lactose daily). The patients were randomly selected on a calendar basis, although no attempt was made to make up tablets in identical form. When the material was subdivided according to the criteria specified above pyridoxine was found superior to the placebo in the following respects: completeness of relief achieved, relief of anorexia and lassitude, and relief of symptoms following abdominal or pelvic irradiation. All these are the most resistant to relief.

Only by the detailed analysis of such criteria in large series of cases will the value of drugs in radiation sickness be clarified.—I am, etc.,

BASIL A. STOLL.

Chester Beatty Research
Institute,
London S.W.3.

REFERENCES

[1] Silverman, A., Kligerman, M. M., Fertig, J. W., and Ellis, K., *Radiology*, 1956, 66, 403.
[2] Finney, R., *Clin. Radiol.*, 1961, **12**, 229.
[3] Stoll, B. A., *Radiology*, 1957, 68, 380.
[4] Ellis, F., and Stoll, B. A., *J. Fac. Radiol. (Lond.)*, 1952, **3**, 207.
[5] Stoll, B. A., *Brit. med. J.*, 1962, **2**, 507.

A Case for Cannabis?

SIR,—In your leading article "A Case for Cannabis?" (29 July, p. 258) you state categorically "Cannabis has no known therapeutic value . . .," and give as the reference to this *Brit. med. J.*, 1964, **2**, 1348. Perhaps your leader writer overlooked *Guy's Hospital Reports*, 1954, **103**, 330.—I am, etc.,

DAVID STAFFORD-CLARK.

York Clinic,
London S.E.1.

⁂Dr. Stafford-Clark rightly draws attention to a case reported by himself and Dr. E. J. Rolls in which alcoholic tincture of cannabis was used in the treatment of a depersonalization syndrome which immediately followed labour. The syndrome had failed to respond to other therapy, and after treatment using cannabis the patient recovered rapidly and completely.

The leading article made the point that little research had been done on the pharmacological activity of cannabis in man, possibly because of its lack of "known therapeutic value." The most recent edition of "Martindale"[1] states, "Cannabis was formerly employed in mania and nervous disorders as a cerebral sedative or narcotic and it has occasionally been used for the relief of migraine and of headache due to hypertension. It is now rarely used as a therapeutic agent. Its action is very unreliable. Different samples of cannabis may vary greatly in potency." At p. 430 of this issue we print a list of publications mentioning cannabis abstracted by Medlars from 2,000 journals in the world literature for the period from 1963–7. Very few of these papers are clinical.—ED., *B.M.J.*

REFERENCE

[1] *Extra Pharmacopoeia*, 1967, 25th edition. London.

SIR,—I would like to commend the good sense of your leading article under the above heading (29 July, p. 258). The subject of drug addiction is part of the bigger one of the misuse of drugs of all kinds. This is one of the largest diseases of modern life; partly iatrogenic and much more a social one. The generality of drugs are overprescribed and overdemanded. They are not treated with respect; adults are careless, children are poisoned, character is eroded, accidents are facilitated, money is wasted, and political control is nonsensical.

As to cannabis, we should remember that it has an evil reputation going back many centuries. Intoxication with "hashish" led to murder, thus the origin of the word "assassin."

Scientific study of the drug is no doubt desirable, but the whole nation needs to look into its own actions and seek for the creative development of beauty, compassion, and indeed hard work for its future (*poiesy*).—I am, etc.,

Exeter. NORMAN CAPENER.

Disinfectants and Plastic Mop Heads

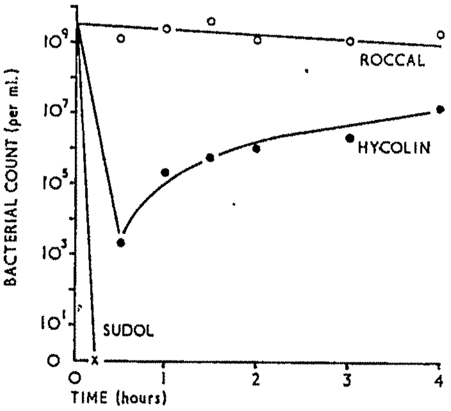
SIR,—There is very little agreement about the best disinfectant to use for hospital cleaning procedures, and cleaning equipment is made of a variety of materials. It is known that some varieties of plastic will interfere with the action of disinfectants, but in view of the lack of advertisement of this problem we would like to report the recent findings in our renal transplantation unit.

The unit consists of single-bedded rooms, the floors of which are individually cleaned each day with a plastic mop which is stored after use in a disinfectant solution in each room. The mop head is made of polyurethane foam and can be autoclaved.

In October 1966 routine culture of a mop head and of the disinfectant solution showed a heavy growth of *Pseudomonas aeruginosa* which was resistant to Roccal (0.05%) the disinfectant in use at that time. The disinfectant was therefore changed to Hycolin (1%), to which the organism was sensitive, and new mop heads were issued. Subsequent culture of the mop heads, however, again grew large numbers of *Pseudomonas aeruginosa*, and since the material of which the mop head was made seemed to be interfering with the action of the disinfectant the compatibility of several disinfectant solutions with the plastic mop head was examined.

The effect of Hycolin, Roccal, and Sudol was tested on four pathogenic bacteria isolated from infections in renal transplant patients. The organisms were *Pseudomonas aeruginosa* (pyocine type 10), *Escherichia coli 0111*, *Staphylococcus aureus* (phage group III), and *Candida albicans*, which were grown overnight in nutrient broth; the following morning the disinfectant solutions were added to give a final concentration of Hycolin 1%, Roccal 0.05%, and Sudol 2.5%. Two cultures were used, one containing the disinfectant solution alone and the second containing in addition a sterilized cube of plastic from the mop head. The bottles were placed on a mixer and quantitative bacterial counts were carried out at 30-minute intervals.

All organisms were killed by the three disinfectants alone in 15 minutes, with the exception of *Pseudomonas aeruginosa*, which was resistant to Roccal. When the plastic was present the *Staphylococcus aureus* and *Candida albicans* were still sensitive to the disinfectant solutions, but *Escherichia coli* was not killed in Roccal and *Pseudomonas aeruginosa* survived in Hycolin. The effects of the three disinfectants on *Pseudomonas aeruginosa* is shown in the Figure; it was found that Sudol was still effective within 15 minutes, but Hycolin, although reducing the bacterial count initially, did not completely eliminate the organism and after 30 minutes sufficient sorption of the disinfectant on to the plastic had occurred to allow the organisms to grow again. A similar effect was seen with *Escherichia coli* and Roccal. It was possible by increasing the working concentration of Hycolin to 5% to eliminate this effect, but in this high concentration toxic effects and hypersensitivity reactions are more likely to occur, and the risks to cleaning staff are increased.



As a result of these experiments it was decided to use Sudol as the disinfectant in ward cleaning procedures and to continue using the same plastic mop.

The purpose of this report is not to advise on the use of a particular disinfectant or mop head but to suggest that care must be taken in the choice of a particular combination. Incompatibility between disinfectant and plastic can be detected only by bacteriological examination, and constant supervision should be carried out.—We are, etc.,

D. A. LEIGH.
CHRISTINE WHITTAKER.

Department of Bacteriology,
St. Mary's Hospital,
London W.2.

Potentiation of Anticoagulants

SIR,—We read with interest the letter of Drs. B. I. Hoffbrand and D. A. Kininmonth (24 June, p. 838) commenting on the potentiating effect of phenylbutazone on coumarin anticoagulants. We should like to report a further example.

A man aged 62 had been treated with warfarin for eight months following a myocardial infarct. His anticoagulant control had been good, and on a dose of 10 mg. daily of warfarin his prothrombin time was between 24 and 28 seconds with a control of 11 to 12 seconds. He attended hospital on 20 June 1967 complaining of severe right sciatic pain and was admitted to the ward.

The previous day, in addition to the usual dose of warfarin, he had taken 400 mg. of phenylbutazone, and on the morning of admission 100 mg. On 21 June his prothrombin time was found to be greater than 60 seconds with a control of 12 seconds, and without further warfarin his prothrombin time was as follows:

22 June	43 seconds (control 12 seconds)
23 June	52 seconds (control 12 seconds)
24 June	24 seconds (control 12 seconds)

Liver function tests, including the bromsulphalein test, were normal.

There seems to be no doubt that the effect of warfarin was potentiated by phenylbutazone in this patient, and it is interesting that the total dose taken was only 500 mg.—We are, etc.,

J. D. EDDY.
J. MACKINNON.

Dudley Road Hospital,
Birmingham 18.

Safer Dental Anaesthesia

SIR,—I am both puzzled and perturbed at the tendency of some of your leading articles to be written with such complete lack of balance. The most obvious of these was " Anaesthesia for Dental Extractions " (25 February, p. 447), which seems to be expressed entirely from the academic point of view. To take but one example, there is the categorical statement, " Undoubtedly the safest method of operating in the oral cavity is under endotracheal anaesthesia. . . ." No exceptions are even suggested, though it is granted that the numbers of patients are too great for its universal application. If strictly true, how does one account for the fact that throughout some 40 years of close association with both dental surgeons and anaesthetists I cannot think of one who, if confronted with the personal problem of the extraction of a septic tooth or teeth in the anterior part of the mouth, would request for himself the " safest method," knowing as he does its possible attendant discomforts.

Similarly, in your article " Safer Dental Anaesthesia " (8 July, p. 64) there is quoted the paragraph[1] that the " administration of general anaesthesia and the performance of dental surgery require the undivided attention of anaesthetist and operator respectively and . . . cannot be combined without risk." You go on to say, " This authoritative statement will surely receive general assent." The word " authoritative " seems to be added for good measure, but as there is nowhere any evidence of any kind to support this statement (and this over the analysis of over 10,000,000 cases) it would have been fairer to leave it out.

What has been omitted from the article is the growing demand on the part of the public for painless conservative dental treatment by means of intravenous medication. The conception and application of this differs so greatly from the general anaesthesia and the performance of dental surgery that, as mentioned in the third recommendation of the Report,[1] it has become a separate entity and is deserving of special study by anyone interested in relieving the patient of mental distress as well as physical pain.

Howe and Hovell[2] make the point, " The recommendations detailed in the report may or may not be sound, but what is certain is that they are based not on facts but on expressions of opinion."

It would indeed seem that some of the pundits who range themselves so strongly against an extension of methods whereby the patient experiences less discomfort and pain during conservative dental procedures do so from a variety of reasons, some of them academic more than practical, and so fall into the " Fruits of Error and False Assumption " as so adequately described by Lord Cohen[3] and also from emotional and illogical reasons similar to those historically recalled by the furore about anaesthesia in childbirth, subsequently upon the introduction of local anaesthesia for dental conservation, and now by the extended use of intermittent methohexitone or the Jorgensen technique.—I am, etc.,

M. W. P. HUDSON.

National Dental Hospital,
University College Hospital,
London W.C.1.

REFERENCES

[1] *Dental Anaesthesia*, Report of a Joint Subcommittee of the Standing Medical and Dental Advisory Committees on Dental Anaesthesia, Ministry of Health, 1967, H M.S O.

[2] Howe, G L., and Hovell, J. H., *Brit. dent. J.*, 1967, 123, 3.

[3] Cohen, Lord, *Proc. roy. Soc. Med.*, 1967, 60, 673.

SIR,—Without going into the main deficiencies of the Government Report on Dental Anaesthesia,[1] which are almost all connected with the expression of personal opinion without acceptable supporting evidence, your leading article on the subject seems to be satisfied with a low order of conciseness and clarity to mete out congratulation (8 July, p. 64).

It has been agreed by the British Dental Association that the subject of training is of greatest importance. The B.D.A. are especially keen on retaining the rights of dentists to give anaesthetics.

Such is the conciseness and clarity of the report that the Council of the B.D.A. issued a paper[2] agreeing with this section. This is tantamount to saying that dental students should receive no practical training in anaesthetics and that dental graduates could not receive any postgraduate training which would enable them to provide a service.

The first point is dealt with in paragraph 31 of the report, but to check the second one must study paragraphs 33, 34, 35, and the reasonable potential capacity of six-month postgraduate courses, which would be unlikely to exceed 50 places a year in the foreseeable future, whereas 700 would be needed.

Little in the report seems to be based on practical experience. The authors claim to examine the criteria for safety " in some detail," yet do not mention the importance of protection of the airway, of effective packing, and of the simple measures one should adopt to prevent, rather than having to treat, emergencies.—I am, etc.,

S. L. DRUMMOND-JACKSON.

London W.1.

REFERENCES

[1] *Dental Anaesthesia*, Report of a Joint Subcommittee of the Standing Medical and Dental Advisory Committees on Dental Anaesthesia, Ministry of Health, 1967, H.M.S.O.

[2] *Conference on General Anaesthesia in Dentistry*, Supplement to *Brit. dent. J.*, 1967, 20 June.

Aversion Therapy of Homosexuals

SIR,—In your issue of 3 June (p. 594) you published a report on the treatment of homosexuality (I did not know it was a disease). The authors are to be congratulated on their honest and sincere report which prompts me to a similar comment.

From 43 persons—allow me not to call them patients, although the " treatment " inflicted upon them entitles them to it—18 appeared for treatment in connexion with a court appearance. Twenty-five had some personality disorder associated with their homosexuality—court appearance or other people's attitude to them. Four presented with symptoms other than their homosexuality. Only seven preferred partners under 16.

It is obvious that, excluding the last two categories, at least 32 persons have been subjected to a treatment of their homosexuality because society disliked their sexual practices. After treatment half of the 43 were converted to " active " heterosexuality. In short, because of these persons' unconventional sexual practices they have been conditioned to conventional ones, so much so that it looks as though fornication has become an end in itself.

If this treatment gives such satisfactory results is there any reason why enthusiasts should not extend it to conditions such as promiscuity or adultery ? And if we extend it to people with less conventional views than ourselves in general we will be in 1984. At a time when lay people begin to have enlightened views on sex and sexual behaviour is it too much to expect the profession at least to follow suit if it is unable to be in the forefront ?—I am, etc.,

Bamford, Rochdale. B. KALCEV.

Results of Augmented Histamine Tests

SIR,—It is scarcely surprising that Mr. R. J. Abernethy and others (22 July, p. 205) should find highly significant correlations between the post-histamine acid output in the whole hour,[1] mid-half-hour,[2] and peak half-hour.[3] In a comparable study[4] " a highly significant correlation was found between the values of the samples 0–40 and 20–60 minutes and the MAO [maximal acid output]," but Carneiro de Moura and Pinto Correia went on to comment on their own highly significant correlations : " In fact, these correlations are spurious because the same component (0–40 or 20–60) appears in both abscissa and ordinate."—I am, etc.,

J. H. BARON.

Institute of Clinical Research,
Middlesex Hospital Medical School,
London W.1.

REFERENCES

[1] Bruce, J., Card, W. I., Marks, I. N., and Sircus, W., *J. roy. Coll. Surg. Edinb.*, 1959, 4, 85.

[2] Kay, A. W., *Brit. med. J.*, 1953, 2, 77.

[3] Baron, J. H., *Gut*, 1963, 4, 136.

[4] Carneiro de Moura, M., and Pinto Correia, J., *Amer. J. dig. Dis.*, 1964, 9, 669.

Folate Deficiency in the Elderly

SIR,—The last statement in Dr. J. D. B. Andrews's letter (22 July, p. 244)—namely, " However, as serum folic levels probably do not accurately reflect tissue state, the diagnosis or exclusion of folate deficiency on serum folate levels alone appears unjustified," demands comment as it seems to carry the air of dismissing the value of serum folate estimations. Dr. Andrews's supposition could be correct, but it would help to hear more supporting facts as a case to the contrary can be made as follows.

For the purposes of this discussion I take the word " accurate " in medicine to mean accurate enough to be of practical value. Professor Leevy *et al.*[1] showed that serum folate levels reflect liver tissue levels surprisingly accurately. Chanarin *et al.*[2] demonstrated similar findings.

It may be that serum folate levels do not reflect tissue levels in tissues other than the liver. If this is so, has Dr. Andrews any facts to support this ? There are abundant publications, too well known to require reference, that patients with low serum folate levels and changes believed to be secondary to folic acid deficiency respond when given folic acid. This is strong supporting evidence that serum folate levels reflect tissue levels accurately enough for practical purposes. The folate level in the central nervous system[3] is three times that of serum and falls when the serum folate falls. This also suggests that serum folate levels can give a helpful reflection of folate levels elsewhere in the body.

The serum estimation of any substance—e.g., potassium—requires sensible interpretation. Estimations used in this way have served us well for years. The day when an easy estimation of tissue substances can be achieved is probably many years off. Meanwhile it would be unwise to reject such guides as are available. We must do the best with those we have ; which probably are accurate enough for practical purposes.—I am, etc.,

A. J. GARDNER.

Atkinson Morley's Hospital,
London S.W.20.

REFERENCES

[1] Leevy, C. M., Baker, H., Ten Hove, W., Frank, O., and Cherrick, G. R., *Amer. J. clin. Nutr.*, 1965, 16, 339.
[2] Chanarin, I., Hutchinson, M., McLean, A., and Moule, M., *Brit. med. J.*, 1966, 1, 396.
[3] Herbert, V., and Zalusky, R., *Fed. Proc.*, 1961, 20, 453.

Dietetic Treatment of Phenylketonuria

SIR,—I read with interest the recent follow-up study of the 57 children with phenylketonuria by Dr. Barbara Clayton and others (15 July, p. 133). The age when treatment is started and the occurrence of epilepsy are certainly two factors affecting a satisfactory outcome to treatment, but the following case may be of interest.

A male infant had a normal birth and at 8 weeks gave a negative reaction to a routine Phenistix test. The occurrence of frequent (4-5 a day) "infantile spasms" caused him to be admitted to the Royal Salop Infirmary under Dr. J. C. Macaulay at 8 months, when he was found to be suffering from phenylketonuria, and he was subsequently put on to a low phenylalanine diet.

In retrospect many of the recognized milestones were delayed. He did not sit on his own until 11 months, he did not start to walk until 18 months, and when I first saw him at the age of 3½ years, although he appeared bright and had a good vocabulary, he was still having a little difficulty with urinary continence during the day. Both parents are intelligent and I would assess the "quality of treatment" and maternal care as good.

At the age of 4½ years the lad was tested on the Stanford Binet scale and an I.Q. of 109% was obtained. He was recently admitted to the local school and at the end of his first term the head-teacher commented that he appeared a bright lad but easily distracted from sustained work, though beginning to settle well. This had been noted during the I.Q. assessment.

It is too early to give any firm prognosis regarding his future at school, but this is a lad who, because of late detection and the occurrence of epilepsy, might not have been expected to have done as well as he has.

This case seems to be worth reporting, as the follow-up study contained only one child (Case No. 20) detected after the age of 6 months and showing evidence of epilepsy who has been placed within the normal educational system, and his last I.Q. fell within the educationally subnormal range.

The presence of "fits" in a child with phenylketonuria would seem to make a favourable outcome unlikely but not an indication for withholding treatment.—I am, etc.,

BRIAN E. DEERE.

County Health Offices,
Newtown, Montgomeryshire.

Cardiac Resuscitation

SIR,—If the problem of who should be resuscitated is a difficult one for nurses in hospital how much more difficult for the first-aider in the factory or in the street. He has not the advantage of seeing seriously ill patients daily to help him in assessing the condition of a collapsed casualty, nor does he usually know of the past and present medical history, which the nurse would have been told on the patient's admission. Why then did the first-aid organizations of St. John, St. Andrew, and the British Red Cross[1] choose to ignore the carefully thought out conclusion of the Symposium on Resuscitation in 1961[2] that cardiac resuscitation should be taught only to "doctors, nurses, and recognized life-savers" ?

There is already too much knowledge to be absorbed in the 16 hours' instruction recommended for the first-aid course, and the result is obvious to anyone regularly involved in examining candidates for the St. John certificate. While the technique of cardiac compression is easily learnt and remembered, the indications for it are often not clearly understood, and one feels that cardiac arrest would seldom be diagnosed correctly. Presumably this would not matter if the procedure was entirely safe, but complications such as fractured ribs, haemothorax, haemopericardium, and visceral damage have been reported with relevantly experienced resuscitators.[3,4] These are not likely to improve the chances of recovery of a severe cardiac infarction or oligaemic shock, and I would suggest that unless far more time and care are spent in teaching resuscitation it is likely to do more harm than good.—I am, etc.,

J. D. BARRETT.

Vauxhall Motors Ltd.,
Luton, Beds.

REFERENCES

[1] *First Aid Authorised Manual St. John Amb. Assoc., St. Andrew's Amb. Assoc., and Brit. Red Cross Soc.*, 2nd ed., 1965. London.
[2] *Acta anaesth. scand.*, 1961, 5, Suppl. No. 9.
[3] Lee, W. R., *Trans. Soc. Occup. Med.*, 1966, 16, 94.
[4] Sykes, M. K., and Ahmed., N., *Lancet*, 1963, 2, 347.

Dopa and Parkinsonism

SIR,—Assuming that the identification of tyramine in excess in the urine of patients with Parkinsonism[1] and the improvement in such patients on feeding dopa[2] can be confirmed, these findings are in keeping with the postulated defect in hydroxylation in this syndrome. Normally the amino-acid phenylalanine is hydroxylated to tyrosine, which is then hydroxylated to dihydroxyphenylalanine (dopa), this finally being decarboxylated to yield dopamine. If a defect in tyrosine hydroxylation exists in Parkinsonism then tyrosine would be decarboxylated to yield tyramine, thus explaining Boulton and colleagues' findings.

Feeding of dopa would result in a return to normal levels of dopamine in the substantia nigra and corpus striatum, thus ameliorating the symptoms. That the symptoms of Parkinsonism may not be solely due to depleted stores of dopamine, however, is suggested by the finding that feeding of phenylalanine aggravated them. This would tend to suggest that an abnormal metabolite of tyrosine is also involved in producing the clinical features.

The occurrence of athetoid movements on feeding dopa is extremely interesting, but it would be rash to speculate on the significance of this.—I am, etc.,

J. WATT.

Royal Edinburgh Hospital,
Edinburgh.

REFERENCE

[1] Boulton, A. A., Pollitt, R. J., and Majer, J. R., *Nature (Lond.)*, 1967, 215, 132.
[2] Cotzias, G. C., Van Woert, M. H., and Schiffer, L. M., *New Engl. J. Med.*, 1967, 276, 374.

Infectivity of Scabies

SIR,—While I am in complete agreement with the views of Dr. Lionel J. Bacon (6 May, p. 373) and Professor J. T. Ingram (20 May, p. 506), it is with some concern that I find the myth of transfer of this infestation by clothing and bedclothes is still being perpetuated. My experience of close contact between cases of scabies and venereal disease in a ship in 1942-3 without a single case of cross infection in spite of the fact that bedding was often shared has been confirmed by my experience since that time.

I was responsible for the care of skin and venereal cases in a ship between September 1941 and October 1943. The crew of 1,500 adult males formed a closed community. During the two-year period visits were made to ports in the temperate and torrid zones. Men were allowed leave either for short periods of four hours or overnight for 12 hours. Their contact with a source of infection was, therefore, either for four hours or for 12 hours. The incidence of scabies and venereal diseases was fairly high. For one six-month period in 1943 the figures were: scabies 106, gonorrhoea 18, urethritis 11, balanitis 10, syphilis 4, soft sore 2 (unfortunately figures for the whole period are not now immediately available to me).

Cases of scabies and venereal disease once diagnosed were segregated in a common mess in the ship and no attempt was made to separate them. They carried out their normal duties. They slept in hammocks and a man coming off duty frequently turned in in the hammock of the man going on duty. No attempt at disinfestation of bedding or clothing was made or possible. During the two-year period no case of cross-infection was found. It was noted that scabies was not contacted when shore leave was limited to four hours, but only when overnight 12-hour leave was given. This was not found with the venereal diseases.

Therefore I am convinced that casual contact cannot lead to transfer of the infestation but that intimate contact with the infected host for some hours is necessary.

Unfortunately, I cannot entirely agree with the views expressed by Dr. J. O'D. Alexander

(17 June, p. 766). In my opinion, treating a case of itching as scabies on suspicion but without confirmation is unwise. The recent interest in scabies has led to a marked increase in the number of patients referred to this hospital for diagnosis following empirical treatment with benzyl benzoate. Where suspicion has not been well founded and the itching has been due to some other cause, time has been lost in arriving at a diagnosis and the symptom, itching, for which treatment was given, has been worsened. Itching is not synonymous with scabies and scabetic infestation can be found without itching. The acarus is the cause, can be seen, and can be killed.—I am, etc.,

Victoria Infirmary,
Glasgow S.2.
R. W. CARSLAW.

Compulsory Treatment of Addicts

SIR,—I am sorry that Dr. H. D. Beckett (24 June, p. 841) has not had an opportunity of referring to my paper on drugs causing dependence[1] where I originally said that "a kindly compulsion will be the first step in treatment" and later gave it as my opinion that "we must separate the addicted 'pusher' from the non-addicted 'pusher.' The addicted pedlar needs treatment, not punishment. But the non-addicted 'pusher' or pedlar is a criminal; he is the murderer of the soul and the mind."

These are the persons who, in Ohio, have been imprisoned for 20–40 years and it is in Ohio that drug addiction has been almost completely eliminated from the State.

Can Dr. Beckett recommend any better method of controlling drug addiction?—I am, etc.,

Great Shelford,
Nr. Cambridge.
N. C. LENDON.

REFERENCE

[1] Lendon, N. C., *Brit. J. Addict.*, 1965, 61, 115.

Regurgitation during Induction

SIR,—Dr. L. Rendell-Baker (20 May, p. 507) questions the safety of "crash intubation" of the trachea under anaesthesia in the presence of a full stomach compared with the safety of awake intubation in similar circumstances.

There is little doubt that of the many different techniques of "crash intubation" that have been described none can be regarded as completely safe. However, it is probable that much of the danger of such intubation could be eliminated if in all cases where a full stomach is suspected three basic safety procedures were undertaken prior to induction of anaesthesia. Firstly, an adequate oesophageal tube (absolute minimum size—10 E.G./18 F..G) is passed into the stomach, and, immediately preceding induction, the contents of the stomach evacuated as far as is possible. Secondly, the patient is placed on a non-slip mattress on a properly tilting theatre table. Thirdly, efficient suction apparatus with wide-bore tubing (without constrictions) is in action, the sucker end being held by a nurse at the head of the patient.

It would seem that in many centres there is a failure on the part of anaesthetists to carry out the above safety procedures, with the result that death during intubation due to the inhalation of stomach contents still remains a not uncommon occurrence. This failure stems no doubt from a mistaken faith in the absolute safety of some one particular technique of intubation.

In seeking to reduce the mortality due to inhalation of stomach contents there is, however, a fundamental question to be considered, a question that has yet to be fully answered. In anaesthesia in the presence of a full stomach under what circumstances does the act of intubation itself occasion more hazard to the patient than is entailed in carrying out the operation with the patient not intubated?—I am, etc.,

Middlesbrough,
Yorks.
D. DENISON DAVIES.

Mortality of the Ambulance Ride

SIR,—Mr. D. Lamont refers in his letter (6 May, p. 374) to the "mortality of the ambulance ride." This merits consideration in its own right.

One of us accompanied a road-accident case with multiple injuries during his transfer by ambulance to an intensive care unit at another hospital, the patient while in our hospital having been resuscitated twice from cardiac arrest and later from secondary shock. Within one mile the jogging up and down of the ambulance ride caused a recurrence of shock despite continued blood transfusion and intermittent positive-negative pressure respiration with a Manley respirator. The blood pressure dropped from 110 to 90 mm. Hg systolic, and the skin became cold. This state persisted throughout the journey, which took 47 minutes, although the roads were good, the speed limited to 20–30 m.p.h. (32–48 km.p.h.), and stopping and starting eliminated by a police escort. The patient's condition improved soon after arrival in the intensive care unit, where he recovered consciousness, but he developed renal failure from which—together with damage to brain and spinal cord—he died five days later. It is impossible to exonerate the ambulance ride from being an important secondary factor contributing to his death.

The jogging of the ambulance ride caused the patient's body to bounce up and down through a range of about 6 in. (15 cm.). It was clearly due to the design of the ambulance suspension, which has not kept pace with that of private cars. As a shock-producing factor it would have been exaggerated by bad road surfaces; by the centrifugal force of rapid cornering; and by any period of time spent ascending a hill, during which the patient's body would have been subjected to the anti-Trendelenburg position and its well-known ill-effects on the supply of blood to the brain, which would in many cases be sufficient to cause respiratory arrest and death.

It would seem to be possible, from our experience as motorists, to reduce these factors by paying some overdue attention to the design of the suspension. The ambulances based on the Citroën Safari, as used on French and Spanish roads, have an obvious claim to investigation because of their well-known merits on bad as well as good roads. In addition, some means of keeping the body horizontal is essential.

Until the ambulance ride ceases to be an important factor in the causation of essentially avoidable death, no acute hospital should be closed if a longer ambulance journey is entailed for seriously ill or injured patients. The distance between intensive care units must also remain a critical factor. It is clear that any serious attempt to prevent essentially avoidable death must also involve on-the-spot skilled resuscitation of the gravely injured patient before transfer to hospital, as suggested by Mr. Lamont.—We are, etc.,

C. H. CULLEN.
W. KEITH DOUGLAS.
A. M. DANZIGER.

Manchester Victoria
Memorial Jewish Hospital,
Manchester 8.

Oculogyric Crises Due to Phenothiazines

SIR,—I was interested to read Dr. J. R. Harries's letter (22 July, p. 241) in which he reported three of these cases, as a similar type of case was seen at Queen Mary's Hospital, Roehampton, last year, in which the phenothiazine drug was thiethylperazine (Torecan).

In June 1966 a 14-year-old boy was referred to the Department of Oral Surgery at Queen Mary's Hospital, Roehampton, with a provisional diagnosis of recurrent dislocation of the temporomandibular joints. He had started taking thiethylperazine 10 mg. and tablets of tetracycline the previous morning, which had been prescribed for a gastrointestinal upset. After two tablets of each he began to have spasms of his facial and tongue muscles which lasted less than a minute and occurred several times an hour. He continued with the tablets, and when he was seen at Queen Mary's Hospital he had taken about six tablets of thiethylperazine and an equal number of tetracycline tablets. He and his parents were in some doubt as to exactly how many of each tablet he had taken.

By this time the "spasms" were almost continuous. Every few minutes his mouth opened widely and he would protrude his tongue. He had no abnormal eye movements. He was apparently distressed by these attacks and would attempt to close his mouth by pushing against his mandible with both hands. He was admitted to hospital, given no more thiethylperazine or tetracycline, and sedated with phenobarbitone. The muscle spasms stopped within an hour, but oddly enough returned for the duration of his parents' visit later that evening.

The following day he had no attacks and the day after that he was discharged home. As far as is known, he has had no similar attacks since then.

I am grateful to Mr. Rowe, consultant oral surgeon, for permission to report this case.

—I am, etc.,

Westminster Hospital,
London S.W.1.
JAMES McIVOR.

SIR,—I feel that my colleagues might be interested to hear of the dramatic side-effects I have recently found in a patient on a minute dose of trifluoperazine (Stelazine). The symptoms were those of acute Parkinsonism, affecting the jaw, tongue, and eye muscles. The patient had had only three spansules of trifluoperazine 2 mg. b.d. for two days. On the evening of the second day she developed a tremor of the hands and inability to close her mouth, symptoms which gave every appearance of being hysterical, but gradually reached the most painful state of spasm.

I have seen these symptoms on two previous occasions, once with perphenazine (Fentazin), 1 mg. t.d.s., and once with prochlorperazine (Stemetil) 5 mg. t.d.s., side effects occurring dramatically on the second day in all three cases.

I injected pethidine 100 mg. i.m. and quickly drove to the surgery to get some benzhexol (Artane). By the time I returned the spasm had been relaxed by the pethidine, but there was still a degree of oculogyric crisis which improved on orphenadrine hydrochloride (Disipal) t.d.s. over the next 24 hours. As this was a fit young woman with no background of hysteria, I feel it is worth drawing attention to these occasional dramatic side effects.

During six years in a psychiatric unit where patients received doses of over 100 mg. of potent tranquillizers, we never saw a case of such severity. Parkinsonism seemed to manifest itself in pill-rolling movements, excess salivation, and some rigidity of the facies.

These three cases which have occurred in our practice over the past five years have all shown that unless the general practitioner is aware of this problem the patient is treated as a hysteric.—I am, etc.,

Bracknell, Berks. M. R. MEDHURST.

Cervical Cytology

SIR,—Dr. R. D. Last's experience of cervical cancer below the age of 35 years (29 July, p. 311) is by no means isolated.

In this department we accept smears from all women aged 25 years and over. In the first six months of this year we examined approximately 1,000 smears from women aged 25–34 years, nearly all from the antenatal and gynaecology clinics of this group. Among them we found five positive smears confirmed by biopsy, and three more still awaiting confirmation. Assuming that at least two of the latter are proved positive (we have had one false positive in 9,000 smears), we have found at least seven positive smears in 1,000 women, a rate which compares very favourably with the national average.

We have also seen 15 biopsies from cases of clinically invasive cervical cancer in the last three years. Of these, one was aged 35 years, two 34 years, and one 24 years.

These figures surely show the only excuse for discouraging smears from women under 35 years is a lack of trained staff to examine them. This difficulty varies from place to place; and if the local laboratory can take on the work, then the Ministry should be prepared to pay for it.—I am, etc.,

J. A. U. MORGAN.

Department of Pathology,
Hackney Hospital,
London E.9.

SIR,—I read with dismay that the Chairman of Council received the report on the development of the cervical cytology service with satisfaction (8 July, *Supplement*, p. 15). It seems extraordinary to be satisfied with a total number of tests in Great Britain scarcely above the number carried out in British Columbia with its tiny population.

I would like to know who proposed that a test every five years offered safety; that there is magic in the age 35, so that a doctor taking a test at or over this age receives a fee, whereas at 34, 24, or even 18 no fee is payable. Whatever the statistical purist may think the individual woman screened every year or (second best) every two years is protected from cervical cancer. If this is accepted then nothing short of a screening service available for all volunteers should be accepted.

I hope Dr. J. C. Cameron (same report) will keep up the pressure on the Ministry and on regional hospital boards.—I am, etc.,

H. C. MCLAREN.

Queen Elizabeth Hospital,
Birmingham 15.

Another Hardship of Hospital Junior Staff

SIR,—May I, through your columns, attempt to point out some of the hardships caused by hospital appointments being made so soon before the vacancy actually falls?

Let me say at once that I do see the disadvantages of appointing hospital junior staff too far in advance. But against this, surely the difficulties that the unfortunate hospital junior staff inevitably suffer as a result of an "eleventh hour" appointment must be weighed.

Their applications are considered perhaps five to six weeks (or even more) prior to the vacancy. But the actual appointments are often made only about three weeks in advance.

The consequences are obvious: there is very little time to pack up one's belongings, find new accommodation and move (possibly with a wife and family). For a minority too, a move must entail finding a new kindergarten. If one has just vacated a flat, one cannot give the one month's notice as is so often stipulated by landladies, the gas and electricity boards, so that one may be asked to pay one or two weeks' "unnecessary" rent.

If one is moving to a town where difficulties in finding accommodation are anticipated —such as Oxbridge (admittedly perhaps an unfair example, but nevertheless one which will illustrate my point)—is it right that appointments for jobs commencing say on 1 October are not made until the first or second week of September?

No doubt these points have been raised before, but I do regret that the consultants en masse are not more sympathetic to them. —I am, etc.,

Plymouth. MICHAEL COSGROVE.

Without Prejudice

SIR,—May I ask you to convey to Pertinax at this time my personal thanks for all the interest and enjoyment he has given me in reading his weekly articles. I always look forward to the post which brings the *B.M.J.*, whereas previously I never cared. When time is short I read "Without Prejudice" and skip the rest; but in better times I read your excellent leading articles, the correspondence pages, perhaps an original paper, and quite often parts of the *Supplement*, and leave Pertinax's article until the end as a bonne bouche.

I ought also to thank the one, unknown to me, who conceived the idea most brilliantly of asking Pertinax to write for the *B.M.J.* This not only added to the interest but also did something to improve the journal as an instrument of education. Perhaps many other readers might appreciate a few additional articles of this type in the *B.M.J.*, not entirely confined to the serious reporting or discussion of purely medical or scientific topics.

Thanks are also due to the one who returned the "Contents" to its previous place on the front cover page from the midst of the advertising jungle where it hid itself for a time a year or two ago, so that I have been able to turn in a jiffy to the Pertinax column.

It is with great sorrow that I read his last little four-letter word, *Vale*, and with a tear I wish him well.—I am, etc.,

Conway, Caerns. T. V. TATTERSALL.

SIR,—It is with profound sorrow that I note the demise of Pertinax.

Pertinax was the one thing about the *B.M.J.* that reminded me that it was written by men, not machines. Though he chose to hide his identity, he certainly did not hide his personality. Compared with the facelessness of the editorials, he was a miracle of sustained levity and frequent erudition. It was surely no accident that he was to be found in the middle pages of the journal, a slender lifeline against ennui, a balm for the weary. I disagreed with most of what he said, but at least he was human.

His absence may mean that the intellectual tenor of the journal will approach the colour of its cover.—I am, etc.,

London W.C.1. GRAHAM WORRALL.

Points from Letters

Minister's Cambridge Speech

Dr. J. H. SWAN (London W.13) writes: In the Minister of Health's speech at Cambridge, at the end of last month, he declared himself once again "wholly against National Health charges" and that those who suggested them had "simply not thought the arguments through." He continued along the old predictable lines that health charges would encourage private treatment which would promote "two standards of medical care." . . . If the Minister persists in his dangerously dogmatic attitude the inevitable outcome will be what he most fears—a National Health Service which is a poor second to flourishing private practice.

Providing Information

Dr. DAVID CHASTELL (Broadstairs, Kent) writes: An attitude is growing up where some psychiatrists and their social workers are refusing point blank to reveal any information about patients to other doctors, be they consultant or general practitioner. Recently I wrote fully informing a psychiatrist that a patient had moved 100 miles away from him and was under my care. Despite three letters, he refused to supply me with any information whatsoever unless I obtained the patient's signed consent first. To do this would, I thought, have negated any value therefrom.

Surely it is fundamental teaching, in this country, that a patient ought to be treated as a whole and any practice of good medicine must take account of all facets, not just an "arm," "leg," or chest." No surgeon would dream of refusing information about the aetiology of a scar on the "belly." Is it not often more important to know the aetiology of a scar on the mind?

Obituary Notices

Colonel C. H. REINHOLD, M.C., F.R.C.S.ED., I.M.S.(RET.)

Colonel C. H. Reinhold, one of the best known and highly regarded officers of the Indian Medical Service, died peacefully at Haslemere, Surrey, on 22 July, at the age of 86.

Carl Henry Reinhold was born on 4 December 1880, and received his medical education at Guy's Hospital, qualifying with the Conjoint diploma in 1903. After a period of hospital residency he entered the Indian Medical Service by examination in 1905.

His early military years were served with the old Punjab Frontier Force. In 1911, during a period of study leave, he took the F.R.C.S.Ed. During the first world war he served with distinction in France and Mesopotamia, gaining a mention in dispatches and a Military Cross for gallantry in action. On the civil side of the I.M.S. after the war Reinhold gained a high reputation in many major civil surgeoncies as an all-round clinician, operative surgeon, and district medical administrator. He held such key posts as Meerut and Dehra Dun, and, finally, was much in the public eye as chief medical officer and civil surgeon of New Delhi. On promotion to the rank of colonel he was appointed inspector-general of civil hospitals of the Punjab, retiring in 1937 on account of age. After retirement he served as station medical officer with the R.A.F. at Odiham, and during the second world war was medical officer to the Bank of England at Whitchurch. He later joined the medical board staff of the Ministry of Pensions.

Throughout his service Reinhold was held in high respect by a host of patients and by his brother officers, who, only a few years ago, invited him to preside over the annual service dinner.

Reinhold married in 1918. His wife died three years ago. There were three sons of the marriage, one of whom, trained at Guy's Hospital, died in an accident in America, and one died in infancy. To the surviving son—himself a former Indian Army officer—and grandchildren we extend our sympathy.—G. R. McR.

S. C. GHOSH, M.B., B.S., F.R.C.S.

Mr. S. C. Ghosh, consultant ear, nose, and throat surgeon to the West Bromwich and the Lichfield, Sutton, and Tamworth groups of hospitals, died suddenly at his home in Sutton Coldfield on 25 June.

Saral Chandra Ghosh was born in India, and he received his medical education at Lucknow University, graduating M.B., B.S. in 1930. He came to London in the early 1930s, and worked for a time at the Institute of Laryngology and Otology before moving to Birmingham in 1936, where he was appointed registrar at the Birmingham and Midland Ear and Throat Hospital. In 1940 he was appointed resident surgical officer at the West Bromwich and District General Hospital, where he obtained a wide experience in general surgery. He returned to ear, nose, and throat surgery in 1943, and joined the school health service. He was assistant ear, nose, and throat surgeon to the Birmingham Children's Hospital from 1944 to 1945, when he joined the staff of the Tamworth General Hospital, and the following year was elected to the senior staff. With the advent of the National Health Service in 1948 he became consultant ear, nose, and throat surgeon to the West Bromwich and district hospital group, and to the Lichfield, Sutton, and Tamworth hospital group. He obtained the F.R.C.S. in 1954, and in 1961 was appointed surgeon to the Good Hope General Hospital at Sutton Coldfield.

J. A. writes: Saral Ghosh was interested in all branches of ear, nose, and throat surgery, and only twelve months ago attended a course in Holland on reconstruction surgery of the nasal pyramid. He was obviously delighted to find yet another new field in his specialty, and talked enthusiastically about cases which he had treated. He was, however, particularly interested in neck surgery, and travelled widely, visiting clinics on the Continent and in Scandinavia. He was a scrupulous, painstaking, and neat surgeon, who developed his own techniques, and gladly demonstrated them to anyone who came to watch him work. Saral Ghosh was a shy, retiring, modest man, with little time or interest for medical politics. He devoted all his energies to the care of his patients. His sincerity, charm, and characteristic boyish smile made him many lasting friends, and he will be greatly missed. He leaves a widow and three sons, and we extend to them our deepest sympathy.

L. R. J. writes: Saral Chandra Ghosh was a man of philosophical disposition, shunning controversy, and of a shy nature. He was a genial man and a kindly friend, devoted to his wife and family, and had a wide range of interests which included Freemasonry. He liked working with his hands, as evidenced by his careful surgery, and he even went to evening classes to learn carpentry. He enjoyed tinkering with cars and was a keen gardener, and he also appreciated music, in particular the Indian classics.

C. E. COBB, M.B., B.S., D.T.M.

Dr. C. E. Cobb, formerly in general practice in Basingstoke, Hants, died on 17 July. He was 72.

Charles Eric Cobb was born on 1 May 1895, and was educated at Dulwich College and St. Thomas's Hospital, London. His education was interrupted by the first world war, and he served as surgeon sub-lieutenant, R.N.V.R., from July to December of 1916, when he was temporarily demobilized and returned to complete his medical studies. As a fourth-year medical student he was selected to hold the responsible post of a resident physician at the London Fever Hospital. On qualifying with the Conjoint diploma in 1918 he was appointed casualty officer and resident anaesthetist at St. Thomas's Hospital before returning to active service as a temporary surgeon-lieutenant, R.N. After demobilization in 1919 he joined the Malayan Medical Service, later becoming senior medical officer for the State of Pahang. He took the D.T.M. in 1920 and graduated M.B., B.S. in 1924. He returned from Malaya in 1931, and in 1932 entered general practice in Basingstoke, where he remained for some thirty years. An active member of the British Medical Association, he was a representative at the Annual Meetings from 1945 to 1947, and chairman of the Aldershot and Basingstoke Division from 1945 to 1948. After his retirement from general practice he continued for a time in ophthalmic medical practice until forced by ill-health to give it up.

Charles Cobb was a much liked and popular person, both as a student and naval surgeon and as a doctor in Malaya and among his many patients and friends in Basingstoke and the adjoining village of Sherborne St. John, where he lived after retirement. He leaves a widow, three daughters, and a son, who is a senior registrar in the ophthalmic department at St. Thomas's Hospital, to all of whom we extend our sympathy.—E. J. S. B.

S. C. BARNES, M.B., CH.B.

Dr. S. C. Barnes, a general practitioner in Wirral, Cheshire, died in hospital on 19 February after a short illness. He was 73.

Samuel Crossley Barnes was born in Lowbands, Gloucestershire, on 28 August 1893. He served in the R.A.M.C. during the first world war, but after demobilization he was unable to embark upon his medical career owing to heavy family responsibilities. His was, indeed, a remarkable achievement, as the opportunity to enter medical school did not arise until he had reached the age of 40 years. He entered Liverpool University, graduating M.B., Ch.B. in 1940, at the beginning of the second world war. After serving as house-surgeon at Birkenhead General Hospital, he entered a busy practice in the Wirral. He was actively engaged as a major in the Home Guard during this time. After a short spell in general practice in Formby, Lancashire, Dr. Barnes returned to the Wirral in 1946, and for the next twenty years he devoted his whole life to his patients. He was an excellent clinician and obstetrician, and his standards of medicine were of the highest order, a fact which was recognized when, in December 1950, he was invited to join the Cohen Committee on general practice, on which he served during the next two and a half years.

Dr. Barnes was an idealist who did not spare himself in the interest of his patients.

His capacity for work was prodigious. On one occasion, during a severe influenza epidemic, he worked for three days and nights without any sleep, at the same time more ill than many of his patients. He sacrificed his leisure and in the end his own health, despite much advice to take things more easily, and he continued to work up to a few days before his death. His care of his patients did not end with medicine, and he would spare no effort to help anyone who had genuine problems. Dr. Barnes had a deep interest in the arts, and was widely read. His favourite relaxation was music and he was an accomplished pianist.

Affectionately known as "Sammy," his passing is mourned by many hundreds of his patients. To his widow we offer our deepest sympathy. Her sacrifice and her devotion to his practice enabled Dr. Barnes to succeed in the calling he had longed to serve.—W. G. R.

J. L. BROWN, M.B., B.CH., B.A.O.

Dr. J. L. Brown, a former general practitioner in Birmingham, died in Selly Oak Hospital on 22 July after a brief illness. He was 79.

John Laird Brown was born near Londonderry in 1888, and was educated at the Royal School, Raphoe, University College, Galway, and Queen's University, Belfast, graduating M.B., B.Ch., B.A.O., in 1912. He entered general practice in South Wales, and in 1921 joined his brother, Dr. J. A. Brown, in Stirchley, Birmingham. Over the years he earned the esteem and lasting affection of the patients of his large practice, from which he retired about two years ago.

John Brown was a kindly and genial man, with an outstanding sense of humour, and a great natural aptitude for making friends. The passing of this notable personality will be deeply regretted, not only by his medical colleagues in Birmingham, but by a host of non-medical friends within and beyond the bounds of the city. In the Midlands he was widely known in golfing circles. He had been president of the King's Norton golf club since 1945, having formerly captained the club and acted for a time as its secretary. He was a past-president of the Midland Counties golf association, and a vice-president of the Worcestershire professional golfers association. A staunch Ulsterman, he was a founder member and a past-president of the Birmingham and District Ulster Association. In addition to golf, the cultivation of roses was one of his hobbies, and from this, being the expert he was, he derived great enjoyment and satisfaction.

Dr. Brown's wife, who had been a wonderful partner in their married life, died in 1952. He leaves a married daughter and two sons, the elder of whom is in practice in Malvern ; the wife of the younger son is also a doctor, in medical practice in Birmingham. The sympathy of all his many friends and colleagues will go out to them.—H. C.

H. F. G. HENSEL, M.R.C.S., L.R.C.P.

Dr. H. F. G. Hensel, general practitioner of Milton Abbas, Dorset, died in hospital on 13 July. He was 62.

Henry Frederick George Hensel was born in London on 24 November 1904. He received his education in Birmingham, and later at Nottingham University, where he read botany and pharmacy, becoming a member of the Pharmaceutical Society. After a short time in business he began his medical studies at the London Hospital, qualifying with the Conjoint diploma in 1935. After holding house appointments at the London Hospital and the Poplar Hospital for Accidents he went to Kashmir under the auspices of the Church Missionary Society, working with Sir Henry Holland in Quetta. While in Kashmir he met and married Elizabeth Davis, a King's College Hospital nurse, the elder daughter of the late Mr. William Davis, of Newbury, Berks. His career in Kashmir was cut short by a serious illness which led to his being invalided home in 1939. In 1940 he settled in Milton Abbas with his family and began his career as a country practitioner, which he was to carry on until the time of his death. In addition to his general practice he was also medical officer at Bryanston and Milton Abbey schools, and was a member of the Medical Officers of Schools Association, as well as being a founder member of the College of General Practitioners.

Henry Hensel was a good doctor, and a gentleman in the true sense of that word. His patients became his friends, and he showed equal care and courtesy to gipsies and gentry alike. Quiet and reserved, he was none the less ready to speak out on issues he felt strongly about. His philosophy of life was based on a practical Christian faith, and, although he did not often air his religious views, he averred even in his last illness that it really did work. His main leisure activities were in the garden he created in Milton Abbas, with its fine collection of rare trees and flowering shrubs, which he delighted to show his friends and visitors. He was a keen botanist, and no mean painter in oils.

He will be greatly missed, not only by his family and partners, but also by his wide circle of friends and by the village community in which he lived, and worked, and worshipped. He is survived by his wife and four children, two of whom are doctors. To all of them we extend our deepest sympathy. —C. E. L.

A. H. SHELSWELL, V.R.D., M.R.C.S. L.R.C.P.

Dr. A. H. Shelswell, formerly a general practitioner in Mitcham, Surrey, and of the fourth generation of doctors in his family, died suddenly in retirement at Marnhull, Dorset, on 1 June at the age of 71.

Arthur Hugh Shelswell, son of Dr. O. B. Shelswell, was born on 7 January 1896. Educated at King's School, Canterbury, and at Guy's Hospital, he interrupted his medical education in the first world war to serve in the Royal Navy as a surgeon probationer. He returned to Guy's after demobilization, and qualified with the Conjoint diploma in 1921. After serving as house-surgeon and house-physician at his hospital he took over his father's practice in Mitcham. When the Wilson Hospital, Mitcham, was opened in 1928 he was one of the original members of the medical staff, and served the hospital loyally until he was called up in 1939. He then served throughout the second world war, and for the last two years he was principal medical officer in H.M.S. *Queen Elizabeth*, with the rank of surgeon-commander. After demobilization he returned to Mitcham, where he continued in general practice until July 1958, finding conditions somewhat different from those he had known.

Dr. Shelswell was a keen rugby player, and played for his school, for Guy's Hospital, and for the Barbarians. As a fellow general practitioner, and one of the early medical officers to the Wilson Hospital, I got to know Hugh Shelswell very well. He was honest, kind, and understanding, and incapable of a mean action. He did not appear to be too happy in the National Health Service, and after 10 years he retired. In 1923 he married Eileen Crampton, a doctor's daughter. They were a very devoted couple. She died in March of this year, and there is no doubt that her loss hastened his end.

Our sympathies go to his two daughters, who have lost both parents in such a short space of time.—I. E.

W. LUMLEY, T.D., L.R.C.P.&S.I., L.M.

Dr. W. Lumley, formerly in general practice in Preston, Lancashire, died on 17 July at Stratford-on-Avon. He was 78.

William Lumley was born in Ireland on 28 June 1889, and received his medical education in Dublin, qualifying with the joint diploma of the Royal College of Physicians and the Royal College of Surgeons in Ireland in 1914. During the first world war he served with the R.A.M.C., mainly on ambulance trains and in ships. After demobilization with the rank of captain he became medical officer on the Peking–Mukden railway from 1920 to 1925. On his return to England he set up in general practice at Preston as partner to the late Dr. Stuart Holden. Between the two world wars he joined the 88th Brigade of the Royal Field Artillery, Territorial Army, in which he held the rank of major, and received the Territorial Decoration. He went to France with the battery at the outbreak of the second world war, but was invalided in 1940, and returned to Preston until his early retirement on account of ill-health.

He married Miss Ethel Henley, at one time matron of the Kilkenny Hospital in Ireland, who predeceased him many years ago. He is survived by his only daughter, Maureen Lumley, a matron in the R.A.F. nursing service, and by two sons.—E. A. L.

A. R. W. writes: Bill retired early on account of ill-health, and returned to Ireland to stay with his aged mother, making frequent returns to Preston to see old friends. Bill was a lovable character, with all the Irishman's pawky humour and wit ; sometimes outspoken, and landing himself (temporarily) in hot water, but leaving no rancour.

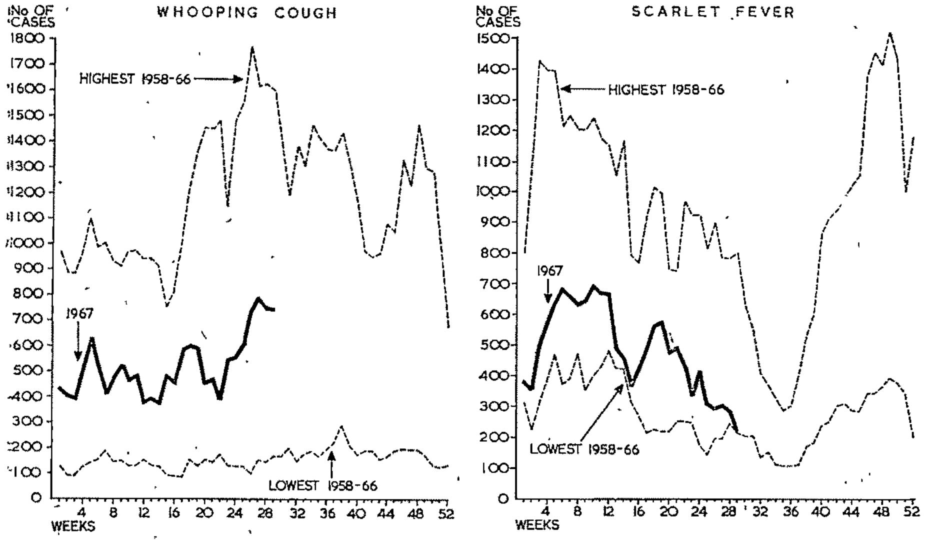
A memorial service for Sir Eardley Lancelot Holland will be held at Chichester Cathedral, at 2.30 p.m., on 16 August.

News and Notes

EPIDEMIOLOGY

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of whooping-cough and scarlet fever in England and Wales. Figures for 1967 are compared with the highest and lowest figures for each week in the previous years shown.



Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available.

	Week Ending 21 July	Week Ending 28 July
Dysentery		
Greater London	58	**77**
Ealing	12	**11**
Wandsworth	4	**10**
Staffordshire	11	**16**
Aldridge–Brownhills U.D.	0	**12**
Warwickshire	21	**25**
Coventry C.B. ...	4	**13**
Yorkshire West Riding ...	49	**35**
Bradford C.B.	11	**12**
Leeds C.B.	19	**12**
Edinburgh	24	**38**
Glasgow	25	**27**
Food-poisoning		
Kent	1	**25**
Lydd M.B.	0	**15**

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **22 July** (No. 29) and corresponding week 1966.

Figures of *cases* are for the countries shown and for Greater London. Figures of *deaths* and *births* are for the whole of England and Wales (London included), Greater London, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0		3	0	0	0	
Dysentery ..	336	58	75	3	1	501	106	54	12	4
Encephalitis, acute ..	11	0		0		3	0		0	
Enteric fever: Typhoid ..	2	0	1	0		3	0	0	1	
Paratyphoid...	1	0	0	0		2	0	0	0	
Food-poisoning	175	35	13	1		144	33	12	5	
Infective enteritis or diarrhoea under 2 years				33	29				17	41
Measles* ..	5,106	281	20	123	178	8,398	812	101	118	221
Meningococcal infection ..	7	0	2	0		4	0	4	1	
Ophthalmia .. neonatorum	13	2	1	0		21	1	0	0	
Pneumonia† ..	82	4	54	2	1	48	9	66	1	
Poliomyelitis, acute: .. Paralytic ..	1	0	0	0		0	0	0	0	
Non-paralytic	0	0	0			0	0	0		
Puerperal fever§	89	27	4	0		83	31	0	0	
Scarlet fever ..	222	32	15	6	7	345	55	13	3	8
Tuberculosis: Respiratory	223	43	34	5		237	64	30	3	
Non-respiratory ..	58	9	8	0		54	8	11	1	
Whooping-cough	745	123	35	9	49	370	54	25	5	15

DEATHS	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0		0	0	0	0		0	0	0
Dysentery ..	1	0		0		1	0		0	
Encephalitis, acute.. ..					0					0
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	5	0	0	0	1	3	1	0	2	1
Influenza ..	3	0	0	0	0	3	0	0	0	0
Measles ..	0		0	0	0	0		0	0	0
Meningococcal infection ..			0					0		
Pneumonia ..	580	100	13	16	4	459	73	16	16	2
Poliomyelitis, acute.. ..	0	0		0	0	0	0		0	0
Scarlet fever ..	0		0	0	0	0		0	0	0
Tuberculosis: Respiratory ..	30	6	3	0	0	28	6	7	0	0
Non-respiratory ..				0	1				0	0
Whooping-cough	1	0	1	0	0	0	0	0	0	0
Deaths 0–1 year	274	32	13	5	6	280	50	23	5	7
Deaths (excluding stillbirths)	9,059	1407	477	106	159	8,891	1385	507	110	129
LIVE BIRTHS	16,082	2679	924	289	551	16,162	2700	823	332	400
STILLBIRTHS	227	30	13			261	32	16		

* Measles not notifiable in Scotland, whence returns are approximate. † Includes primary and influenzal pneumonia. § Includes puerperal pyrexia.

MEDICO-LEGAL

Antibiotic in Cow's Milk

[FROM OUR LEGAL CORRESPONDENT]

When milk is sold containing an antibiotic it is no defence to a prosecution under the Food and Drugs Act, 1955, that the milk was sold in the same state as it came from the cow.

This is the effect of a ruling of the Divisional Court of the Queen's Bench Division on an appeal by a public health inspector against dismissal by the magistrates at Oswestry of a summons alleging that Central Dairies, Newton, Montgomeryshire, had supplied milk to a retailer which was not of the substance required. Penicillin had been found in two pints of milk. (*Birmingham Post*, 7 July).

The case was remitted to the magistrates for further hearing. In accordance with their rights under the Act, the dairy firm had brought in the Milk Marketing Board, their suppliers, as third parties. The magistrates will have to determine whether primary responsibility for testing milk for antibiotics lies with the Milk Marketing Board or with wholesalers.

Endowment for Private Beds

[FROM OUR LEGAL CORRESPONDENT]

The Court of Appeal has held[1] to be valid a bequest of £35,000 to Barnet Group Hospital Management Committee made on terms that half the fund shall be applied in endowing beds for paying patients in Finchley Memorial Hospital.

As the evidence was that the hospital had 20 paying beds and did not require any more, Mr. Justice Cross in the court below had held that so far as the gift related to the endowment of beds it was invalid. But the Court of Appeal held that "endowment of beds" went beyond the mere physical provision of beds and the buildings to put them in: the phrase included the provision of better beds, bedding, furnishings, decoration and soundproofing of rooms, the provision of telephones and television, sitting- and dining-rooms, and better food. All these purposes were charitable purposes for the benefit of infirm paying patients, and the bequest was valid. The appeal of the Barnet Group Hospital Management Committee was allowed.

---

[1] *The Times*, 7 July 1967.

MEDICAL NEWS

Peerage for Hospital Chairman

LADY PATRICIA LLEWELYN-DAVIES, Chairman of the Hospital for Sick Children, Great Ormond Street, London, has been made a life peer. Her parliamentary career began in 1950 when she resigned from the Civil Service to become prospective Labour candidate for Wolverhampton, South-west, in 1951. Since then she has contested Wandsworth, Central (1955 and 1959). She was educated at Liverpool College, Huyton, and Girton College, Cambridge. Her husband, LORD LLEWELYN-DAVIES, who is professor of architecture at University College, London, was made a life peer in 1963.

[Universal Pictorial Press

University of the West Indies

Professor D. B. JELLIFFE, director of the Caribbean Food and Nutrition Institute, University of the West Indies, has been appointed honorary professor of community nutrition at the university. Professor Jelliffe qualified from Middlesex Hospital in 1943. After a period in the Sudan Medical Service, he held lectureships in paediatrics at the University College, Ibadan, and in Jamaica. In 1954 he became W.H.O. professor in paediatrics at the All-India Institute of Hygiene and Public Health in Calcutta. He was then appointed visiting professor of tropical medicine at Tulane University, New Orleans. From 1959 to 1967 he held the Unicef chair of paediatrics and child health at Makerere Medical School, Kampala. Professor Jelliffe was elected F.R.C.P.(Lond.) in 1961. He is a member of the W.H.O. expert panel on nutrition. His latest monograph, *The Assessment of the Nutritional Status of the Community*, was published last year.

New Chair at Keppel Street

Dr. R. F. L. LOGAN, reader in social medicine at Manchester University, has been appointed to the Chair of Organization of Medical Care at the London School of Hygiene and Tropical Medicine from 1 October.

Dr. Logan, who is 49, graduated M.B. with honours at Queen's University, Belfast, in 1940. After house appointments in Southampton and Salford he served with the Royal Netherlands Marine. In 1947 as a Nuffield Fellow in industrial medicine he studied adolescent workers with the M.R.C. social medicine research unit under Professor J. N. MORRIS. The same year he took the D.I.H., M.R.C.P., and M.D.(Belf.). In 1950 he organized the university health service in Manchester as lecturer in occupational health. He was awarded a Rockefeller travelling fellowship in 1955 and visited the U.S.A. and Canada. Returning to Manchester, he took up his present readership in social medicine in charge of teaching in the Darbishire House experiment. Since 1963 he has been director of the first medical care research unit and consultant to the World Health Organization. He is joint author of *The Demand for Medical Care*.

M.R.C. Advisory Boards

The Medical Research Council has made the following appointments to its advisory boards as from 1 October: *Biological Research Board*, Professor A. S. V. BURGEN, F.R.S. (Department of Pharmacology, Cambridge University); Professor K. BURTON (Department of Biochemistry, University of Newcastle upon Tyne); Professor P. M. B. WALKER (Department of Zoology, Edinburgh University). Professor J. L. GOWANS, F.R.S. (Sir William Dunn School of Pathology, Oxford), already a member of the board, will succeed Professor W. D. M. PATON, F.R.S., as chairman. *Clinical Research Board*, Professor A. W. KAY (Regius Professor of Surgery, Glasgow University). *Tropical Medicine Research Board*, Professor W. MELVILLE ARNOTT (Department of Medicine, Birmingham University); Dr. D. J. LEWIS (M.R.C. External Scientific Staff, British Museum (Natural History)).

Advice on Hospital Scientific Services

A committee to advise on hospital scientific and technical services in Great Britain has been set up by the MINISTER OF HEALTH and the SECRETARY OF STATE FOR SCOTLAND. Its terms of reference are: "To consider the future organization and development of hospital scientific and technical services in National Health Service hospitals and the broad pattern of staffing required and to make recommendations." The chairman will be: Sir SOLLY ZUCKERMAN, Chief Scientific Adviser to the Cabinet Office. Other members are: Professor A. R. CURRIE, Regius Professor of Pathology, Aberdeen University; Dr. R. GADDIE, Chief Biochemist, the General Hospital, Birmingham; Professor J. E. ROBERTS, Middlesex Hospital, Professor of Physics, London University; Mr. A. B. SCOTT, Secretary, United Manchester Hospitals Board of Governors; Professor J. P. SHILLINGFORD, Hammersmith Hospital, Consultant Physician, and Director, Medical Research Council's cardiovascular research unit; and Dr. S. SHONE, Senior Administrative Medical Officer, Sheffield Regional Hospital Board. The secretary of the committee will be Mr. R. P. S. HUGHES, of the Ministry of Health.

Family Planning Services

The Minister of Health, Mr. KENNETH ROBINSON, has drawn the attention of local health authorities in England and Wales to the National Health Service (Family Planning) Act, which came into force on 28 June (see *B.M.J.*, 6 May, p. 385). He has asked them to review their family-planning arrangements, including the giving of information by health visitors and others in the course of their daily work.

A.M.A. Policy on Abortion

The A.M.A. House of Delegates, at its meeting in June, adopted a statement opposing induced abortions except when:

> "(1) There is documented medical evidence that continuance of the pregnancy may threaten the health or life of the mother, or
>
> "(2) there is documented medical evidence that the infant may be born with incapacitating physical deformity or mental deficiency, or
>
> "(3) there is documented medical evidence that continuance of a pregnancy resulting from legally established statutory or forcible rape or incest may constitute a threat to the mental or physical health of the patient;
>
> "(4) two other physicians chosen because of their recognized professional competence have examined the patient and have concurred in writing; and
>
> "(5) the procedure is performed in a hospital accredited by the Joint Commission on Accreditation of Hospitals."

In adopting the statement, the House recognized that there are many physicians who on moral or religious grounds oppose therapeutic abortion in any circumstances.

Emergency Bed Service

In the year 1966–7 applications for admission to hospital totalled 53,311, compared with 59,496 the previous year. These figures are given in the annual report, which contains a reminder that cases can be accepted by the service only when the patient has been seen by a doctor within the last 24 hours.

British Heart Foundation

Research grants, totally about £77,000, are announced by the British Heart Foundation. They are as follows:

Physiology and Biochemistry of the Heart and Circulation: Professor C. W. M. Adams, Guy's Hospital Medical School, London, £6,875; Dr. G. de J. Lee, Radcliffe Infirmary, Oxford, £11,260; Professor R. J. Linden, Leeds University, £9,050; Dr. G. Manley, Radcliffe Infirmary, Oxford, £1,615; Dr. E. N. O'Brien, Institute of Diseases of the Chest, Brompton Hospital, London, £2,400; Professor A. G. Shaper, Makerere University College, Kampala, Uganda, £2,200; Dr. E. A. Wren, Birmingham University, £382.

Pathology of the Heart: Dr. G. Williams, Manchester University, £3,000.

Fundamental Research on Structure and Function of the Heart: Professor R. Walmsley, St. Andrews University, £4,000.

Pulmonary Heart Disease: Professor J. M. Bishop, Queen Elizabeth Hospital, Birmingham, £7,385.

Surgical Treatment of Coronary Arterial Disease: Mr. J. S. Bailey, Westminster Hospital, London, £2,500.

Development of Artificial Heart Valves: Mr. L. D. Abrams, Queen Elizabeth Hospital, Birmingham £2,500.

New Techniques for Diagnosis and Treatment: Dr. A. Guz, Charing Cross Hospital, London, £6,400; Professor R. E. Steiner, Royal Postgraduate Medical School, London, £3,845.

Problems of Replacement Surgery: Mr. D. Longmore, National Heart Hospital, London, £4,000; Mr. A. E. Thompson and Mr. D. N. Ross, St. Mary's and National Heart Hospitals, London, £4,500; Sir Thomas Holmes Sellors, Mr. D. N. Ross, and Mr. D. B. Longmore, National Heart and Guy's Hospitals, London, £5,000.

Heart Disease in a Tropical Environment: Professor K. L. Stuart, University of the West Indies, Jamaica, £656.

Research workers seeking support for programmes of original investigation are invited to write for an application form to the Administrative Medical Director, British Heart Foundation, Tavistock House North, Tavistock Square, London W.C.1. The closing date for applications is 6 October.

Cambridge Student Health Association

The objects of the Cambridge Student Health Association, which has recently been formed, include the sponsoring of student health education and of research into student health. Dr. BRIAN DAVY is president and Dr. A. A. CRAIGEN is secretary of the association.

U.K. Branch of P.M.A.

At a meeting of Pakistani doctors in London on 15 July at B.M.A. House it was resolved to form a branch of the Pakistan Medical Association in the United Kingdom. The chairman of the organizing committee is Dr. M. A. QADEER KHAN, 18 Leinster Square, London W.2.

People in the News

▶ Professor D. WHITTERIDGE, F.R.S., professor of physiology at Edinburgh University, is to visit the Vallabhbhai Patel Chest Institute, University of Delhi, India, under the Royal Society visiting professorships scheme.

Coming Events

International Union Against Tuberculosis and Royal Netherlands Tuberculosis Association.—International Tuberculosis Conference, 3–7 October, Amsterdam. Details from Conference Secretariat, K.N.C.V., P.O.B. 146, The Hague, Netherlands.

Societies and Lectures

For attending lectures marked ● a fee is charged or a ticket is required. Applications should be made first to the institution concerned.

Wednesday, 16 August

STOKE MANDEVILLE HOSPITAL.—(1) 12.15 p.m., Dr. A. S. Hall: clinical cases. (2) 6 p.m., Dr. M. Mayne: case demonstration.

Friday, 18 August

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. K. M. Citron: clinical demonstration.

Universities and Colleges

ROYAL COLLEGE OF SURGEONS OF ENGLAND

At a meeting of the council held on 3 August, with Sir Hedley Atkins, president, in the chair, Sir Miles Clifford, K.B.E., was admitted to the Honorary Fellowship of the College.

The re-election of Mr. Terence Ward as dean of the Faculty of Dental Surgery and the election of Mr. Norman Rowe as vice-dean of the Faculty was reported.

Mr. R. E. Horton, of the United Bristol Hospitals, Mr. F. G. Smiddy, of Leeds General Infirmary, and Mr. R. H. Livingston, of the Royal Victoria Hospital, Belfast, were admitted as members of the Court of Examiners.

Dr. J. R. Batchelor, of Guy's Hospital, was admitted honorary research professor in the College in respect of his appointment as director of the McIndoe memorial research unit, Queen Victoria Hospital, East Grinstead.

The Lady Cade medal for 1966 was awarded to Air Vice-Marshal G. H. Morley.

A Moynihan lectureship was awarded to Professor W. G. Bigelow, of Toronto.

The appointment of Sir Thomas Holmes Sellors as Tudor Edwards memorial lecturer for 1968 was reported.

The Hallett prize was presented to Dr. A. L. G. Peel, of the University of Cambridge.

Handcock prizes were awarded to P. J. Leopard, of Guy's Hospital Medical School, and to R. T. Watson, of St. Thomas's Hospital Medical School (Macloghlin Scholar in 1961).

A diploma of membership was granted to M. H. Mehta.

Deaths

Harwood-Yarred.—On 22 July 1967, at St. Thomas's Hospital, London, William Henry Harwood-Yarred, M.B., aged 90.

Correction

In the leading article "Changed Character of Osteomyelitis" (29 July, p. 255), in the first reference the second author's name should read "CAHEN, I.," and in the second reference the second author's name should read "KIRKALDY-WILLIS, W. H."

New Issues of Specialist Journals

Obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London W.C.1.

BRITISH JOURNAL OF OPHTHALMOLOGY

Contents of the August issue are as follows:

Ciliary Artery Involvement in Giant Cell Arteritis. P. A. MacFaul.
Occult Temporal Arteritis. J. F. Cullen.
Papilloedema in Sarcoidosis. D. Geraint James, M. A. Zatouroff, Joan Trowell, and F. Clifford Rose.
Complicated Cataract Extraction in Fuchs's Heterochromic Uveitis. D. M. Ward and C. T. Hart.
A Method of Trabeculotomy. I. M. Strachan.
Thyroid Disease and Glaucoma. H. Cheng and E. S. Perkins.
Examination for Posterior Subcapsular Cataracts in Patients Treated with Topical Steroids. John Williamson and M. J. Jasani.
Ocular Tension and Diabetes Mellitus. James L. K. Bankes.
Occlusion of a Pre-retinal Arterial Loop. R. B. Harcourt and N. A. Locket.
Orbital Foreign Body Simulating a Malignant Melanoma. C. N. Banks.
Ophthalmological Synopses.
Fixation Device for Central Field Examination. H. M. Symons.
Stand for Applanation Tonometer Prisms. J D. Abrams.
Reviews. Notes.

Volume 51, No. 8. Yearly subscription (12 numbers) inland £8 8s., overseas £9. With *Ophthalmic Literature* and Index (7 numbers) inland £15, overseas £16.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON W.C.1. TELEPHONE: 01-387 4499. TELEGRAMS: *Aitiology, London W.C.1.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs.

ADVERTISEMENT AND SUBSCRIPTION ORDERS should be addressed to The Manager at B.M.A. House, London, or at 415 Bourke Street, Melbourne, Victoria, Australia.

MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the British Medical Association, B.M.A. House, London, or to the Scottish Secretary, B.M.A. Scottish Office, Drumsheugh Gardens, Edinburgh.

BRITISH MEDICAL JOURNAL

LONDON SATURDAY 19 AUGUST 1967

Pointers

Kwashiorkor: Added iron and high protein diet are valuable aids to recovery, according to Dr. E. B. Adams and colleagues, from Durban (p. 451). Drs. G. C. Cook and M. S. R. Hutt, from Kampala, Uganda, found no evidence that liver disease develops after recovery from treated kwashiorkor in Uganda (p. 454). Leader at p. 446.

Enteropathy in Psoriasis: Professor Sam Shuster and colleagues found the incidence and degree of steatorrhoea were related to the extent of skin involvement (p. 458).

Chronic Bronchitis: Acute exacerbations were related to rhinovirus infection in 14% of Dr. A. C. Stenhouse's cases (p. 461).

Chronic Onychomycosis: Dr. R. R. Davies and colleagues found griseofulvin effective particularly in the finger-nails, and there was no evidence that drug resistance develops (p. 464).

Hypercalciuria: Related to dietary intake according to Dr. M. Peacock and colleagues (p. 469).

Leptospirosis: Major B. Simpson and colleagues found long-term prognosis after acute renal lesions to be good (p. 472).

Intrinsic Factor Secretion: Medical vagotomy did not affect histamine-stimulated output while surgical vagotomy reduced both this and basal output in Dr. J. F. Adams and colleagues' patients (p. 473).

Triploid Chromosome: Hydatidiform mole and coexistent foetus both with this constitution (p. 476).

Autoimmune Disease: Dr. G. L. Asherson's concluding article (p. 479).

Plus ça change: Account of International Congress of Medicine in 1867 by Professor W. H. McMenemey (p. 487).

Is There an Alternative? Mr. A. McWilliam discusses the quinquennial system of financing universities from State funds (p. 489).

Dialysis and Transplantation: Current work reported at Paris Conference (p. 491).

Clamp Like Fingers: Professor R. Y. Calne describes atraumatic clamp for controlling vessels with finger pressure (p. 492).

Pregnancy Tests: To be accepted on request from general practitioners (p. 504). Leader at p. 448.

Negotiations with the Minister: Hospital staffs' work load, research, and mileage allowance are discussed in Joint Second Report (*Supplement*, p. 119).

Accuracy of Mortality Statistics

It is sometimes forgotten that the elaborate mortality statistics published annually by the Registrar General (the latest report[1] runs to nearly 450 pages) depend for the most part on what medical practitioners write on death certificates. Inaccuracy at this stage is inevitably reflected in the final tabulations. From time to time doubts are expressed about the reliability of this information, and interest in the subject has recently been stimulated by the publication of a report from the General Register Office[2] already briefly described.[3]

The clinical staff of 75 selected hospitals were asked to complete dummy death certificates in respect of all patients who died during a six-month period in 1959. Each certificate was completed before the necropsy findings were known, and the stated cause of death was then compared with the pathologist's opinion based on the clinical notes and the post mortem result.

Disagreement was noted in rather more than half the cases, and even when clinicians were "fairly certain" of the cause of death there was disagreement in 44%. According to the pathologists, the clinicians failed to record more than half the biliary cancers, at least a third of the cases of tuberculosis, bronchitis, bronchiectasis, and lymphosarcoma, and nearly a fifth of the lung cancers and peptic ulcers. On the other hand, a substantial proportion of the deaths ascribed by the clinicians to cerebral haemorrhage, cerebral embolism and thrombosis, pneumonia, and diabetes were considered by the pathologists to be due to other causes.

Some caution is needed in using these results to judge the reliability of national mortality statistics. The conditions of the investigation were unusual in that clinicians did not have the help of the necropsy findings which they normally have in about a quarter of the deaths they certify. Furthermore, patients who die in hospital probably present greater problems in diagnosis than do those who die at home. Also relevant is the fact that coroners certify an appreciable proportion of deaths (17% in 1963) and rarely do so without seeking a pathologist's opinion. On the other hand, about half of all deaths occur at home and are certified by medical practitioners who rarely have the advantage of post mortem reports. With all these points in mind it seems fair to conclude that the number of deaths for which the cause is not accurately determined is far from negligible.

Mistakes in diagnosis, however, are not the only cause of inaccuracy of death certificates. In a recent paper,[4] based on the 1,216 deaths which occurred in 1962 in the area of the Oxford Record Linkage Study, M. R. Alderson and T. W. Meade examined the extent of agreement between the principal condition treated in hospital (recorded usually by hospital registrars) and the certified cause of death (usually completed by house-officers). A substantial discrepancy between the two diagnoses was found in 39% of the cases. The authors therefore examined the hospital notes of a random sample of 105 cases. They considered that the principal

© *British Medical Journal*, 1967. All reproduction rights reserved.

condition treated was wrongly stated in 14 and that the certified cause of death was incorrect in 23. Most of the errors were due to failure to distinguish between the main disease and the complications of the disease or incidental conditions.

Even when an accurate diagnosis has been made and has been correctly recorded on the death certificate, difficulty may still arise in the coding of the cause of death. This may lead to serious discrepancies, particularly when international comparisons of mortality rates are attempted. Some idea of the extent of this type of error has recently become available.[5] A sample of 1,000 completed death certificates was sent to five European countries for coding and the results were compared with the coding carried out by the World Health Organization Centre for Classification of Disease in London. The discrepancy rate ranged from 15 to 34%. It seems that although the rules for coding are clearly stated in the International Classification of Disease[6] their interpretation varies from country to country. For example, aneurysm of the thoracic aorta of unspecified cause should, according to the rules, be classified under syphilis, but in some countries where the condition is thought nearly always to be arteriosclerotic these deaths were classified under disease of arteries.

The latest revision of the International Classification of Disease will soon be published and will contain more precise instructions about coding the cause of death when several diagnoses are recorded. This should help to remove some of the errors. But for any substantial improvement in the accuracy of mortality statistics we must look to the doctors who sign the death certificates.

[1] *The Registrar General's Statistical Review of England and Wales for the Year 1965*, Part 1, Tables, Medical, 1967. London.

[2] Heasman, M. A., and Lipworth, L., *Accuracy of Certification of Cause of Death*, Studies on Medical and Population Subjects, No. 20, 1966. General Register Office, London.

[3] *Brit. med. J.*, 1966, 2, 1465.

[4] Alderson, M. R., and Meade, T. W., *Brit. J. prev. soc. Med.*, 1967, 21, 22.

[5] *W.H.O. Chronicle*, 1967, 21, 11.

[6] *Manual of the International Statistical Classification of Diseases, Injuries, and Causes of Death*, 1957, vol. 1, pp. 357–371. World Health Organization, Geneva.

Anaemia in Kwashiorkor

Kwashiorkor is still one of the most important medical problems of childhood in many tropical areas. The anaemia associated with it has long presented a dual challenge, for it is notoriously resistant to therapy and the mechanism by which it is caused is still not generally agreed. The article by E. B. Adams and his colleagues at page 451 of the *B.M.J.* this week is the latest in a long series of studies of these two problems.

When in 1937 attention was first drawn[1] to the anaemia of kwashiorkor it was attributed to protein malnutrition. However, the response of the anaemia to treatment with protein was disappointing, so other causes were sought. The high incidence of helminthic, malarial, and other infections in patients with kwashiorkor led some workers to suggest that it was the secondary infection rather than the kwashiorkor that was responsible for the anaemia. But this explanation was also open to objections. The anaemia of kwashiorkor is found in virtually all regions, whereas the incidence and type of secondary infections vary widely. H. C. Trowell and his colleagues[2] pointed out that infection with hookworms was very common among patients with kwashiorkor in East Africa but that it did not often cause severe anaemia until after the second year of life, whereas kwashiorkor was most frequently encountered before this time. They also observed that kwashiorkor was frequently seen in patients having no evidence of active malaria. Now Adams and his colleagues have completed a study in an area where malaria is rare, and have reached the conclusion that in their patients infection played no part in the production of the anaemia.

It has also been suggested that deficiencies of folic acid, vitamin B_{12}, and iron might be responsible in part for the anaemia. In 1954 Adams[3] reported that considerable numbers of patients with kwashiorkor benefited from treatment with folic acid, but the present study has shown that though folate deficiency may occur in kwashiorkor there is no evidence that the degree of anaemia is related to it. Iron deficiency was also excluded as a prime cause of the anaemia ; Adams and his colleagues found stainable iron in the marrow of all but two of their patients. However, treatment with iron prevented iron deficiency developing when treatment with a high protein diet was given, probably because increased red cell production then drains the iron from the storage depots.

The conclusion reached by Adams and his co-workers is that protein deficiency is the main cause of the anaemia. This and their exclusion of iron deficiency and specific haemopoietic factors as the prime causes support the findings of A. W. Woodruff[4] in his study of the natural history of anaemia associated with protein malnutrition, and further support comes from the work of D. M. Allen and R. F. A. Dean.[5]

How then should this anaemia be treated ? Clearly infections should be eradicated whether or not they have a causative role in the anaemia. Bacterial and malarial infections should be treated at once—respiratory infections are a common cause of death in kwashiorkor. Caution is needed, however, in the use of anthelmintics. Drugs used for hookworm infection tend to produce a variety of complications which can be fatal to ill-nourished children. Unless the condition is mild it is usually best to postpone anthelmintic treatment until recovery from kwashiorkor is well under way.

Iron deficiency may develop during treatment or may be present on admission ; it too should be treated. Again there is a tendency for the remedy to produce nausea when given orally, and Adams and his colleagues recommend that iron-dextran solution should be given by intramuscular injection. Though folate deficiency does not appear to limit haematological progress it is well to guard against it by a daily dose of 15 mg. folic acid. When anaemia is severe a slowly given transfusion of packed erythrocytes may be life saving. Detailed attention to fluid and electrolyte balance is always essential.

[1] Trowell, H. C., *Arch. Dis. Childh.*, 1937, 12, 193.

[2] —— Davies, J. M. P., and Dean, R. F. A., *Kwashiorkor*, 1954, p. 103. Edward Arnold, London.

[3] Adams, E. B., *Brit. med. J.*, 1954, 1, 537.

[4] Woodruff, A. W., ibid., 1955, 1, 1297.

[5] Allen, D. M., and Dean, R. F. A., *Trans. roy. Soc. trop. Med. Hyg.*, 1965, 59, 326.

[6] Dean, R. F. A., and Skinner, M., *J. trop. Pediat.*, 1957, 2, 215.

Fundamental to the whole treatment is administration of a high protein diet, if need be by intragastric tube and drip feeding. Here the recommendations laid down by Dean and M. Skinner[6] for kwashiorkor of various grades of severity have met widespread acceptance.

The aims of treatment of kwashiorkor are now agreed, and, as Dr. G. C. Cook and Professor M. S. R. Hutt show on page 454, there is no evidence in Uganda that liver disease is a sequel to treated kwashiorkor. Nevertheless, the mass prevention of the condition and widespread availability of treatment are still unsurmounted problems.

Thymic Function and Disease Processes

The thymus arises as a paired structure from the entoderm of the third and fourth branchial pouches. By the end of the second intrauterine month its epithelial nature is clearly evident, and shortly afterwards lymphocytes make their appearance. It rapidly grows in utero, but the greatest maximum weight is not achieved until puberty. From puberty there is a gradual loss of thymic parenchyma and replacement with fat. However, the thymus never completely disappears. The growth curve of the thymus[1] shows that this organ must be of some importance in developmental biology, and that whatever its functions may be they are likely to be most active in early life.

Though it is a lymphoid organ, the thymus differs from other lymphoid tissues both structurally and functionally. Apart from possessing epithelial cells and Hassall's corpuscles and a very high mitotic activity among the cortical lymphocytes, the thymus contains few plasma cells and no lymph follicles with germinal centres. Neither will these latter structures develop after injection of antigen.[2,3] Lymphopoiesis is therefore not effected by antigenic stimulation, and the primary stimulus to proliferation of thymic lymphocytes arises in the thymus itself.[4] Another peculiarity of this organ is the extent and often extreme rapidity with which it will undergo reduction in size in conditions of stress, including serious illness, radiotherapy, the administration of corticosteroids and radiomimetic drugs, and in pregnancy and lactation. This type of involution is due to massive depletion of its lymphoid population and is mediated through the adrenal and pituitary glands.[5,6] The discovery of thymic lesions in patients with thyroid disease, adrenal dysfunction, or acromegaly[7,8] is further evidence that mechanisms for endocrine control may effect thymic structure. Failure to appreciate the effects of stress and hormonal influences, together with the fact that there is a wide variation in the weight of the thymus at different ages,[1] may lead to erroneous diagnoses of hyperplasia, persistent thymus, and aplasia.

It has been known for some time that thymic lesions exist in myasthenia gravis.[7-9] About 10% of patients with this disease have thymomas,[10] and most of the remainder show microscopic abnormalities in the form of medullary lymph follicles with germinal centres, and increased numbers of plasma cells. In the last decade several diseases have been described in association with abnormalities of the thymus. They include the Swiss type of agammaglobulinaemia with thymic aplasia,[11,12] the disgammaglobulinaemias, pure red-cell aplasia and other haemopoietic abnormalities associated with thymoma[13-15] and systemic lupus erythematosus (S.L.E.), and rheumatoid arthritis,[16,17] in which there are derangement of architecture and changes in the epithelial cells. The thymic changes present in myasthenia gravis and S.L.E. are better termed dysplastic[18] in contrast with the true hyperplasia seen in, for example, thyrotoxicosis.[7] The recent report of a child with subacute leucoencephalitis in whom remission was obtained by thymectomy[19] is yet another instance of a disease with autoimmune features and thymic change. It is interesting in this context that damage to the frontal lobes and thymic lesions have previously been described.[20,21]

Some experimental findings are also relevant. In 1944 it was reported that a strain of mice " spontaneously " developed thymic leukaemia and that this process was thymus-dependent,[22] and in 1956 a lymphocyte-stimulating factor was isolated.[23] Experiments with neonatally thymectomized mice established the notion that the thymus is essential to the normal development and function of the lymphoid system. A circulation of lymphocytes between thymus, thoracic duct, lymph nodes, and spleen was suggested, and a thymic hormonal effect demonstrated.[24,25] All the evidence thus points to the thymus playing a key role in the control of immune reactivity.

Furthermore, it has been suggested that there are two centres directing immunity, one being the thymus, which is concerned with cellular immunity, the other being the bursa of Fabricius (a thymus-like structure found in birds) or its equivalent in man—possibly tonsil or appendix—which controls antibody production.[26] Current concepts of thymic function were recently summarized by Burnet.[27] It is suggested that the thymus is the centre of lymphoid-cell differentiation, making immigrant stem cells from the bone marrow differentiate along immunological pathways, and that the immunocytes so formed are differentiated in such a way as to activate the genetic loci associated with antibody production. Another suggestion is that more than one humoral factor is secreted by the thymus, whose effects control lymphopoiesis in the thymus itself and perhaps in bursa-of-Fabricius-

[1] Hammar, J. A., *Z. mikr.-anat. Forsch.*, 1926, **6**, 107.
[2] Bjørneboe, M., Gormsen, H., and Lundquist, F., *J. Immunol.*, 1947, **55**, 121.
[3] Fagraeus, A., and Gormsen, H., *Acta path. microbiol. scand.*, 1953, **33**, 421.
[4] Metcalf, D., in *The Thymus: Wistar Institute Symposium Monograph*, ed. Defendi, V., and Metcalf, D., No. 2, 1964, p. 53. Philadelphia.
[5] Selye, H., *Brit. J. exp. Path.*, 1936, **17**, 234.
[6] Baillif, R. N., *Amer. J. Anat.*, 1949, **84**, 457.
[7] Sloan, H. E., jun., *Surgery*, 1943, **13**, 154.
[8] Castleman, B., in *Thymectomy for Myasthenia Gravis*, ed. H. R. Viets, and R. S. Schwab, 1960. Illinois.
[9] Weigert, C., *Arch. Psychiat. Nervenkr.*, 1901, **34**, 1063.
[10] Castleman, B., *Ann. N.Y. Acad. Sci.*, 1966, **135**, 496.
[11] Hitzig, W. H., and Willi, H., *Schweiz. med. Wschr.*, 1961, **91**, 1625.
[12] Freycon, F., Jeune, M., Larbre, F., and Germain, D., *Rev. franç. etud. clin. biol.*, 1961, **6**, 817.
[13] Good, R. A., Martinez, C., and Gabrielsen, A. E., in *The Thymus in Immunobiology*, ed. R. A. Good, and A. B. Gabrielsen, 1964, p. 3. New York.
[14] Freeman, Z., *Brit. med. J.*, 1960, **1**, 1390.
[15] Havard, C. W. H., and Parrish, J. A., *J. Amer. med. Ass.*, 1962, **179**, 228.
[16] Mackay, I. R., and de Gail, P., *Lancet*, 1963, **2**, 667.
[17] Hutchins, G. M., and Harvey, A. M., *Bull. Johns Hopk. Hosp.*, 1964, **115**, 355.
[18] Mackay, I. R., in *The Thymus: Experimental and Clinical Studies*, ed. G. E. W. Wolstenholme, and R. Porter, 1966, p. 449. London.
[19] Kolář, O., Obručník, M., Běhounková, L., Musil, J., and Pěničková, V., *Brit. med. J.*, 1967, **3**, 22.
[20] Ascenzi, A., *J. Neuropath. and exp. Neurol.*, 1961, **20**, 1191.
[21] Messimy, R., *Rev. neurol.*, 1939, 71, 1.
[22] McEndy, D. P., Boon, M. C., and Furth, J., *Cancer. Res.*, 1944, 4, 377.
[23] Metcalf, D., *Brit. J. Cancer*, 1956, **10**, 442.
[24] Miller, J. F. A. P., Osoba, D., and Dukor, P., *Ann. N.Y. Acad. Sci.*, 1965, **121**, 95.
[25] —— *Science*, 1964, **144**, 1544.
[26] Peterson, R. D. A., Cooper, M. D., and Good, R. A., *Amer. J. Med.*, 1965, **38**, 579.
[27] Burnet, F. M., in *The Thymus*, 1966, p. 520. London.

like organs and the viability of immunocytes leaving the thymus to colonize secondary lymphoid organs.

As to the role of the thymus in disease, most of these clinical syndromes are linked with disorders of immunity and production of autoantibodies as in myasthenia gravis,[28-30] systemic lupus erythematosus, rheumatoid arthritis, thyroid disease,[31] and even the red-cell aplasia associated with thymoma.[32] The rudimentary epithelial thymus associated with the Swiss type of agammaglobulinaemia can be considered to be the clinical counterpart of neonatal thymectomy in animals, and there are now more than twenty syndromes in man with disordered production of antibody and in which abnormalities of the thymus, or bursa-like equivalents, or both have been described.[33] So far as diseases with an autoimmune basis are concerned, the role of the thymus is less clear, but two main hypotheses, not necessarily mutually exclusive, have been advanced. Burnet[34] suggests that autoimmunity may result from the proliferation of forbidden clones of immunocytes within the thymus, and regards the presence of lymph follicles with germinal centres in the thymus as evidence of such a process. An alternative hypothesis[35] suggests that chronic thymitis due to an antigen–antibody reaction within the gland itself results in defective thymic function in dealing with autoimmune lymphocytes. The finding of a neuromuscular blocking agent in the thymuses of myasthenic patients[36] is cited as further evidence of deranged function.

As to the association of thymoma with the development of autoimmunity, it has been postulated[35] that the neoplastic process itself initiates autoimmune disease. This supposition is borne out by the common finding of lymph follicles with germinal centres in thymic tissue adjacent to thymoma in myasthenia gravis but not in thymoma alone.[37] So far there is no clinical counterpart to the "spontaneous" thymic leukaemias in mice known to be due to transmission from parent to offspring of a virus,[38] but there is some suggestion that in children with sex-linked congenital agammaglobulinaemia there is increased risk of development of leukaemia and lymphoma.[39]

Thus it can be seen that the role of the thymus in the production of disease is complex, which explains the variable results of thymectomy and the development of autoimmune disease after thymectomy for myasthenia gravis.[40 41] R. A. Good's concept that there are at least two central origins for peripheral lymphoid tissue is attractive, for, as he points out,[42] the proper functioning of these systems would be vulnerable to failure of development, arrest of differentiation, or arrest of stimulus to proliferate, and defects at any of these levels would be expected to cause disorders of immunological function. This hypothesis could also account for the known genetic basis to many of the autoimmune diseases.[43 44]

---

[28] Van der Geld, H., Feltkamp, T. E. W., Van Loghem, J. J., Oosterhuis, H. J. G. H., and Biemond, A., *Lancet*, 1963, **2**, 373.

[29] —— and Strauss, A. J. L., ibid., 1966, **1**, 57.

[30] Wright, R., Kerr, J. H., *Clin. exp. Immunol.*, 1967, **2**, 93.

[31] Irvine, W. J., and Sumerling, M. D., *Lancet*, 1965, **1**, 996.

[32] Roland, A. S., *Amer. J. med. Sci.*, 1964, **247**, 719.

[33] Good, R. A., in *The Thymus*, 1966, p. 470. London.

[34] Burnet, F. M., and Holmes, M. C., *J. Path. Bact.*, 1964, **88**, 229.

[35] Goldstein, G., *Lancet*, 1966, **2**, 1164.

[36] Parkes, J. D., McKinna, J. A., ibid., 1966, **1**, 388.

[37] Bernatz, P. E., Harrison, E. G., and Clagett, O. T., *J. Thorac. Cardiovasc. Surg.*, 1961, **42**, 424.

[38] Gross, L., *Proc. Soc. exp. Biol. (N.Y.)*, 1951, **76**, 27.

[39] Page, A. R., Hansen, A. E., and Good, R. A., *Blood*, 1963, **21**, 197.

[40] Alarcón-Segovia, D., Galbraith, R. F., Maldonado, J. E., and Howard, F. M., jun., *Lancet*, 1963, **2**, 662.

[41] Simpson, J. A., *J. Neurol. Neurosurg. Psychiat.*, 1964, **27**, 485.

[42] Good, R. A., *et al.*, in *The Thymus*, 1966, p. 181. London.

[43] Wolf, J. K., Gokcen, M., and Good, R. A., *J. Lab. clin. Med.*, 1963, **61**, 230.

[44] de Vaal, O. M., and Seynhaeve, V., *Lancet*, 1959, **2**, 1123.

Tests for Pregnancy

From the time of ancient Egypt, when the urine of a pregnant woman was known to induce the flowering of plants,[1] many tests for pregnancy have been based on demonstrating the presence of increased amounts of chorionic gonadotrophin in the urine. Some of these tests have relied on the response of animals (such as mice, rabbits, rats, frogs, or toads) to the injection of small quantities of urine. Nevertheless, these methods are time-consuming, and the animal colonies which they require are inconvenient and expensive to maintain. Thus for many years workers have been trying to develop an effective in-vitro method for detecting human chorionic gonadotrophin. An immunological technique was tried by W. Liepmann as long ago as 1903,[2] but there was little success in this field until 1960, when four groups of workers independently reported three different immunological procedures. Of these the haemagglutination-inhibition method[3] has been most generally adopted. This uses sheep red cells that have been mixed with human chorionic gonadotrophin, and an antibody to chorionic gonadotrophin that has been prepared in rabbits. To perform the test the antibody is mixed with a small amount of the patient's urine, and then the sensitized sheep red cells are added. If the patient is pregnant the chorionic gonadotrophin present in the urine reacts with the antibody—which is therefore unable to agglutinate the sensitized red cells. If the patient is not pregnant, on the other hand, there is no competition for the chorionic gonadotrophin, and agglutination of the red cells takes place. The result is recognized after two hours from the pattern formed by the cells at the base of the tube ; a similar test, in which latex particles sensitized with human chorionic gonadotrophin replace the red cells, can be performed on a slide in two minutes.

Convenience and economy would be of little value if the haemagglutination-inhibition method were appreciably less reliable than the well-tried Hogben or female xenopus toad test, the accuracy of which may exceed 99%.[4] Comparative studies have shown an accuracy of 97% for the tube test[5] and 94% for the slide test,[6] though in an investigation confined to patients with suspected pregnancy less than 10 days after the first missed period lower degrees of accuracy were observed.[7] In a further study, by J. Powell and his colleagues, it was concluded that an immunological test was definitely superior to a biological method.

For routine work a pregnancy test that can be completed in two hours, obviates the need for an animal colony, costs in reagents only between two and five shillings per patient, is often positive within a week of the first missed menstrual period, yet rivals the accuracy of earlier methods, has not unexpectedly proved popular. The Hogben test is still occasionally used to determine the titre of human chorionic gonadotrophin in patients with hydatidiform mole and choriocarcinoma, and for checking equivocal results, though immuno-assay is increasingly preferred. Nevertheless, the demand for pregnancy tests is now so great that some laboratories are compelled to exercise selection over those patients to be tested. It is impossible to dictate stringent criteria for the choice of patients; the clinician must judge the need, but should indicate the reasons for his decision to the laboratory staff. A circular from the Ministry of Health (see page 504) now recommends pathology laboratories to accept requests for pregnancy tests on referral from general practitioners.

---

[1] Hon, E. H., *A Manual of Pregnancy Testing*, 1961, p. 3. London.

[2] Liepmann, W., *Dtsch. Med. Wschr.*, 1903, **29**, 80.

[3] Wide, L., and Gemzell, C. A., *Acta endocr. (Kbh.)*, 1960, **35**, 261.

[4] Barr, W. A., *J. Obstet. Gynaec. Brit. Cwlth*, 1963, **70**, 551.

[5] Hutcherson, W. P., Schwartz, H. A., and Bates, Helen M., *Amer. J. Obstet. Gynec.*, 1964, **89**, 70.

[6] Sato, T., and Greenblatt, R. B., ibid., 1965, **91**, 31.

[7] Powell, J., Stevens, V. C., Dickey, R. P., and Ullery, J. C., ibid., 1966, **96**, 844.

[8] Kew, M. C., Seftel, H. C., and Bloomberg, B. M., *Lancet*, 1967, **1**, 902.

Tests making use of tanned red cells require skill and care for their performance, and interference with the sedimentation pattern of the erythrocytes may result from such commonplace factors as vibration of the tube or the presence of proteinuria.[8] Above all the clinician should appreciate that both the biological and immunological tests detect the presence of human chorionic gonadotrophin or of luteinizing hormone, which is not necessarily due to pregnancy, and the results of these tests must always be interpreted with this thought in mind.

Mao's Medicine

In the course of a civilization that stretches much further back than our own in the West the conduct of affairs in China has often seemed to have an enigmatic quality. The present revolutionary ferment is no exception, and perhaps one of the oddest features of it is that its mainspring should be those two characteristic nineteenth-century immigrants to England, Marx and Engels.

The strident confusion of voices from China today and the difficulty of communications hinder any clear interpretation of events, especially as different parts of that vast country are in conflict with each other over their allegiances. But recently the effect of "the great proletarian cultural revolution" has led to notable changes in that once estimable record of medicine in China, the *Chinese Medical Journal*, published in Peking as the official organ of the Chinese Medical Association. Instead of the 10 or so articles of high clinical and scientific standard to which readers of that periodical were accustomed, the journal under the new title *China's Medicine*[1] is now mostly devoted to political exhortation, while the original articles are reduced to two or three at the back. The article having pride of place in the first issue is headed "China Successfully Conducts Guided Missile–Nuclear Weapon Test," and the second article, which is a speech delivered by Mao Tse-tung himself in 1957, is "On the Correct Handling of Contradictions among the People." An editorial statement announces that "Our people are out to eradicate all the old ideas, old culture, old customs, and old habits of the exploiting classes and foster the new ideas, new culture, new customs, and new habits of the proletariat." It goes on to say that *China's Medicine* will bring its readers:

> "The works of Chairman Mao Tse-tung, the greatest Marxist-Leninist of our era, who has led the Chinese people's revolution from victory to victory.
>
> "Experience in medical research and clinical practice guided by the invincible thought of Mao Tse-tung.
>
> "Reports on implementation of the policy of medicine in the service of the workers, peasants and soldiers, prevention first, and health work in integration with mass movements, especially the prevention and treatment of commonly-seen diseases in the countryside.
>
> "Advances in the synthesis of modern medicine and traditional Chinese medicine.
>
> "Experience in the Patriotic Health Movement among the masses of the people.
>
> "New people and new things on the medical front resulting from the creative study and application of Mao Tse-tung's thought.
>
> "French and Spanish summaries of the main medical articles.
>
> "News and notes and medical activities."

These aims are repeated in the second issue to reach us recently,[2] which also includes at the end two carefully documented articles from the Chinese Academy of Medicine on the treatment of choriocarcinoma.

Clearly the Chinese Medical Association at the time of writing is backing Mao Tse-tung, but to the Western reader such subservience to political inspiration, whatever its source, as *China's Medicine* promises would seem certain to bring great harm to the development and practice of medicine. No doubt the phase will pass, as the corruption of biology by the Michurin–Lysenko movement did in Russia. It may even leave in its wake some real benefit if it concentrates the attention of both medical experts and politicians on the improvement of public sanitation and hygiene in China. But at present there can be little doubt that rational medicine whose aim is to relieve suffering in the individual and the community is going through a difficult time there.

---

[1] *China's Medicine*, 1966, Nos. 1–3.

[2] Ibid., 1967, No. 4.

Studies of Platelets

In-vitro tests of platelet behaviour have been used for three main purposes: firstly, to study the basic properties of platelets; secondly, to measure platelet activity in various diseases; and, thirdly, to screen potential antithrombotic agents. Many test methods have been described, but most of them depend on either the ability of platelets to stick to glass surfaces and to each other, or the way in which they change the density of the electrical charge on their surfaces.

H. P. Wright[1] showed that when whole blood was rotated in a glass bulb the platelet count fell progressively, and that this fall could be used as a measure of platelet adhesiveness. A. J. Hellem[2] showed that a similar fall occurred when whole blood passed through a column filled with glass beads. Both these systems depend on an accurate platelet count being done, but they do allow the behaviour of platelets to be studied in their natural suspending medium, whole blood. Platelet adhesiveness, measured by modifications of these techniques, has been shown to be increased in ischaemic heart disease,[3] cerebrovascular disease,[4] multiple sclerosis,[5] and venous thromboembolism.[6] Decreased adhesiveness has been found in uraemia[7] and scurvy.[8] By using Salzman's column method reduced adhesiveness has been demonstrated in von Willebrand's disease,[9] but other methods have given divergent results in this condition.

The second method for studying platelet behaviour measures their ability to stick to each other and form aggregates. G. V. R. Born[10] showed that this could be monitored by measuring the changes which occur in the optical density of platelet-rich plasma as platelet clumps form and disperse. In the preparation of the plasma by differential centrifugation selective recovery of platelets occurs, so the platelets studied may not be representative of those in the whole blood. Many factors have been found to influence aggregation, and there is considerable patient-to-patient and day-to-day variability.[11] Tests of aggregation have therefore proved disappointing in studying individual patients. Nevertheless, they are useful for the diagnosis of thrombasthenia, where none of the usual agents such as adenosine diphosphate, noradrenaline, and collagen induces clumping. Moreover, differences in aggregation between groups of patients have been observed, for after operation[12] and myocardial infarction[13] increased intensity of aggregation develops. A heterogeneous group of persons has also been described[14] whose platelets respond normally to adenosine diphosphate but who show little response to other aggregating agents.

The third method measures the surface-charge density of platelets by determining their electrophoretic mobility. J. R. Hampton and J. R. A. Mitchell[15] showed that agents which cause aggregation induce changes in mobility, while they found that increased sensitivity to adenosine diphosphate and to noradrenaline occurs in a wide range of acute illnesses.[16] A selective increase in sensitivity to adenosine diphosphate alone occurs in patients with ischaemic heart disease, peripheral vascular disease, and with those conditions which predispose to the development of vascular disease.[17] The changes in sensitivity are due to factors in the plasma, and abnormal sensitivity can be conferred on normal platelets by suspending them in fresh plasma from a patient whose platelets are abnormal.

With the exception of thrombasthenia, which is an intrinsic platelet disease, many of the abnormalities detected in platelet behaviour in various diseases could result from changes in other blood constituents, and not from abnormalities in the platelets themselves. For example, the adhesion of platelets to glass depends on the presence of red cells as a source of adenosine diphosphate,[2, 18, 19] and it has been suggested that changes in the function of the red cells might be responsible for some of the variations in platelet adhesion in certain diseases.[19] In multiple sclerosis, where platelet adhesiveness is increased,[5] E. A. Caspary and his colleagues have recently shown that the red cells have an increased osmotic fragility.[20]

None of the above tests is appreciably affected by anticoagulant therapy, and early claims that linolenic acid and clofibrate reduced platelet adhesiveness have not been confirmed,[21, 22] Nevertheless, many drugs used as vasodilators have been shown to inhibit aggregation and to modify the changes in surface charge induced by adenosine diphosphate and noradrenaline.[23] The naturally occurring vasodepressor prostaglandin E_1 has been shown to be a potent inhibitor of platelet activity, both in vitro[24, 25] and in vivo.[25]

Though these in-vitro tests of platelet behaviour are still not sufficiently precise and discriminatory to be used in diagnosis—except perhaps in von Willebrand's disease and thrombasthenia—they have proved of considerable value in the study of the basic properties of platelets. Moreover, they may contribute to the eventual development of potent antithrombotic agents.

---

[1] Wright, H. P., *J. Path. Bact.*, 1941, **53**, 255.
[2] Hellem, A. J., *Scand. J. clin. Lab. Invest.*, 1960, **12**, Suppl. 51.
[3] McDonald, L., and Edgill, M., *Lancet*, 1957, **2**, 457.
[4] Millar, J. H. D., and Dalby, A. M., *8th Intl. Cong. Neurol.*, 1965, Vienna.
[5] Field, E. J., and Caspary, E. A., *Lancet*, 1964, **2**, 876.
[6] Hirsh, J., and McBride, J. A., *Brit. med. J.*, 1965, **2**, 797.
[7] Salzman, E. W., and Neri, L. L., *Thrombos. Diathes. haemorrh. (Stuttg.)*, 1966, **15**, 84.
[8] Born, G. V. R., and Wright, H. P., *Lancet*, 1967, **1**, 477.
[9] Salzman, E. W., *J. Lab. clin. Med.*, 1963, **62**, 724.
[10] Born, G. V. R., *J. Physiol. (Lond.)*, 1962, **162**, 67P.
[11] Harrison, M. J. G., Emmons, P. R., and Mitchell, J. R. A., *J. Atheroscler. Res.*, 1967, **7**, 197.
[12] Emmons, P. R., and Mitchell, J. R. A., *Lancet*, 1965, **1**, 71.
[13] O'Brien, J. R., Heywood, J. B., and Heady, J. A., *Thrombos. Diathes. haemorrh. (Stuttg.)*, 1966, **16**, 752.
[14] Hardisty, R. M., and Hutton, R. A., *Lancet*, 1967, **1**, 983
[15] Hampton, J. R., and Mitchell, J. R. A., *Brit. med. J.*, 1966, **1**, 1074.
[16] —— —— ibid., 1966, **1**, 1078.
[17] —— —— *Lancet*, 1966, **2**, 764
[18] Caspary, E. A., ibid., 1965, **2**, 1273.
[19] Harrison, M. J. G., and Mitchell, J. R. A., ibid., 1966, **2**, 1163.
[20] Caspary, E. A., Sewell, F., and Field, E. J., *Brit. med. J.*, 1967, **2**, 610.
[21] Borchgrevink, C. F., Berg, K. J., Skaga, E., Skjæggestad, Ø., and Stormorken, H., *Lancet*, 1965, **2**, 980.
[22] O'Brien, J. R., and Heywood, J. B., *Thrombos. Diathes. haemorrh. (Stuttg.)*, 1966, **16**, 768.
[23] Hampton, J. R., Harrison, M. J. G., Honour, A. J., and Mitchell, J. R. A., *Cardiovasc. Res.*, 1967, **1**, 101.
[24] Kloeze, J., in *Proc. Nobel Symposium II*, 1966, Stockholm.
[25] Emmons, P. R., Hampton, J. R., Harrison, M. J. G., Honour, A. J., and Mitchell, J. R. A., *Brit. med. J.*, 1967, **2**, 468.

Appointment in Surrey

On 27 May the British Medical Guild published an advertisement in the *B.M.J.* recommending doctors not to apply for public health appointments until a firm acceptable offer of an increase has been made in the pay of all public health medical officers. At the wish of the Council of the B.M.A. the *B.M.J.* stopped advertising vacancies for public health appointments from that date.

Most local authorities have made no attempt to fill senior medical posts since the Guild notice was published, and it is known that the advertisement of a number of vacancies of this kind has been postponed until the ban is lifted. The local authorities associations, who appoint the Management Side of Whitley Committee C, have asked[1] to meet the B.M.A. on 17 August, and this suggests that the dispute may be settled before long.

Surrey County Council, however, chose to seek applications for the position of county medical officer of health, and an appointment has been made. This has drawn protests from the B.M.A. and the South-West London and Surrey Local Medical Committee. The B.M.A. wrote to the Chairman of the Surrey County Council asking that the post be readvertised when the Guild notice is withdrawn, and the L.M.C. pointed out that the County Council's action would prejudice the good relationship between the local authority medical services and family doctors in Surrey. The Chairman of the Surrey County Council has agreed to meet a deputation from the B.M.A. but has stated that he sees no prospect of readvertising the appointment.

These reactions by the profession could have been foreseen by the County Council. It was aware that the professional association representing medical officers of health had advised them not to apply for vacancies, that many doctors who might have intended to apply for the post would be placed in a very difficult position, and the doctors in the public health service in Surrey would take exception to the job being offered while the Guild notice was in force. The new appointment will not be taken up until late in November,[2] so there was no need for haste. The County Council's reckless action has provoked a situation to which there is no easy solution.

---

[1] *Brit. med. J. Suppl.*, 1967, **3**, 98.
[2] *Daily Telegraph*, 11 August 1967

Papers and Originals

Observations on the Aetiology and Treatment of Anaemia in Kwashiorkor*

E. B. ADAMS, M.D., B.SC., F.R.C.P.; J. N. SCRAGG, M.D., D.C.H.; B. T. NAIDOO, M.MED.
S. K. LILJESTRAND; V. I. COCKRAM, B.SC.

Brit. med. J., 1967, 3, 451–454

Anaemia has been shown to develop in experimental animals deprived of proteins or essential amino-acids (Cartwright, 1947), but there is little evidence that protein deficiency is ever the cause of anaemia in man. Though protein is the major deficiency in kwashiorkor, there is an inadequate supply of other nutrients and infection is common. It might be expected, therefore, that anaemia in kwashiorkor is multifactorial. Morphological descriptions support this view. In the considerable body of literature which has accumulated its features are reported as normocytic, hypochromic, macrocytic, megaloblastic, or hypoplastic—singly or in combinations—but as yet there is little clear evidence regarding causation, and treatment is largely empirical.

We report here the results of an investigation of the part played in the production of this anaemia by infection and by deficiencies of iron, vitamin B_{12}, and folic acid; speculate on the role of protein deficiency as an aetiological factor; and make recommendations about treatment.

Clinical Materials and Methods

Sixty African children suffering from kwashiorkor were investigated in a ward used specially for this purpose. All had oedema, dermatosis, and lowered plasma proteins (mean albumin 1 g./100 ml.). They were admitted to the series if their haemoglobins were less than 10.5 g./100 ml., without any other form of selection. As controls we used 40 African infants of comparable age and apparently in good nutritional health.

On admission, Heaf tests and *x*-ray examination of the chest were carried out in all cases. Other infections were diagnosed on clinical grounds and confirmed by appropriate pathological tests. Twenty patients were found to be suffering from acute concomitant infection when first seen—namely, pneumonia, which was the commonest, gastroenteritis, and bacillary and amoebic dysentery. All 60 infants were given tetracycline in a dose of 125 mg. six-hourly whether or not there was evidence of acute infection. Despite this, three developed pneumonia in hospital and one later had amoebic dysentery. In seven infants the course of the disease was complicated by measles.

Our haematological methods have been reported elsewhere (Adams and Scragg, 1965), with the exception of serum folate estimations, which were carried out as described by Waters and Mollin (1961), and neutrophil lobe averages, for which we adopted the method of Herbert (1962). Clinical and haematological progress was observed for at least four weeks while the children were on a high-calorie diet of full-strength cow's milk with added glucose and potassium acetate. Feeds were offered four-hourly in unlimited amounts. Supplements of folic acid and vitamin B_{12} were not given except in two infants who required treatment with folic acid during the course of their illness. Six patients needed blood transfusion.

By random selection 32 infants received intramuscular iron dextran (Imferon) in six injections during the first two weeks, the total dose being 9 ml. When comparing the results of this group with those of the remainder we excluded the two patients who were given folic acid and the six who were transfused.

Results

Severity of the Anaemia

The mean haemoglobin on admission and the mean of the lowest levels reached in all cases, together with the controls for comparison, are given in Table I. In most of the infants the haemoglobin level dropped shortly after admission, the biggest fall among those who survived being 3.3 g./100 ml. In almost a quarter of the series (14) the lowest haemoglobin was below 6 g./100 ml. Severe anaemia must therefore be regarded as a common feature of kwashiorkor.

TABLE I.—*Severity of the Anaemia (Hb g./100 ml.)*

Haemoglobin	Controls (40)	Kwashiorkor (60)	
		Admission	Lowest
Mean	10·7	8·0	6·8*
Range	6·5–12·4	4·5–10·4	3·7–10·4
Under 9 g. ..	2	45	60
„ 6 g. ..	0	6	14

* Mean of 39 patients (10 died. Hb did not fall in 11).

Role of Infection

The mean haemoglobin on admission in infants with infection was the same as in those without infection, and there was no significant difference between the means of the lowest haemoglobin levels recorded in the two groups (Table II). It may be concluded, therefore, that infection played no part in the

TABLE II.—*Haemoglobin on Admission in Relation to Infection (Hb g./100 ml.)*

	Mean Hb on Admission	Mean Lowest Hb
Patients with infection (20)	8·0	6·7
„ without „ (38)	8·0	7·0

2 patients who died have been excluded because necropsies were not done and infection was in doubt.

---

* From the Departments of Medicine and Paediatrics and Child Health, University of Natal, Durban, South Africa.

production of anaemia. This is not surprising, since the infections were mostly acute, whereas it is chronic infection which is likely to cause anaemia.

The presence of infection on admission did not affect subsequent haematological progress. The mean rise in haemoglobin over four weeks in such patients was 1.1 g./100 ml., as compared with 0.82 g./100 ml. in infants without infection. In a group of six suffering from intercurrent infection during treatment, however, the rise in haemoglobin was negligible. As would be expected, the presence of infection decreased the chances of survival: among the 20 infants admitted with infection six died (30%), but only two deaths (15%) occurred in the remainder.

Iron Deficiency

Examination of marrow specimens for haemosiderin showed that iron-deficiency anaemia was uncommon before treatment started (Table III). Stainable iron was present in all patients except two in whom iron-deficiency anaemia was confirmed by the absence of sideroblasts and by the plasma iron patterns. A striking feature of the common plasma iron pattern in kwashiorkor is the diminution of total iron-binding capacity and the high percentage saturation—above 70% in a third of the infants, and complete in one case. The number of controls with apparent iron deficiency (judged on percentage saturation) is also worth noting (Table III).

TABLE III.—*Iron Status on Admission. Bone Marrow Haemosiderin Present in 58 Out of 60 Cases*

Plasma Iron Patterns		Plasma Iron (μg. per 100 ml.)	Saturation (%)
Controls (20)	Mean	46	22
	Range	8–112	3–58*
Kwashiorkor (59)	Mean	51	57
	Range	12–152	8–100†

* 7 under 16.
† 19 out of 59, 70% saturated or more.

We previously drew attention to the characteristic plasma iron pattern in kwashiorkor and the infrequency of iron-deficiency anaemia before treatment is started (Adams and Scragg, 1965). We pointed out that after treatment with high-protein diet the picture of iron deficiency commonly emerges, presumably because there is a rise in total red cell mass and the stores are drained of iron. It was for this reason that we divided the 60 infants in this series into two groups by random selection on admission, treating about half with iron. The results are summarized in Table IV. It will be seen that the use of iron prevented the development of iron deficiency and produced a much better mean rise in haemoglobin at the end of an observation period of four weeks.

TABLE IV.—*Results of Randomized Clinical Trial*

Diet Only	Iron-treated
28 patients, 5 died	32 patients, 5 died
1 iron-deficient on admission	1 iron-deficient on admission
9 iron-deficient after 4 weeks	0 iron-deficient after 4 weeks
Mean Hb rise, 0·28 g./100 ml.	Mean Hb rise, 1·42 g./100 ml.

Iron deficiency diagnosed by absence of haemosiderin and sideroblasts in the marrow and saturation less than 16%.

Incidence of Megaloblastic Anaemia

Examination of the bone marrow for morphological changes showed partial megaloblastic erythropoiesis in 17 infants (28%). In these cases erythropoiesis was predominantly normoblastic in type, but giant metamyelocytes were present in all, and in some there were intermediate megaloblasts as well. None was fully megaloblastic. In this group the neutrophil lobe average was slightly higher (2.93) than it was in those with fully normoblastic erythropoiesis (2.64) and in the controls (2.60).

It is noteworthy, however, that the mean haemoglobin on admission was almost the same (7.9 g./100 ml.) in patients with these bone marrow changes as it was when erythropoiesis was entirely normoblastic (8.1 g./100 ml.), suggesting that megaloblastic erythropoiesis plays no significant part in determining the severity of the anaemia of kwashiorkor before treatment with protein is started.

A point worth noting is the fact that where partial megaloblastic change in the marrow was present on admission the mean haemoglobin rise after four weeks' treatment was virtually the same as in the normoblastic group (see Table V). This occurred irrespective of whether iron had been given or not. Furthermore, the presence of these bone marrow abnormalities on admission did not significantly alter the prognosis: there were 3 deaths among 17 infants with partial megaloblastic erythropoiesis (18%) compared with 7 in the remaining 43 (16%).

TABLE V.—*Effect of Partial Megaloblastic Erythropoiesis on Mean Hb Rise After Four Weeks*

	Mean Hb Rise (g./100 ml.)	
	Iron-treated	Diet Only
Partial megaloblastic erythropoiesis	1·83 (7)	0·56 (5)
Normoblastic erythropoiesis	1·18 (17)	0·05 (13)

Number of cases in parentheses.

Vitamin-B_{12} Deficiency

Table VI gives the results of serum vitamin-B_{12} estimations, from which it is apparent that deficiency of this substance seldom occurs in kwashiorkor, confirming our previous observations (Adams and Scragg, 1962). The high values before treatment are probably related to fatty infiltration of the liver.

TABLE VI.—*Serum Vitamin-B_{12} Levels (μμg./100 ml.)*

	Mean	Range
Controls (22)	519	160–1,500
Kwashiorkor patients:		
On admission (48)	1,089	185–4,000
„ discharge (40)	532	135–1,710

Folic Acid Deficiency

Table VII, which gives the serum folate results, shows that folate deficiency was a common finding. Compared with the controls, a much higher proportion of patients with kwashiorkor had subnormal values, one-fifth being less than 3 mμg./ml. while more than half were under 5 mμg./ml., the upper limits of definite and probable folate deficiency according to Herbert (1966).

TABLE VII.—*Serum Folate Levels (mμg./100 ml.)*

	Mean	Range
Controls (39)	10·7	2·8–24·8 (1 under 3; 4 under 5)
Kwashiorkor patients:		
On admission (54)	5·6	0·4–19·0 (10 under 3; 31 under 5)
At 4 weeks (44)	5·2	0·7–13 (11 under 3)

There was a broad correlation between folate levels and the appearance of the bone marrow. Partial megaloblastic erythropoiesis was observed in 5 out of 10 cases in which the folate was under 3 mμg./ml., in 7 out of 21 with values between 3 and 4.9 mμg./ml., and in 3 out of 23 with normal serum folate activity. The neutrophil lobe average was slightly higher (2.83 mμg.)

among those with low folate levels than it was in the group with normal values (2.6 mμg.) and in the controls (2.6 mμg.).

Nevertheless there was no evidence that the degree of anaemia on admission was related to folate deficiency. The mean haemoglobin in 10 cases in which the folate level was less than 3 mμg./ml. was 8.1 g./100 ml.; in 21 cases with serum folate activity between 3 and 4.9 mμg./ml. the mean haemoglobin was 8.3 g./100 ml., and the same mean was found among the 23 cases with normal folate levels. Moreover, the mean haemoglobin rise over the first four weeks of treatment in those infants who had low serum folate values on admission compared favourably with the mean rise in those infants with normal serum folate levels (see Table VIII). There were no deaths among the 10 patients with serum folates less than 3 mμg./ml., though only one was treated with folic acid.

TABLE VIII.—*Effect of Serum Folate Levels on Mean Hb Rise After Four Weeks*

	No.	Mean Hb Rise (g./100 ml.)
Serum folate on admission <3·0 mμg./ml. ..	9	1·05
„ „ „ „ >5·0 „ ..	14	0·80

Discussion

Role of Protein Deficiency

This is by no means an exhaustive study of the many possible factors which might lead to anaemia in kwashiorkor. We have not, for instance, investigated in depth the role of haemolysis, and we cannot express an opinion on the therapeutic value of vitamin E, for which claims have been made (Majaj *et al.*, 1963; Marvin and Audu, 1964; Sandstead *et al.*, 1965). Nor have we attempted to assess the place of riboflavin, deficiency of which may give rise to anaemia and reticulocytopenia due to red cell hypoplasia (Lane and Alfrey, 1965) though its therapeutic use in kwashiorkor is disputed (Allen and Dean, 1965). We are impressed, however, by the similarity between the anaemia found in protein-deficient Rhesus monkeys (Sood *et al.*, 1965) and our own observations in kwashiorkor, and we believe we have circumstantial evidence to support the opinions of Ghitis *et al.* (1963b) and Allen and Dean (1965) that protein deficiency is the main cause of the anaemia in this disease.

Allen and Dean investigated 100 infants with kwashiorkor in Uganda. Though some of their patients, unlike ours, were infested with hookworm and malaria, the series as a whole was similar. They showed a definite relation between the lowest haemoglobin and the total plasma protein. Though we cannot confirm this from our experience, the facts all seem to link the anaemia with lack of protein. The relation must of necessity remain speculative, since definitive proof is clearly impossible in humans, though in animals the evidence is strong (Bethard *et al.*, 1958; Ghitis *et al.*, 1963a). In the present paper we show that there is no reason to attribute the anaemia found on admission to deficiencies of iron or vitamin B_{12}; and though partial megaloblastic erythropoiesis may be seen on examining the bone marrow, and folate deficiency is not uncommon, it has been pointed out that the degree of anaemia is comparable to that observed among the rest of the patients in whom erythropoiesis was normoblastic and folate levels were within the normal range. Infection has also been ruled out as a major cause of anaemia. Moreover, in this series, and in others we have previously reported (Adams, 1954; Adams and Scragg, 1962, 1965), we have noted a common haematological pattern after treatment with high protein diets, whether there was evidence of concomitant deficiencies or not. The underlying pattern was not related to the use of iron, folic acid, or vitamin B_{12}. The reticulocyte count rises shortly after protein feeding begins; in the present series this occurred as frequently in patients on diet only as it did in those receiving additional iron. The haemoglobin level often drops at first but later rises steadily over a period of many weeks to reach a normal or near-normal value, provided deficiencies of iron or folic acid do not manifest themselves. A typical example of uncomplicated progress to recovery is shown in Fig. 1.

Fall in Haemoglobin and Need for Blood Transfusion

The drop in haemoglobin which occurs soon after protein feeding starts is generally slight, but it may be severe and abrupt. We have assumed, with some justification (Cronje *et al.*, 1961; Adams and Scragg, 1965), that this is partly the result of the expansion in blood volume which follows the rise in plasma proteins. When the fall in haemoglobin is small and anaemia only moderate in degree it can be ignored. An abrupt drop, however, is an indication for immediate blood transfusion. Such episodes are alarming and sometimes herald death. To obviate them requires awareness of their occurrence and constant vigilance, and we therefore advise regular estimations of haemoglobin every five days in all cases. When the initial haemoglobin is less than 6 g./100 ml. transfusion is also a wise precaution. Falls in haemoglobin of 3 g./100 ml. were observed in some infants who survived, and prompt transfusion may have saved their lives. In one case delay in giving blood probably contributed to the patient's death.

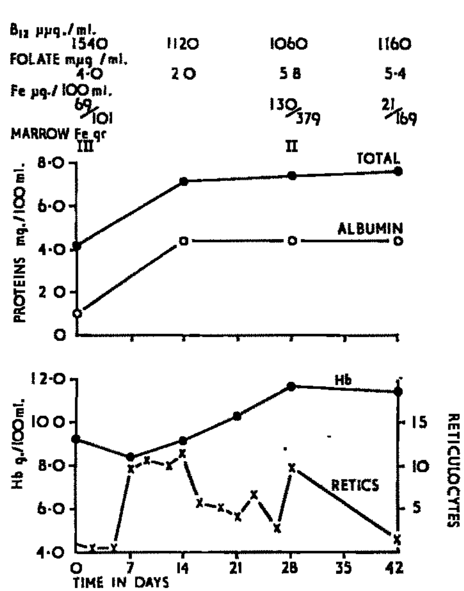


FIG. 1

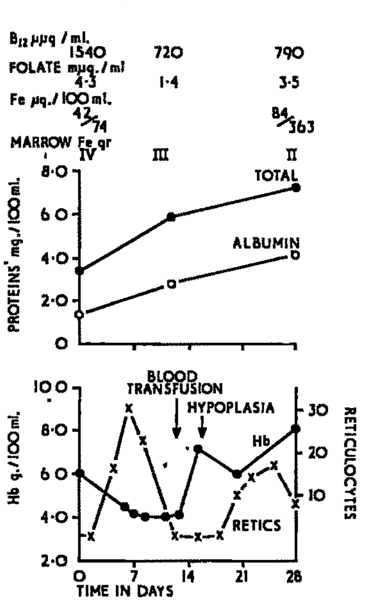


FIG. 2

FIG. 1.—Patient on diet only. FIG. 2.—Patient on diet and given blood transfusion.

It is unlikely that change in blood volume is the only cause of increasing anaemia. In some cases of kwashiorkor the haemoglobin drops because of the development of hypoplasia of the bone marrow (Lien-Keng and Tumbelaka, 1960; Neame and Simson, 1964). Reticulocytes disappear from the peripheral blood and red cell precursors from the marrow, but after a few days or a week the marrow recovers spontaneously, reticulocytosis occurs, and the haemoglobin rises. Such episodes give a double reticulocyte peak to the haematological pattern with a trough of reticulocytopenia in between. In the present series there were five examples, one of which is shown in Fig. 2. Their occurrence raises the question of haemolysis as an aetiological factor, since similar hypoplastic crises are found in haemolytic anaemias. We have not studied this aspect of the problem fully.

In the 60 infants reported here the mean serum bilirubin on admission was within the normal range (0.82 mg./100 ml.) and the initial reticulocyte count was usually only slightly raised (mean 3%), both values being little higher than corresponding control means of 0.54 mg./100 ml. and 1.6%. For this reason it seemed unlikely that the anaemia was predominantly haemolytic. When temporary marrow hypoplasia occurs, however, it does not affect the haemoglobin appreciably unless the red cell survival time is considerably reduced, which has been shown by Hoffenberg (1967, personal communication) to be the case in kwashiorkor. A haemolytic element should therefore be added to the factors which may contribute to the anaemia in this disease, though its importance remains to be clarified.

Iron and Folic Acid as Supplements During Treatment

We previously demonstrated (Adams and Scragg, 1965) that iron deficiency may occur in the recovery phase of kwashiorkor and we have now shown that it can be prevented by administration of iron. Since the detection of iron deficiency with any degree of certainty may require sophisticated tests which are not practicable except as research procedures, we recommend the administration of intramuscular iron to all infants with this disease, a total of 9 ml. of iron dextran being given over the first two weeks. In view of the high proportion of controls who appeared to be iron-deficient, judged on plasma iron patterns, it may well be that the occurrence of iron deficiency in kwashiorkor is not related to the disease itself but to the general iron status of infants in the age group at risk.

The case for supplements of folic acid is less easy to substantiate. It has been seen that partial megaloblastic erythropoiesis and subnormal serum folate levels are not uncommon findings on admission. Though they do not appear to limit haematological progress over the first four weeks, their existence can hardly be regarded with complacency. We have incomplete information about their long-term effects, but occasionally have observed the full picture of megaloblastic anaemia emerging later on. We therefore believe that the addition of folic acid to protein feeding is sound therapy in kwashiorkor, and recommend a routine supplement of 5 mg. thrice daily in all cases.

Summary

From a controlled clinical trial evidence is submitted in favour of the addition of iron to treatment with high-protein diet in kwashiorkor. Though iron-deficiency anaemia is seldom present on the patient's admission, routine treatment with iron prevents its development during the recovery phase.

No evidence was found that vitamin-B_{12} deficiency plays a part in the production of anaemia in kwashiorkor, and there was little support for the view that its severity may be related to the presence of infection, though this complication undoubtedly affects prognosis adversely.

Partial megaloblastic erythropoiesis and folate deficiency are shown to be common findings without playing a major part in the aetiology of the anaemia. Nevertheless, reasons are given justifying the use of folic acid supplements in all cases.

The common haematological pattern during recovery from kwashiorkor, no matter whether haematinics are added or not, suggests that protein deficiency is the main cause of the anaemia.

We thank Professor H. L. Wallace for access to patients under his care and for helpful criticism, and the Medical Superintendent, King Edward VIII Hospital, for facilities. The work was supported by a grant from the Council for Scientific and Industrial Research.

REFERENCES

Adams, E. B. (1954). *Brit. med. J.*, **1**, 537.
—— and Scragg, J. N. (1962). *J. Pediat.*, **60**, 580.
—— —— (1965). *Brit. J. Haemat.*, **11**, 676.
Allen, D. M., and Dean, R. F. A. (1965). *Trans. roy. Soc. trop. Med. Hyg.*, **59**, 326.
Bethard, W. F., Wissler, R. W., Thompson, J. S., Schroeder, M. A., and Robson, M. J. (1958). *Blood*, **13**, 216.
Cartwright, G. E. (1947). Ibid., **2**, 111.
Cronje, R. E., Savage, D. J., and Theron, J. J. (1961). *Proc. Nutr. Soc. Sth. Afr.*, **2**, 27.
Gritis, J., Piazuelo, E., and Vitale, J. J. (1963a). *Amer. J. clin. Nutr.*, **12**, 452.
—— Velez, H., Linares, F., Sinisterra, L., and Vitale, J. J. (1963b). Ibid., **12**, 445.
Herbert, V. (1962). *Trans. Ass. Amer. Phycns*, **75**, 307.
—— (1966). *J. clin. Path.*, **19**, 12.
Lane, M., and Alfrey, C. P. (1965). *Blood*, **25**, 432.
Lien-Keng, K., and Tumbelaka, W. A. F. J. (1960). *Ann. paediat. (Basel)*, **194**, 257.
Majaj, A. S., Dinning, J. S., Azzam, S. A., and Darby, W. J. (1963). *Amer. J. clin. Nutr.*, **12**, 374.
Marvin, H. N., and Audu, I. S. (1964). *W. Afr. med. J.*, **13**, 3.
Neame, P. B., and Simpson, J. C. (1964). *S. Afr. J. Lab. clin. Med.*, **10**, 27.
Sandstead, H. H., *et al.* (1965). *Amer. J. clin. Nutr.*, **17**, 27.
Sood, S. K., Deo, M. G., and Ramalingaswami, V. (1965). *Blood*, **26**, 421.
Waters, A. H., and Mollin, D. L. (1961). *J. clin. Path.*, **14**, 335.

The Liver after Kwashiorkor*

G. C. COOK,† M.D., B.SC., M.R.C.P.; M. S. R. HUTT,‡ M.D., F.R.C.P., F.C.PATH.

Brit. med. J., 1967, 3, 454–457

In many tropical areas a widespread belief persists that malnutrition in infancy often predisposes to hepatic cirrhosis. Evidence has been put forward for a progression from the fatty liver of kwashiorkor (Trowell *et al.*, 1954) to the development of cirrhosis (Davies, 1948; Ramalingaswami, 1964). There is a considerable weight of opinion against such a course of events in man (Gillman and Gillman, 1951; Higginson *et al.*, 1957; Waterlow and Bras, 1957; Brock, 1966). This last view is, however, supported by only one adequate long-term follow-up investigation, which included liver histology (Suckling and Campbell, 1957). In that study, which was carried out in a non-tropical country—South Africa—there was no evidence of cirrhosis in liver biopsy specimens obtained from 20 children five years after recovery from kwashiorkor.

The present investigation was designed to study liver structure and function in 50 African children four years or more after they had had kwashiorkor.

Patients and Methods

Details of the 50 patients investigated are given in Table I. Fifty-five households were visited, but five children were found

---

* From the Mulago Hospital and the Medical Research Council's Malnutrition Unit, Kampala, Uganda.
† Lecturer in Medicine, Makerere University College, Kampala, Uganda.
‡ Professor of Pathology, Makerere University College, Kampala, Uganda.

TABLE I.—*Details of Children Investigated After Recovery From Kwashiorkor*

No. Studied	Sex		Age at Diagnosis of Kwashiorkor (yr) (Mean and Range)	Length of Time between Kwashiorkor and Present Study (yr) (Mean and Range)	Present Age (yr) (Mean and Range)	Present Body Weight (kg.) Expressed as Percentage of Standard* for Same Age (Mean and Range)	Present Height (cm.) Expressed as Percentage of Standard* for Same Age (Mean and Range)
	M	F					
50	29	21	1·8 (0·7–4·7)	7·0 (4·0–11·3)	8·8 (5·5–13·0)	82·3 (56·9–99·5)	92·1 (81·4–101·0)

* Compared with standard weights and heights for upper-class Baganda schoolgirls (Burgess and Burgess, 1964).

to have died since the first admission: in no case did the history preceding death suggest that severe liver disease had been responsible. Eighteen of the children had been studied in an investigation of the jejunum after recovery from kwashiorkor (Cook and Lee, 1966). All of the 50 children lived within a 60-mile (96-km.) radius of Kampala. They had all been in-patients with kwashiorkor at the M.R.C. Malnutrition Unit, and good case-notes of the previous admission were available. They were taken at random from the admission register of children who left the unit alive. Of the 50 children 33 were from the local Baganda tribe, 14 from the Bahutu tribe of Rwanda, and 3 from other tribes. The severity of the preceding kwashiorkor was divided into four grades on clinical and laboratory criteria (Dean, 1960). Two had had very severe, 30 severe, 14 moderately severe, and 4 mild kwashiorkor.

They were readmitted to the Mulago Hospital for the present follow-up study. Details of the investigation were explained to the parents before the children were admitted. Though there was no evidence of severe malnutrition or vitamin deficiency in any of the children, most had some long-term sequelae of their kwashiorkor, for the mean weights and heights were reduced when compared with standard data for well-nourished Baganda schoolgirls. Weights were reduced more than heights (Table I); the correlation coefficient (r) between individual weights (kg.) and heights (cm.) in the 50 children was +0.893. Twenty-three of the children had also been studied in an investigation which revealed that intravenous glucose tolerance was impaired in most of them (Cook, 1967a), probably owing to pancreatic insufficiency (Cook, 1967b). Three patients had sickle-cell disease and four had the sickle-cell trait. One child had a congenital dislocation of the right hip. Another had had paralytic poliomyelitis since his earlier admission. Parotid enlargement was present in 11 children, slight hepatomegaly in 11, and splenomegaly in 15 (gross in 7). Twenty-one children had hepatomegaly and/or splenomegaly. There was no other clinical evidence of hepatocellular disease in any of the children. Four children with splenomegaly had a strongly positive, and one a positive, fluorescent malarial antibody titre (Voller and Bray, 1962) (Table II). A titre of 1:1,600 was taken to be strongly positive, and one of 1:800 to be positive.

TABLE II.—*Serum Fluorescent Malarial Antibody Titres in Children After Kwashiorkor*

No. Examined	Serum Dilution*				
	1 : 100 or <1 : 100	1 : 200 or >1 : 200	1 : 400 or >1 : 400	1 : 800 or >1 : 800	1 : 1,600 or >1 : 1,600
50	26	2	8	5	9

* Control serum titre <1 : 100.

Haemoglobin (Table III) and total and differential white cell count were done in all of the children. Total count was normal in all except five: four had a leucocytosis and one a leucopenia. Twenty-seven had an eosinophilia, accompanied in seven by a neutropenia. Serum bilirubin, aspartate and alanine aminotransferase, and alkaline phosphatase were estimated in all. Total plasma-protein, amino-acid ratio, and hydroxyproline index (Whitehead, 1964, 1965) were also measured (Table III). Three had an abnormality in both the amino-acid ratio and the hydroxyproline index. Brucella agglutinins were estimated in five patients who had granulomata in the liver biopsy specimens. Chest *x*-ray films and straight *x*-ray films of the abdomen were taken in all of the children. The heart shadow was normal in every one; four had pulmonary consolidation (three in the right upper lobe and one in the lingula), and one had bilateral hilar lymphadenopathy. No child had pancreatic calcification.

TABLE III.—*Haemoglobin and Biochemical Tests of Nutritional Status in Children After Kwashiorkor*

No. Tested	Haemoglobin (g./100 ml.) (Mean and Range)	Total Plasma-protein* (g./100 ml.)		Amino-acid Ratio†		Hydroxyproline Index‡	
		Mean and Range	No. Abnormal	Mean and Range	No. Abnormal	Mean and Range	No. Abnormal
50	12·1 (7·1–16·0)	7·4 (6·0–9·4)	12	2·1 (1·1–3·7)	8	2·9 (0·8–5·9)	12

* Normal range >7 g./100 ml. † Normal range <3. ‡ Normal range >2.

Aspiration liver biopsies were obtained by an anterior subcostal approach under local anaesthesia with a 1.9-mm. Menghini needle (Menghini, 1958). We believe that this investigation was justified; for in Uganda a considerable proportion of liver biopsy specimens from paediatric patients reveal a treatable disease—such as tuberculosis or schistosomiasis. Indeed, during the present study two cases of active tuberculosis were diagnosed as a result of liver biopsy. There were no complications. All the biopsy specimens were adequate for histological assessment, and all except four were between 1 and 4 cm. in length. They were immediately fixed in 10% formol-saline solution and embedded in paraffin wax. Sections were cut at 5–7 μ. They were stained with haematoxylin and eosin, a reticulin stain, and by Perls's technique for free iron. The presence of malarial pigment was confirmed by demonstrating double refractility under polarized light. All biopsy specimens were examined on several occasions by both authors, and were compared with biopsies from six European children of mean age 10.3 (range 8 to 13) years who had no evidence of liver disease, and who had never lived in a tropical area. All six children had presented with symptoms and signs suggesting liver disease; in three the final diagnosis was extrahepatic venous obstruction, in one Gilbert's disease, and in the other two no conclusive diagnosis was reached, but liver disease was considered to have been excluded.

Results

Liver Histology

Table IV summarizes the results. No evidence of cirrhosis was found in any of the biopsy specimens. None of the abnormalities present in the specimens could be associated with any of the different tribes.

Twenty-one biopsy specimens were relatively normal when compared with the specimens from the six European children

TABLE IV.—*Summary of Histological Findings in Liver Biopsy Specimens from Children After Kwashiorkor*

No. Examined	Parenchyma			Portal Tracts			Sinusoids			
							Excessive Infiltrate			
	Excessive Fat	Nuclear Irregularity	Granulomata	"Stellate" Fibrosis	Excessive Infiltrate	Malarial Pigment	Lymphocytes	Eosinophils	Malarial Pigment in Kupffer Cells	Excessive Kupffer Cell Hyperplasia
50	1	17	5	6	2	29	7	11	23	8

who had never lived in tropical areas. Most of these, however, had mild periportal fibrosis and/or portal infiltration with lymphocytes, and others had, in addition, occasional plasma cells and eosinophils in the portal areas. These changes were not severe enough, however, to produce expansion of the portal tracts. Most specimens showed slight Kupffer-cell hyperplasia and/or hypertrophy, and some showed a slight increase in sinusoidal lymphocytes. Apart from these changes, and the presence of some malarial pigment, nothing else abnormal was found.

The other 29 biopsy specimens showed similar changes, but all of these also had more striking abnormalities when compared with the European children.

Parenchymal Cells

In one biopsy specimen which also had "stellate" fibrosis radiating from the portal areas there was an excess of fat in the parenchymal cells (Fig. 1). That child had had very severe kwashiorkor, and both biochemical tests of current nutritional status were abnormal. Variability in nuclear size and staining with occasional double nuclei was present in 17 biopsy specimens; in 10 there was marked focal nuclear vacuolation. Nuclear vacuolation was also noted in two of the European specimens. Nuclear irregularity was present in one biopsy specimen which also showed "stellate" fibrosis. There was no association between the presence of nuclear irregularity and the severity of the preceding kwashiorkor. No evidence of cell necrosis in any biopsy specimen was found. Of the 17 with nuclear irregularity, five had lowered plasma proteins and five had an abnormality in one of the biochemical tests of current nutrition.

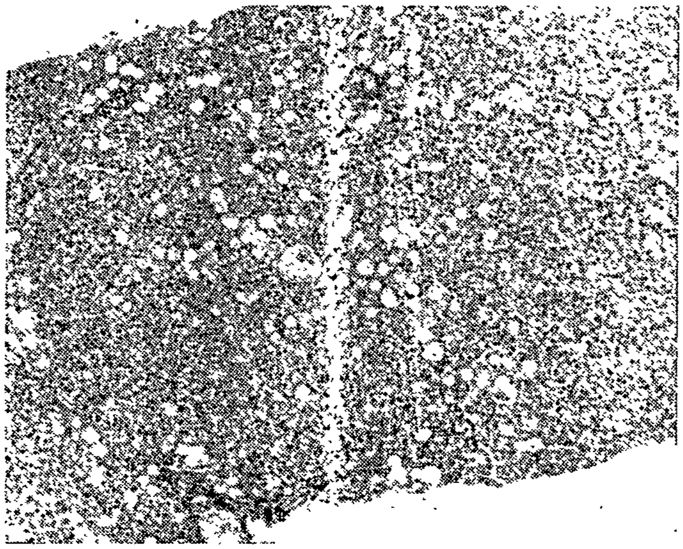


FIG. 1.—Liver biopsy specimen from the only child in the investigation to show an excess of fat in the parenchymal cells. (H. and E. ×20.)

Portal Tracts

Stellate fibrosis spreading from more than one portal tract was found in six biopsy specimens (Fig. 2); one was from a very severe, four from severe, and one from a moderately severe case of kwashiorkor. These six patients had first been admitted between 1.1 and 2.7 (mean 1.7) years of age, and the time between treatment and follow-up was from 5.5 to 8.5 (mean 6.4) years. Three of these cases had an abnormality in one of the biochemical tests of current nutrition (one of them in both tests). In no case was there any widespread linking of the fibrous tissue between adjacent tracts. In several other biopsy specimens a distinct increase in fibrous tissue was present when compared with the controls, but was confined to the tracts. Excessive infiltration with round cells, mainly lymphocytes, causing marked enlargement of several tracts was seen in two specimens.

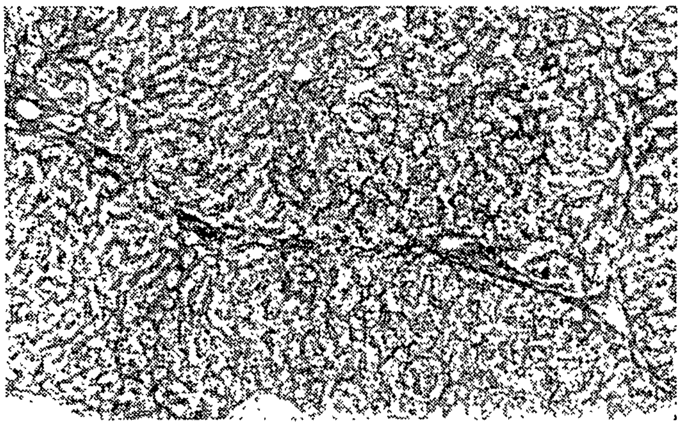


FIG. 2.—Liver biopsy specimen from one of the six children showing "stellate" fibrosis radiating from the portal areas. This specimen showed the most severe change in the present investigation. (Reticulin stain. ×20.)

Sinusoids

In seven specimens sinusoidal lymphocytes were greatly increased in number; four of these cases had splenomegaly and three, moreover, had a strongly positive malarial antibody titre. Malarial pigment was present in five of those seven biopsy specimens. Nine of the 11 specimens with an increase in sinusoidal eosinophils had a high eosinophil count in the peripheral blood. In eight specimens Kupffer cells were greatly enlarged and increased in number; three of these cases had a strongly positive malarial antibody titre.

Malarial pigment was present in the Kupffer cells or in the portal areas of 29 biopsy specimens (Table IV). There was none in the specimens from the children with sickle-cell disease. Twelve children with malarial pigment in the biopsy specimen had splenomegaly. The malarial antibody titre was strongly positive in five and positive in three of these. An excess of free iron in the Kupffer cells was seen in one specimen, from a patient with sickle-cell disease. "Granulomata" were seen in the parenchyma in five biopsy specimens. One was a classical epithelioid granuloma; this case and one other with a granuloma had consolidation of the right upper lobe which was due to tuberculosis. In four cases the "granulomata" consisted of small collections of chronic inflammatory cells grouped around a focus of degenerated parenchymal cells. The possibility that these represent schistosomal granulomata was considered, but ova were not demonstrated on serial sectioning. None of these patients showed a raised brucella antibody titre.

Biochemical Tests of Liver Function

Serum bilirubin was normal in all except one child with sickle-cell disease in whom it was 1.9 mg./100 ml. (normal range <1 mg./100 ml.). Serum aspartate and alanine aminotransferase were normal in all except one child, in whom they were slightly raised (normal range <40 units). Serum alkaline phosphatase was higher than the normal adult range in all except 11 children (mean 19.3, range 7–36 King–Armstrong units). Levels in normal children are usually elevated when compared with the adult range of 3–13 units (Varley, 1962).

Discussion

The only permanent abnormality in the 50 liver biopsy specimens was "stellate" fibrosis in six; in none of these was there a disturbance in the normal liver architecture. It is impossible from this study to relate this fibrosis to the past malnutrition. There was no evidence of cirrhosis, and all biopsy specimens were adequate for histological assessment. The cause of the focal variation in nuclear size in the parenchymal cells is unknown, but was less marked in the present series than in a random group of adult Ugandan African inpatients studied at the Mulago Hospital (Cook and Hutt, 1967). It can be a non-specific result of increased cell turnover (Popper and Schaffner, 1957), and also occurs in malnutrition, as deficiency of riboflavine and pyridoxine has been shown to produce gross nuclear irregularity in the hepatic parenchymal cells of the baboon (Foy *et al.*, 1966). There is, however, no good reason to incriminate current malnutrition in the present study.

Apart from slight portal changes, the only consistent difference between the biopsy specimens in this follow-up study and those from the European children was in the reticuloendothelial components, especially the Kupffer cells. These changes are probably due to parasitic diseases, especially malaria. Malarial pigment was found in the Kupffer cells and/or portal areas in approximately 60% of the biopsy specimens, of whom less than half had splenomegaly and only eight had a positive or very positive malarial antibody titre. In three children there was an association between splenomegaly, increased sinusoidal lymphocytes, and a strongly positive malarial antibody titre. Gebbie *et al.* (1964) have reported a significant association between gross splenomegaly, an increase in sinusoidal lymphocytes, and a strongly positive malarial antibody titre, but without malarial pigment in the liver biopsy specimen ; this probably represents an unusual reticuloendothelial reaction to chronic malarial infection.

This study, despite the fact that at a follow-up examination some of the children were still malnourished and others had evidence of anaemia, malaria, tuberculosis, and other infections, demonstrates that, apart from a few differences which are presumably reversible, liver histology of most Ugandan children after kwashiorkor is very similar to that of European children who have not lived in the tropics.

Despite the widespread belief in many tropical areas that infant malnutrition may account for cases of cirrhosis in later life, the present study in tropical Africa confirms the view of most other workers (Higginson *et al.*, 1957 ; Suckling and Campbell, 1957 ; Bras, 1961) that treated kwashiorkor does not predispose to permanent liver damage. The possibility that prolonged untreated kwashiorkor may proceed to cirrhosis (Davies, 1948 ; Ramalingaswami, 1964) cannot be eliminated by the present study. Most of the children studied had, however, had severe kwashiorkor, and in some cases this had probably been present for a year or more. Only one biopsy specimen still contained an excess of fat in the parenchymal cells. Davies (1951) has suggested that the development of cirrhosis may be a delayed phenomenon and takes place only after the disappearance of fat in kwashiorkor. While this is possible, the absence of any evidence of cirrhosis in six biopsy specimens taken 10 years or more after the treatment of severe or very severe kwashiorkor indicates that progression to cirrhosis must be a rare occurrence. Since it is not possible to obtain an accurate estimate of either the frequency of recovery from untreated kwashiorkor or the overall incidence of adult cirrhosis in Uganda, it must be questioned whether a large enough number of cases has been studied to rule out progressive liver disease in some children after kwashiorkor.

The results of the present investigation apply only to Uganda. There is evidence that liver pathology in kwashiorkor may vary in different areas. In New Guinea, atrophy and vacuolation of parenchymal cells is more obvious than the fatty infiltration (Venkatachalam and Ivinskis, 1957 ; Bailey, 1966) which is so consistent a finding in Uganda.

High serum alkaline phosphatase levels were found in approximately 75% of the children, owing presumably to increased osteoblastic activity in bone.

The good general nutritional status of most of the children here studied after recovery from kwashiorkor, but while continuing to live in the poor socio-economic environment in which they developed kwashiorkor, is striking (Suckling and Campbell, 1957).

Summary

Hepatic histology and biochemical tests of liver function have been studied in 50 Ugandan children, 4.0 to 11.3 (mean 7.0) years after admission to hospital with kwashiorkor. The kwashiorkor had been severe in 32 of the children.

Liver biopsy specimens all showed slight differences when compared with biopsies from six European children who had never lived in tropical areas. Six patients had some " stellate " fibrosis radiating from the portal areas, and in one case there was an excess of fat in the parenchymal cells, but in none was there any evidence of cirrhosis or progressive liver disease.

The liver-function tests gave normal results in most. Serum alkaline phosphatase was elevated, compared with adult levels, in 39 of the children.

There is no evidence from this study that progressive liver disease and cirrhosis are long-term sequelae of treated kwashiorkor in Uganda. The possibility that cirrhosis may follow prolonged *untreated* kwashiorkor has not been eliminated.

We thank Mr. Y. M. Semindi for finding the children for this investigation, and Drs. R. A. Tozer and N. J. Mody for the haematology and liver-function tests respectively. Mr. G. R. Howells was responsible for the plasma proteins and biochemical tests of nutritional status, and Dr. D. E. Wykoff for the fluorescent malarial antibody reactions. Dr. P. J. Scheuer, of the Royal Free Hospital, London, sent us the liver biopsy specimens from the six European children that were used as controls. We are grateful to Professor R. A. McCance, F.R.S., for valuable discussion concerning the manuscript.

REFERENCES

Bailey, K. V. (1966). *Med. J. Aust.*, **1**, 572.
Bras, G. (1961). *Fed. Proc.*, **20**, Suppl. No. 7, p. 353.
Brock, J. F. (1966). *Ann. intern. Med.*, **65**, 877.
Burgess, A. P., and Burgess, H. J. L. (1964). *Hum. Biol.*, **36**, 177.
Cook, G. C. (1967a). *Nature (Lond.)*. In press.
—— (1967b). Awaiting publication.
—— and Hutt, M. S. R. (1967). Unpublished.
—— and Lee, F. D. (1966). *Lancet*, **2**, 1263.
Davies, J. N. P. (1948). Ibid., **1**, 317.
—— (1951). In *Liver Injury*, edited by F. W. Hoffbauer, pp. 151-205. New York.
Dean, R. F. A. (1960). *J. Pediat.*, **56**, 675.
Foy, H., Gillman, T., Kondi, A., and Preston, J. K. (1966). *Nature (Lond.)*, **212**, 150.
Gebbie, D. A. M., Hamilton, P. J. S., Hutt, M. S. R., Marsden, P. D., Voller, A., and Wilks, N. E. (1964). *Lancet*, **2**, 392.
Gillman, J., and Gillman, T. (1951). *Perspectives in Human Malnutrition*, pp. 214–245. New York.
Higginson, J., Grobbelaar, B. G., and Walker, A. R. P. (1957). *Amer. J. Path.*, **33**, 29.
Menghini, G. (1958). *Gastroenterology*, **35**, 190.
Popper, H., and Schaffner, F. (1957). *Liver : Structure and Function*, pp. 87–93. London.
Ramalingaswami, V. (1964). *Nature (Lond.)*, **201**, 546.
Suckling, P. V., and Campbell, J. A. H. (1957). *J. trop. Pediat.*, **2**, 173.
Trowell, H. C., Davies, J. N. P., and Dean, R. F. A. (1954). *Kwashiorkor*, pp. 128–144. London.
Varley, H. (1962). *Practical Clinical Biochemistry*, 3rd ed., p. 385. London.
Venkatachalam, P. S., and Ivinskis, V. (1957). *Med. J. Aust.*, **1**, 275.
Voller, A., and Bray, R. S. (1962). *Proc. Soc. exp. Biol. (N.Y.)*, **110**, 907.
Waterlow, J. C., and Bras, G. (1957). *Brit. med. Bull.*, **13**, 107.
Whitehead, R. G. (1964). *Lancet*, **1**, 250.
—— (1965). Ibid., **2**, 567.

Small Intestine in Psoriasis

SAM SHUSTER,* M.B., PH.D., M.R.C.P. ; A. J. WATSON,† M.D., M.C.PATH. ; JANET MARKS,‡ B.A., B.M., M.R.C.P.

Brit. med. J., 1967, 3, 458–460

We have shown that patients may develop an enteropathy as a result of extensive skin disease (Shuster and Marks, 1965). Some of the patients whose cases we described had psoriasis, and so it became important to find out whether bowel abnormalities were a common feature of this disease.

Patients and Methods

Twenty-three female and 19 male patients were studied. Their ages ranged from 15 to 72 years. The total length of history of psoriasis ranged from 3 weeks to 50 years, and the duration of the most recent episode from 1 week to 20 years. All patients had been admitted to hospital for treatment and were studied consecutively, apart from a few who declined the investigation. None of the patients had a history of diarrhoea or bulky stools. The extent of the rash was assessed visually on admission.

Faecal fat excretion was measured in 26 patients. With the patient on a normal ward diet, which was estimated to contain about 100 g. of fat a day, faeces were collected for five consecutive days. The mean daily faecal fat excretion was measured by the method of Van de Kamer, ten Bokkel Huinink, and Weyers (1949), a mean fat excretion of more than 5 g. being regarded as abnormal.

D-*Xylose absorption* was measured in 10 patients. After an overnight fast 25 g. of D-xylose was given and urine was collected over the next five hours. In some cases a sample of blood was taken two hours after the dose of sugar. Xylose in the blood and urine was measured by the method of Roe and Rice (1948), excretion of less than 4.1 g. of xylose in the urine in five hours being regarded as abnormal (Fourman, 1948).

Mucosal Biopsy of Small Intestine

With the use of a Crosby capsule (Crosby and Kugler, 1957) a peroral biopsy specimen of small-intestinal mucosa was obtained from 26 patients, including 12 who had had a faecal fat examination. The position of the capsule was first verified radiologically ; in most cases it was in the proximal loop of the jejunum, but occasionally it was in the fourth part of the duodenum. The specimen was retrieved with the minimum of delay and was transported to the laboratory in ice-cold buffered sucrose solution (0.22 M). With the aid of a stereoscopic dissecting microscope the specimen was then spread out, mucosal surface upwards, on a flat piece of cellulose sponge and divided in two. One piece was immediately frozen by dropping it in liquid nitrogen and was stored at −70° C. in a small airtight container for subsequent histochemical examination. The interval between the firing of the capsule and the quenching of the selected part of the biopsy specimen in liquid nitrogen ranged from 7 to 10 minutes.

The remaining part of the specimen was fixed in 10% formol-calcium for at least 24 hours. Mucus and intestinal debris were then gently removed from the mucosal surface by means of a soft brush, and the mucosa was examined through the dissecting microscope and photographed. After processing through to paraffin wax, histological sections were cut at a thickness of 5 microns. Care was taken to ensure that the sections were cut in a plane perpendicular to the muscularis mucosae in order to obtain a true measure of villous height in relation to the crypt depth.

Correct orientation in the paraffin block was facilitated by the method of fixation, which prevented the specimen from becoming curled or folded. Finally, the sections were stained by various methods, including haematoxylin and eosin, and the periodic-acid–Schiff method.

Dissecting Microscope Appearances

We have followed the terminology of Booth, Stewart, Holmes, and Brackenbury (1962). Finger-shaped villi are self-explanatory. Leaves are a heterogeneous group of villi which are broadened in one cross-sectional diameter. Straight mucosal ridges appear to be an exaggeration of the leaf-shaped forms and the dividing line between them is arbitrary. We define ridges as having a ratio of width to height of greater than three to one. Ridges which pursue a winding course are described as convoluted. A mucosa from which all villi and ridges have disappeared is conventionally described as flat.

Histological Appearances

Partial villous atrophy (Doniach and Shiner, 1957) is the histological counterpart of a convoluted mucosa as seen by the dissecting microscope (Booth *et al.*, 1962). In normal jejunal mucosa the villi are at least twice as tall as the crypts are deep (Hourihane, 1966), and we consider partial villous atrophy to be present when there is shortening of the villi, with or without lengthening of the crypts. This is usually accompanied by an increased number of plasma cells and eosinophils in the lamina propria, and sometimes the surface epithelium is infiltrated by lymphocytes. Occasionally there are foci of irregularity of the surface epithelium similar to that found in subtotal villous atrophy.

Classification

Our classification is based on the stereomicroscopical and histological appearances and is summarized as follows:

(1) Normal: Fingers and narrow leaves.

(2) Equivocal: Broad leaves and short straight ridges. May show increase of chronic inflammatory cells in lamina propria.

(3) Abnormal: (*a*) *Convoluted.* Predominance of angulated ridges. Surface epithelium focally abnormal, increased inflammatory cells, and partial villous atrophy. (*b*) *Flat.* No villi, but mosaic pattern and prominent crypt openings. Surface epithelium abnormal, with increased inflammatory cells.

---

* Professor of Dermatology, Royal Victoria Infirmary, Newcastle upon Tyne 1.
† Senior Lecturer in Pathology, Royal Victoria Infirmary, Newcastle upon Tyne 1.
‡ Lecturer in Dermatology, Royal Victoria Infirmary, Newcastle upon Tyne 1.

Histochemical Studies

Frozen sections from the unfixed material were cut at a thickness of 10 microns in a cryostat cabinet maintained at a temperature of −20° C. *Leucine aminopeptidase* was demonstrated by the method of Nachlas, Crawford, and Seligman (1957) L-leucyl-4-methoxy-β-napthylamide being used as substrate (Rosenblatt, Nachlas, and Seligman, 1958). *Non-specific alkaline phosphatase* was demonstrated after the method of Burstone (1958a) with naphthol-ASMX-phosphate as substrate. *Adenosine triphosphatase* was demonstrated after the method of Padykula and Herman (1955) with $CaCl_2$ in the incubating medium at a concentration of 0.227 M. *Non-specific acid phosphatase* was demonstrated by the method of Burstone (1958b) with naphthol-ASMX-phosphate as the substrate. *Succinate dehydrogenase* was demonstrated after the method of Nachlas, Tsou, de Souza, Cheng, and Seligman (1957). *Glucose-6-phosphate dehydrogenase* was demonstrated by the method of Hess, Scarpelli, and Pearse (1958) with the use of MTT tetrazolium salt. *Non-specific esterase* was demonstrated by the method of Novikoff and Goldfischer (1961).

Results

Fig. 1 shows that 15 of the 26 patients examined excreted more than 5 g. of fat a day in their faeces. Both the incidence and the degree of steatorrhoea were clearly related to the extent of the psoriasis. There was no apparent relation to age, sex, and total duration of psoriasis, or to the duration of the most recent episode. D-Xylose excretion was abnormal in 4 of the 10 patients in whom it was measured, and three of these abnormal results were in patients with steatorrhoea (Table I).

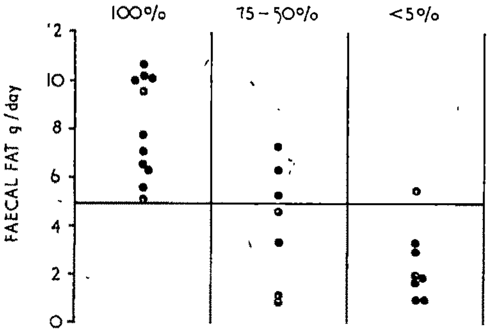


FIG. 1.—Relation between faecal fat excretion and proportion of skin surface affected by psoriasis.

The stereomicroscopical appearances of the small-intestinal mucosa are summarized in Table II. In 12 patients (46%) the mucosa was frankly abnormal with a convoluted appearance (Fig. 2) and histologically showed partial villous atrophy. Most of the abnormal mucosae were found in the younger age group ; none of the patients had a flat mucosa. Unlike the steatorrhoea, the degree of mucosal abnormality was not apparently related to the extent of the psoriasis (Fig. 3).

TABLE I.—*Faecal Fat Excretion and Urinary D-Xylose Excretion in Patients with Psoriasis*

Case No.	Faecal Fat (g./day)	Plasma D-Xylose (mg./100 ml.)	Urinary D-Xylose (g./5 hours)
1	3·0	39	0·3
2	10·1	27	1·7
3	7·8	11·8	2·2
4	10·6	43	3·8
5	—	41	4·2
6	5·4	—	5·2
7	6·4	—	5·6
8	1·0	—	5·7
9	9·6	—	5·8
10	1·9	—	7·1

TABLE II.—*Mucosal Abnormalities in 26 Patients with Psoriasis*

Normal	Equivocal	Abnormal	
		Convoluted	Flat
10	4	12	0

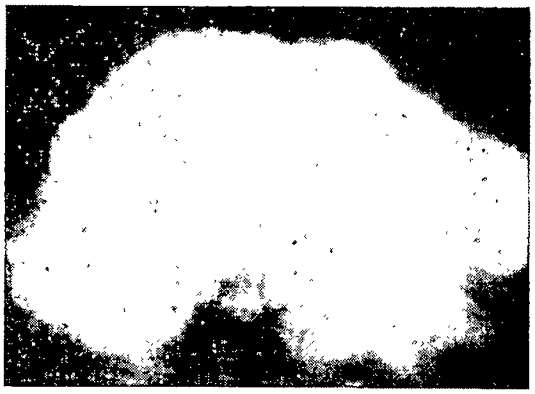


FIG. 2.—Dissecting microscope (×12) appearance of convoluted jejunal mucosa from patient with psoriasis.

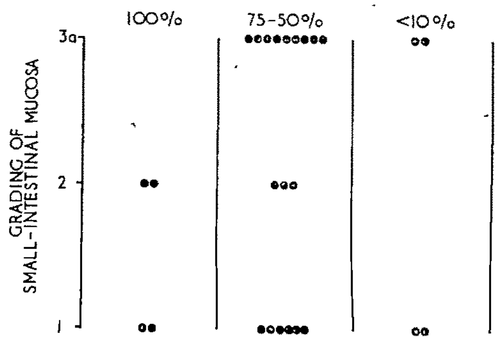


FIG. 3.—To show lack of correlation between mucosal involvement and proportion of skin surface affected by psoriasis.

An abnormality was noted in 12 of the 24 patients whose mucosal biopsies were examined for enzyme activity. This abnormality occurred mainly in patients with a convoluted mucosa. The columnar cells of the surface epithelium covering the free ends of the villi showed loss or inhibition of three membrane enzymes associated with the brush borders of the cells—that is, leucine aminopeptidase, non-specific alkaline phosphatase, and adenosine triphosphatase (Fig. 4). The activity of these enzymes was normal in the brush border other than at the free ends of the villi. Furthermore, the affected cells showed no abnormality in the activity or distribution of the other enzymes studied. In one patient a second biopsy taken six weeks after the first again showed the abnormality. The affected cells showed no unusual features in haematoxylin-and-eosin-stained paraffin sections, and the brush borders gave their usual deep staining reaction with the periodic-acid–Schiff method.

Discussion

Steatorrhoea is common in patients with psoriasis, and this disease and eczema are the main known causes of dermatogenic enteropathy (Shuster and Marks, 1965 ; Watson, Marks, and Shuster, 1967 ; Shuster, 1967a, 1967b). In the present study a convoluted mucosa, together with a histological appearance of partial villous atrophy, was found in 12 out of 26 patients with psoriasis. Though a convoluted mucosa has been found in apparently normal Asians living in India (Baker, Ignatius, Mathan, Vaish, and Chacko, 1962) and Singapore (England and O'Brien, 1966), it was not found in Europeans living in the same area. In a recent study of malabsorption in Scotland (Girdwood, Williams, McManus, Dellipiani, Delamore, and

Kershaw, 1966) none of the 52 control subjects showed a ridged or convoluted jejunal mucosa. It appears, therefore, that our finding of a convoluted mucosa in 46% of our patients with psoriasis is significant. Though none of our patients had a flat mucosa with subtotal villous atrophy we would not wish to exclude the possibility that this may occur.

The steatorrhoea is closely related to the extent of skin involvement (Fig. 1), whereas the mucosal abnormality is not so related (Fig. 3). It is likely, therefore, that there is no relation between degree of steatorrhoea and severity of mucosal abnormality, though our present data on this point are incomplete.

The enteropathy of psoriasis is characterized, therefore, by steatorrhoea with partial villous atrophy or an apparently normal mucosa. In this respect psoriatic enteropathy resembles tropical sprue rather than coeliac disease (England and O'Brien, 1966), as do other forms of dermatogenic enteropathy (Shuster, 1967a, 1967b; Watson *et al.*, 1967).

Many of the biopsy specimens were found to have lost activity of membrane enzymes in the brush borders of the absorptive cells over the free ends of the villi. The possibility of an artifact cannot be completely excluded, though we have been unable to incriminate any variation in our laboratory procedures. In one patient two biopsies were taken at an interval of several weeks and the abnormality was present in both. The site of the abnormality raises the possibility that it has resulted from the action of the intestinal contents on the cell surface. Alternatively there may be some intrinsic abnormality of the epithelium. Though this histochemical abnormality has been found most commonly in patients with psoriasis, it has also been seen in a few patients with eczema, pemphigoid, and dermatitis herpetiformis (unpublished observations), and further investigations are in progress.

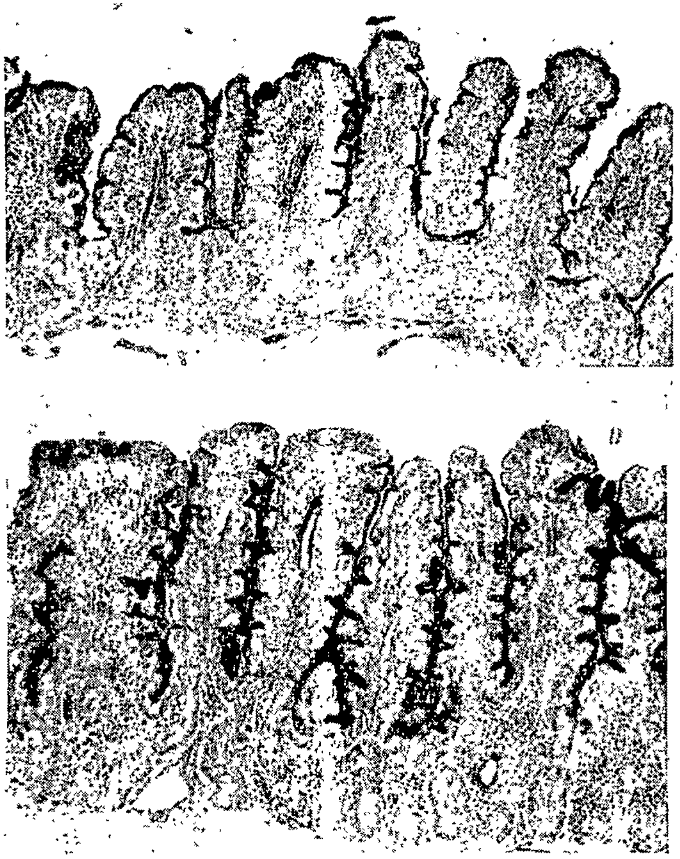


FIG. 4.—Microscopical appearances (×63) of jejunal mucosa from two patients with psoriasis. Above: normal distribution of adenosine triphosphatase activity in surface epithelium of villi. Below: loss of adenosine triphosphatase activity in surface epithelium over free ends of villi.

As with the other forms of dermatogenic enteropathy the immediate cause of the intestinal disorder of psoriasis is speculative (Shuster, 1967a, 1967b). Since the incidence and degree of the steatorrhoea are related to the extent of the skin disease, and since it regresses when the rash is treated topically (Shuster and Marks, 1965), the steatorrhoea is clearly secondary to the skin disease. We do not yet know whether the jejunal mucosa likewise reverts to normal after treatment.

The true incidence and severity of psoriatic enteropathy are unknown; the findings in the present study may reflect the severity of the rash in patients referred to our unit, and much further work will need to be done to define the practical importance of psoriatic and other dermatogenic enteropathies.

Summary

Small-intestinal structure and function were investigated in patients with psoriasis. Faecal fat excretion was measured in 26 and D-xylose absorption in 10; jejunal biopsy appearances were studied in 26. The incidence and degree of steatorrhoea were related to the extent of skin involvement. A convoluted appearance was found in 46% of the jejunal mucosae examined, and a number of these showed a loss of enzyme activity in the brush border of the absorptive cells at the free ends of the villi.

We are grateful to our colleagues at the Royal Victoria Infirmary and the North-east Region for referring patients to us. We are also grateful to Professor A. L. Latner, in whose department the fat and xylose estimations were carried out. We wish to thank Mr. J. R. Maclennan and Mr. J. A. Stewart for valuable technical assistance.

The work was supported by a grant from the Medical Research Council, which we are happy to acknowledge.

REFERENCES

Baker, S. J., Ignatius, M., Mathan, V. I., Vaish, S. K., and Chacko, C. C. (1962). In *Intestinal Biopsy*, Ciba Foundation Study Group No. 14, edited by G. E. W. Wolstenholme and M. P. Cameron. London.

Booth, C. C., Stewart, J. S., Holmes, R., and Brackenbury, W. (1962). Ibid.

Burstone, M. S. (1958a). *J. Histochem. Cytochem.*, **6**, 87.

—— (1958b). *J. Nat. Cancer Inst.*, **21**, 523.

Crosby, W. H., and Kugler, H. W. (1957). *Amer. J. dig. Dis.*, **2**, 236.

Doniach, I., and Shiner, M. (1957). *Gastroenterology*, **33**, 71.

England, N. W. J., and O'Brien, W. (1966). *Gut*, **7**, 128.

Fourman, L. P. R. (1948). *Clin. Sci.*, **6**, 289.

Girdwood, R. H., Williams, A. W., McManus, J. P. A., Dellipiani, A. W., Delamore, I. W., and Kershaw, P. W. (1966). *Scot. med. J.*, **11**, 343.

Hess, R., Scarpelli, D. G., and Pearse, A. G. E. (1958). *Nature (Lond.)*, **181**, 1531.

Holt, S. J. (1958). In *General Cytochemical Methods*, edited by J. F. Danielli, vol. 1, p. 375. New York and London.

Hourihane, D. O'B. (1966). In *Recent Advances in Pathology*, 8th ed., edited by C. V. Harrison, p. 320. London.

Nachlas, M. M., Crawford, D. T., and Seligman, A. M. (1957). *J. Histochem. Cytochem.*, **5**, 264.

—— Tsou, K.-C., de Souza, E., Cheng, C.-S., and Seligman, A. M. (1957). Ibid., **5**, 420.

Novikoff, A. B., and Goldfischer, S. (1961). *Proc. nat. Acad. Sci. (Wash.)*, **47**, 802.

Padykula, H. A., and Herman, E. (1955). *J. Histochem.*, **3**, 161.

Roe, J. H., and Rice, E. W. (1948). *J. biol. Chem.*, **173**, 507.

Rosenblatt, D. H., Nachlas, M. M., and Seligman, A. M. (1958). *J. Amer. chem. Soc.*, **80**, 2463.

Shuster, S. (1967a). In *3rd. Symposium on Advanced Medicine*, edited by A. M. Dawson. Royal College of Physicians London. In press.

—— (1967b). *Lancet*, **1**, 907.

—— and Marks, J. (1965). Ibid., **1**, 1367.

Van de Kamer, J. H., ten Bokkel Huinink, H., and Weyers, H. A. (1949). *J. biol. Chem.*, **177**, 347.

Watson, A. J., Marks, J. M., and Shuster, S. (1967). Unpublished observations.

Rhinovirus Infection in Acute Exacerbations of Chronic Bronchitis: A Controlled Prospective Study*

A. C. STENHOUSE,† B.MED.SC., M.B., M.R.C.P., M.R.A.C.P.

Brit. med. J., 1967, 3, 461–463

Natural rhinovirus infection in adults is usually associated with an afebrile coryzal syndrome (Hobson and Schild, 1960; Hamre and Procknow, 1961; Reilly *et al.*, 1962; Forsyth *et al.*, 1963), and, depending on the population studied, rhinoviruses as a group are associated with 8 to 25% of minor upper respiratory illnesses in adults and from 5 to 20% of such illnesses in children (Tyrrell and Bynoe, 1961; Johnson *et al.*, 1962; Kendall *et al.*, 1962; Bloom *et al.*, 1963; Hamparian *et al.*, 1964). Forsyth *et al.* (1963) found in Servicemen from whom rhinoviruses were isolated that 50% experienced chest pain and 86% reported a cough. Taylor-Robinson *et al.* (1963) and Hamparian *et al.* (1964) each reported the isolation of a rhinovirus from an adult with bronchitis. In the collaborative study on the aetiology of acute respiratory infections in Great Britain from 1961 to 1964, 179 patients were reported as having bronchitis. No indication was given regarding the age of the subjects, but 23% were associated with infective agents and in four instances rhinoviruses were isolated (Medical Research Council, 1965b). In a direct study of 15 chronic bronchitis patients over a period of two and a half years, Eadie *et al.* (1966) studied 75 acute respiratory illnesses and reported the isolation of 12 rhinoviruses. Eleven rhinoviruses were isolated from 47 illnesses affecting the chest, whereas only one rhinovirus was isolated from 28 illnesses not affecting the chest. The only other study of acute exacerbations of bronchitis which employed techniques for rhinovirus isolation failed to detect these agents (Carilli *et al.*, 1964).

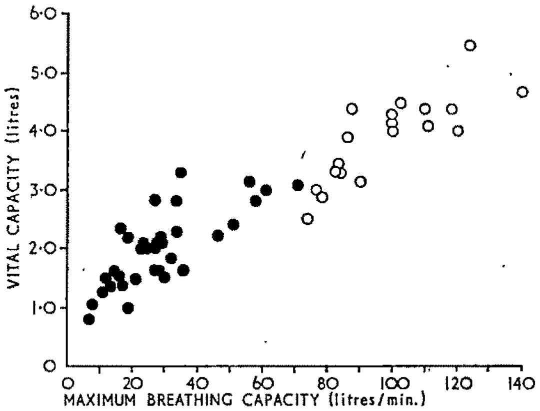
The purpose of this paper is to report the findings of a controlled prospective study designed to determine the significance of rhinovirus infection on the aetiology of acute exacerbations in patients with chronic bronchitis and to describe the clinical picture associated with such infections.

Materials and Methods

Clinical

Thirty-four patients attending the bronchitis clinic, the Royal Hospital, Sheffield, and 19 control subjects enrolled from the staffs of the Sheffield Fire Board and Lodge Moor Hospital, Sheffield, were studied between 18 August 1964 and 1 May 1965. Each patient and subject completed the short questionary on respiratory symptoms (*Brit. med. J.*, 1960) approved by the Medical Research Council Committee on the Aetiology of Chronic Bronchitis. The chronic bronchitis patients fulfilled the criteria for chronic bronchitis as defined by the American Thoracic Society (1962) and Medical Research Council (1965a), and they were clearly able to distinguish between quiescent and exacerbation periods. They comprised 31 men and three women, with a mean age of 61 (range 51 to 73) years. On the basis of the subclassification suggested by the Medical Research Council (1965a) one patient was classified under simple chronic bronchitis, and of the 33 who exhibited airways obstruction, 5 produced mucopurulent sputum and 28 mucoid sputum. The control subjects, comprising 2 women and 17 men with a mean age of 51 (range 32 to 60) years, were shown on the basis of questionary findings and ventilatory function studies to be free of chronic bronchitis or other respiratory disease.

Subjects of both groups were seen at monthly intervals and in addition were asked to report as soon as possible after the onset of an acute infection of the upper or lower respiratory tract. On each occasion that a subject was seen a clinical form was completed. The presence of any upper or lower respiratory tract symptoms during the previous month and the state of the subject at the time of completion of the form were noted. In the chronic bronchitis patients the nature and amount of sputum produced, together with the occurrence of wheeze and shortness of breath, were recorded invariably, and at hospital visits the maximum breathing capacity and the vital capacity were measured by a Poulton Barry SP126 (McKerrow *et al.*, 1960). The mean vital capacity and maximum breathing capacity in the chronic bronchitis patients and control subjects are shown in the Chart.



Mean vital capacity and maximum breathing capacity in chronic bronchitic and control groups. ● = Chronic bronchitis patients. ○ = Control subjects.

The term "acute exacerbation of chronic bronchitis" embraces a spectrum of clinical disorders and was defined in this study as "an alteration in the quiescent state of the patient with an increase in either the quantity or purulence of the sputum."

Virological

On each occasion that subjects were seen a throat swab was obtained and a nasal washing with phosphate-buffered saline made. The throat swabs and nasal washings were placed in a transport medium containing 10% bovine serum albumin and kept at 4° C. Specimens were either inoculated into tissue-culture tubes within three hours of collection or frozen at −70° C. and stored until tested. Sputum specimens obtained from bronchitic subjects were placed at 4° C. for three hours and rendered non-toxic for tissue culture by emulsification in transport medium. They were then centrifuged at 2,000 r.p.m. for 30 minutes and the supernatant fluids stored at $-70°$ C. Blood was obtained by venepuncture, and after separation the serum was stored at $-20°$ C.

---

* This study is included in material to be presented in a thesis as partial fulfilment of the M.D. degree of the University of Otago, New Zealand.

† Wellcome Research Fellow, University Department of Medicine, the Royal Hospital, Sheffield, and the University of Sheffield, Virus Research Laboratory, Lodge Moor Hospital, Sheffield. Present address: Wellcome Virus Research Laboratory, Colonial War Memorial Hospital, Suva, Fiji.

Secondary rhesus monkey kidney, human embryo kidney, human diploid (WI-38 and HEL 7 strains), and Bristol HeLa cells were used during this investigation. With the use of standard isolation procedures the HeLa tissue cultures were shown to contain mycoplasma agents. The laboratory procedures for tissue culture and virus isolation studies paralleled the methods described by the Medical Research Council (1965b).

Rhinoviruses isolated at 33° C. were recognized by their inability to grow at 37° C. in an alkaline medium, and lack of haemadsorption with human group O cells. Subsequently an acid stability test at *p*H 3 was performed (Dimmock and Tyrrell, 1962), and when calculated by the method of Reed and Muench (1938) a hundredfold or greater reduction in titre was taken as evidence of acid lability (Tyrrell and Chanock, 1963). If the rhinovirus was isolated in, or could be propagated in, rhesus monkey kidney cells it was designated as an M strain; otherwise it was classified as an H strain of rhinovirus. Isolates suspected of being herpes simplex virus were identified by neutralization with type-specific antiserum. Homologous rhinovirus neutralization was performed with serial fourfold dilutions of acute and convalescent serum inactivated at 56° C. for 30 minutes, starting at 1 in 8. Serum dilutions were incubated for one hour at room temperature with 50 to 100 50% tissue-culture infective doses ($TCID_{50}$) of homologous virus. Two WI-38 tubes were inoculated with 0.2 ml. of virus-serum mixture and were rolled at 33° C. Complete suppression of cytopathic effect after 10 days' incubation was used to determine the end-points.

Results

Virus Isolations

A total of 299 specimens from the chronic bronchitis patients and 109 specimens from the controls were obtained during the course of the study. Each specimen consisted of a nasal washing and throat swab; a sputum sample was also examined from the bronchitis patients. From the chronic bronchitis patients 237 specimens were taken during periods of quiescence or at more than 10 days after the onset of the acute respiratory symptoms. From the control subjects 88 specimens were examined when they were well. Of the 62 specimens obtained from the chronic bronchitis patients 10 days or less after the onset of an acute respiratory infection 56 had an acute exacerbation of bronchitis, and 38 of these were associated with upper respiratory symptoms. The 21 specimens from the control subjects were collected within six days of the onset of an acute upper respiratory illness.

Nineteen viruses were isolated during the course of the study, and 18 of these were rhinoviruses and one was a strain of herpes simplex isolated in human embryo kidney cells from the sputum of a patient 14 days after the onset of an acute exacerbation of bronchitis. No agents were isolated by means of the haemadsorption technique.

Table I shows the number of rhinoviruses isolated in relation to the clinical state of the chronic bronchitic and control subjects at the time of isolation. During quiescence five rhinoviruses were isolated from the patients and one from the control subjects in the absence of clinical illness, giving isolation rates of 2.1 and 1.1% for the patients and control subjects respectively. During acute exacerbations eight rhinoviruses were isolated from the patients and four were isolated from the control subjects at the time of an acute respiratory infection, giving an isolation rate of 14.3% for bronchitic subjects and 19% for control subjects. No viruses were isolated from the throat swabs or nasal washings collected more than six days after the onset of an acute respiratory infection except those unrelated to acute symptoms. The two rhinovirus strains isolated from the sputum were not recovered from nasal washings or throat swabs taken at the same time, and one of these was isolated 10 days after the onset of acute respiratory symptoms. Of 18 rhinovirus strains 13 were reisolated after storage for 4 to 12 months at $-70°$ C.

TABLE I.—*Number of Rhinoviruses Isolated in Chronic Bronchitic and Control Subjects in Relation to the Clinical State*

Subjects	No. of Specimens Tested	No. of Rhinoviruses Isolated	Percentage Isolated
Chronic bronchitic:			
Quiescent	237	5	2·1
Acute exacerbations of bronchitis ..	56	8	14·3
„ upper respiratory infections	6	0	—
Control:			
No illness	88	1	1·1
Acute respiratory infection	21	4	19·0

Neutralizing Antibody Titres

Table II summarizes the results of homologous neutralization tests carried out on six paired sera from subjects whose throat swabs or nasal washings yielded a rhinovirus. One of the patients from whom a rhinovirus was both isolated and reisolated in the quiescent state showed a high level of neutralizing antibody in the acute serum.

TABLE II.—*Homologous Neutralization Titres* in Six of the Subjects Yielding a Rhinovirus*

Neutralizing Antibody Titres		$TCID_{50}$ in Test
Acute	Convalescent	
<8	32	50
<8	16	100
<8	32	50
<8	8	100
<8	16	100
64	64	50

* Reciprocal values of titre given.

Clinical Picture

All the eight chronic bronchitic patients from whom a rhinovirus was isolated during an acute respiratory illness developed an acute exacerbation of bronchitis. This was characterized by increased production of sputum—purulent in six of the eight patients—increased wheeziness, shortness of breath, and cough. Five experienced substernal chest pain typical of tracheitis and six had mild rhinorrhoea. The control subjects, on the other hand, presented with an afebrile or febrile rhinorrhoea in association with a rhinovirus infection.

A clinical description of two of the acute illnesses associated with recovery of a rhinovirus from the chronic bronchitis patients is given.

Case 1.—A 62-year-old man experienced increased wheezing and coughing on 28 December 1964. Next day he developed rhinorrhoea, a mild sore throat, and substernal chest pain. His sputum increased in volume without becoming purulent, and he was more short of breath. A diagnosis of a common cold with acute tracheobronchitis was made. An H rhinovirus was isolated from his sputum obtained on 30 December. No virus was found in the throat swab or nasal washings taken at the same time. His symptoms gradually improved over the following week.

Case 2.—On 8 November 1964 a 50-year-old man developed malaise; he became more wheezy, and his sputum increased in volume and was purulent. When examined six days later he had improved slightly and there were no symptoms or signs of an upper respiratory infection. A diagnosis of acute exacerbation of bronchitis was made, and an M rhinovirus was isolated from a throat swab taken on 14 November 1964.

Discussion

Before rhinoviruses can be claimed to be a cause of acute exacerbations of bronchitis a modernized version of Koch's postulates must be fulfilled (Tyrrell, 1963).

Firstly, the respiratory secretions of a comparable group of patients and healthy subjects must be tested under similar conditions for the rhinoviruses. A comparison of the isolation rates of rhinoviruses of the chronic bronchitis patients and the control subjects during acute respiratory infections indicates that both groups are infected to a similar extent. The rhinovirus isolation rate of 2% for the chronic bronchitis patients in the quiescent phase and of 1% for the control subjects in the absence of clinical symptoms is in accord with previously published results from asymptomatic subjects (Hobson and Schild, 1960 ; Hamre and Procknow, 1961 ; Hamparian *et al.*, 1964). This indicates, firstly, that in both the chronic bronchitic and control groups the rhinoviruses are probably responsible for the disease produced, and, secondly, that the respiratory secretions of the chronic bronchitic subjects do not harbour rhinoviruses to any greater extent than normal subjects.

The results of the clinical studies show that in the bronchitic subjects rhinovirus infections result in acute exacerbations of bronchitis, while normal persons present a febrile or afebrile rhinorrhoea. These findings are in accord with the observations of Eadie *et al.* (1966), who reported that rhinovirus infections were more often associated with respiratory illnesses which affected the chest than with those which did not. These observations are supported by the findings of Cate *et al.* (1965), who, using a Collison atomizer, which gives a small-particle aerosol, showed experimentally that the lower respiratory tract of adults is quite sensitive to rhinovirus infection by producing, in volunteers, a tracheobronchitis with a low dose (16 to 11 $TCID_{50}$) of a rhinovirus.

The lower isolation rate of rhinovirus from the chronic bronchitis patients during acute exacerbations as compared with the findings of Eadie *et al.* (1966) is likely to be due to the earlier reporting of illness and the more frequent visitation of their patients. Of the 62 acute respiratory illnesses in the present study only six showed no evidence of involvement of the lower respiratory tract, as compared with 25 out of 75 reported by Eadie *et al.* (1966). This may be a reflection of a more advanced stage of the disease of the patients in the present study, but it is difficult to compare directly the ventilating function studies in the two groups. The report by Eadie *et al.* (1966) of the isolation of five rhinoviruses from the sputum, three of which were not recovered from a throat swab taken on the same occasion, is confirmed by the present study, where two rhinoviruses were isolated from the sputum but not from the throat swab or nasal washing, and indicates that attempts at sputum isolation are worth while.

The second modified Koch's postulate which it is desirable to fulfil is the demonstration of a rise in the titre of the homologous rhinovirus antibody during convalescence, indicating that infection was active at the time at which symptoms occurred and the virus isolation was made. In this study five out of six specimens tested showed a rise in titre of the homologous antibody in the convalescent specimen. The single exception occurred in a patient in the quiescent phase from whom a rhinovirus was isolated and subsequently reisolated from the throat swab. In this instance both the initial serum specimen and one taken four weeks later neutralized the homologous virus to a titre of 1 in 64. The possibilities are that this specimen was contaminated at the time of collection, that a subclinical reinfection occurred, or that the patient continued to excrete the virus for some time after infection—a situation which at present is only speculative.

These results indicate that in normal subjects rhinovirus infection gives rise to an afebrile or febrile coryzal syndrome while in chronic bronchitic patients an acute exacerbation of bronchitis is produced. It is likely that a more complete understanding of the nature of the agents responsible for the initiation of acute exacerbations will parallel the application of advances in techniques for the isolation of viruses from acute respiratory infections as a whole.

Summary

In a controlled prospective study employing virus isolation and homologous neutralizing antibody levels an association between rhinovirus infection and acute exacerbations of bronchitis in chronic bronchitic patients is described. Eight of 56 (14%) of such illnesses yielded rhinoviruses. The isolation of five rhinoviruses from 237 specimens (2.1%) from the same patients in the quiescent phase is in accord with previously published figures on the isolation rate of rhinoviruses from normal asymptomatic subjects.

The chronic bronchitis patients during rhinovirus infection present clinically with an acute exacerbation with or without an associated upper respiratory illness. This pattern of clinical illness is contrasted with a control group who presented a febrile or afebrile rhinorrhoea.

It is a pleasure to record my appreciation of the help received from Professor C. H. Stuart-Harris in all phases of this study and for the permission given to investigate patients under his care. I should like to thank the Chief Technician, Mr. J. Skelton, and the technical staffs of the Virus Research Laboratory, Lodge Moor Hospital, and of the department of medicine, the Royal Hospital, Sheffield, for their considerable part in this study ; in particular, Miss Lynda Bebbington for her excellent assistance at all times. I should also like to express my thanks to Dr. G. C. Schild, of the department of bacteriology, the University of Sheffield, for many helpful discussions, and to Dr. D. A. J. Tyrrell, of the Common Cold Research Unit, Salisbury, for continual advice and helpful comments on this paper.

References

American Thoracic Society (1962). *Amer. Rev. resp. Dis.*, **85**, 762.
Bloom, H. H., Forsyth, B. R., Johnson, K. M., and Chanock, R. M. (1963). *J. Amer. med. Ass.*, **186**, 38.
Brit. med. J., 1960, **2**, 1665.
Carilli, A. D., Gohd, R. S., and Gordon, W. (1964). *New Engl. J. Med.*, **270**, 123.
Cate, T. R., Couch, R. B., Fleet, W. F., Griffith, W. R., Gerone, P. J., and Knight, V. (1965). *Amer. J. Epidem.*, **81**, 95.
Dimmock, N. J., and Tyrrell, D. A. J. (1962). *Lancet*, **2**, 536.
Eadie, M. B., Stott, E. J., and Grist, N. R. (1966). *Brit. med. J.*, **2**, 671.
Forsyth, B. R., Bloom, H. H., Johnson, K. M., and Chanock, R. M. (1963). *New Engl. J. Med.*, **269**, 602.
Hamparian, V. V., Leagus, M. B., Hilleman, M. R., and Stokes, J. (1964). *Proc. Soc. exp. Biol. (N.Y.)*, **117**, 469.
Hamre, D., and Procknow, J. J. (1961). *Brit. med. J*, **2**, 1382.
Hobson, D., and Schild, G. C. (1960). Ibid., **2**, 1414.
Johnson, K. M., Bloom, H. H., Chanock, R. M., Mufson, M. A., and Knight, V. (1962). *Amer. J. publ. Hlth*, **52**, 933.
Kendall, E. J. C., Bynoe, M. L., and Tyrrell, D. A. J. (1962). *Brit. med. J.*, **2**, 82.
McKerrow, C. B., McDermott, M., and Gilson, J. C. (1960). *Lancet*, **1**, 149.
Medical Research Council (1965a). Ibid., **1**, 775.
—— (1965b). *Brit. med. J.*, **2**, 319.
Reed, L. J., and Muench, H. (1938). *Amer. J. Hyg.*, **27**, 493.
Reilly, C. M., *et al.* (1962). *Ann. intern. Med.*, **57**, 515.
Taylor-Robinson, D., Johnson, K. M., Bloom, H. H., Parrott, R. H., Mufson, M. A., and Chanock, R. M. (1963). *Amer. J. Hyg.*, **78**, 285.
Tyrrell, D. A. J. (1963). *Amer. Rev. resp. Dis.*, **88**, Suppl., p. 77.
—— and Bynoe, M. L. (1961). *Brit. med. J.*, **1**, 393.
—— and Chanock, R. M. (1963). *Science*, **141**, 152.

Mycological and Clinical Evaluation of Griseofulvin for Chronic Onychomycosis

R. R. DAVIES,[*] M.SC., PH.D.; J. D. EVERALL,[†] M.R.C.P., M.R.C.S.; ELIZABETH HAMILTON,[*][‡] B.SC., PH.D.

Brit. med. J., 1967, **3**, 464–468

When griseofulvin became available in 1959 a critical evaluation of its use in chronic tinea of the nail was begun. Since then 122 patients have been treated with a standard dose[§] (0.5 g. t.d.s. for one month followed by 0.5 g. b.d.) for a minimum of six months and 74 for two years. As the trial progressed it became evident that a longer course of treatment was required than that suggested in earlier reports on the efficacy of the drug—namely, Williams *et al.* (1958) and Blank *et al.* (1959). It was therefore decided to treat for two years and to follow up the patient for a further year without treatment. Those failing to take the drug consistently throughout the lengthy period of treatment were transferred to an "intermittent-dose group."

Methods

At the patient's first visit numerous relevant clinical facts were recorded, and towards the end of the trial the blood and stool porphyrin levels were measured. All the nails of the hands and feet were examined mycologically and clinically, as were the soles, outer toe clefts, thumb crutches, and any other apparently affected site.

For the detailed mycological investigations parings were collected into sterile Petri dishes from all the nails, the clinically normal as well as the dystrophic, and skin scrapings were taken from the soles, webs, thumb crutches, and any other site that seemed to be infected. At least nine pieces of nail from each site were cultured—six in malt extract agar containing 40 μg. of chloramphenicol per ml. and 0.5 mg. of cycloheximide per ml. and three in peptone glucose agar containing 40 μg. of chloramphenicol per ml. Three or four small pieces of nail from each site were examined by direct microscopy in 30% potassium hydroxide (KOH). Skin scrapings were similarly investigated. The patients were thoroughly examined clinically at six-week intervals and the detailed mycological investigations were undertaken every six months.

When cultures were obtained the in-vitro sensitivities of the fungi were tested to investigate the possibility of their developing an increased resistance to the antibiotic during the course of treatment and to determine whether the sensitivity of the infecting organism to the antibiotic was reflected in the patient's response to therapy.

Results

When the trial was concluded 122 patients with mycologically proved onychomycosis had been treated for not less than six months. In 68 (56%) the infecting organism was *Trichophyton rubrum* (Castellani) Sabouraud, and in 22 (18%) it was *T. mentagrophytes* (Robin) Blanchard. From the nails of six patients both these species were isolated; and in 26, despite repeated attempts, no fungus was ever grown, though the presence of mycelium in KOH preparations was clear evidence of onychomycosis.

The number of patients treated with the standard dose or intermittent dose (defaulters) for various periods is shown in Table I.

TABLE I

Fungus	Dose	Months of Treatment				Months Followed	
		6	12	18	24	30	36
T. rubrum ..	Standard	47	41	38	32	23	15
	Intermittent	21	20	16	9	8	6
T. mentagrophytes	Standard	7	7	5	4	3	0
	Intermittent	15	13	11	11	7	7
T. rubrum + *T. mentagrophytes*	Standard	4	4	4	4	1	1
	Intermittent	2	2	1	1	1	1
No culture group	Standard	5	4	3	2	2	2
	Intermittent	21	18	12	11	8	4

Therapeutic Response in Patients with *T. rubrum* Infections

Response to treatment may be judged from two sets of criteria—by the clinical observation of dystrophy, and the mycological evidence of mycelium in KOH preparations or the isolation of dermatophyte fungi. When fungus is observed or is isolated from a dystrophic nail it is irrefutable evidence of infection; on the other hand the failure to discover fungus in the parings from a particular nail is not necessarily evidence that the whole nail is uninfected. However, where the nail has been repeatedly examined for fungus by two methods over a period of many months the possibility of missing an infection must be small, and in this respect it is noteworthy that during these studies dermatophyte fungi were found in clinically normal nails. Nail dystrophy, even in patients with some onychomycosis, is not necessarily due to fungal infection but might arise from a variety of causes. Since even a cosmetic improvement in the case of infected finger-nails is desirable, particularly in women, the clinical and more exact mycological findings are presented separately.

As *T. rubrum* was the commonest cause of onychomycosis in the patients studied, the response of those infected with this organism is described in detail; that of the other groups is briefly summarized.

Nail Infections Before Treatment

In 50 of the 68 patients onychomycosis involved both toe-nails and finger-nails, in 16 it was confined to the feet, and in 2 to the finger-nails alone. One patient, a 20-year-old male Chinese student, seemed exceptional in that all the finger-nails of his right hand were severely dystrophic, and though *T. rubrum* was isolated from each of the nails it was never obtained from any other site despite repeated attempts, and there were no clinical signs of infection elsewhere. He was the only patient with a nail infection who did not also have an infection of the smooth skin when first seen.

---

[*] Wright-Fleming Institute of Microbiology, St. Mary's Hospital Medical School, London W.2.

[†] Royal Marsden Hospital, London S.W.3.

[‡] Now at 65 Greencourt Road, Petts Wood, Kent.

[§] The griseofulvin used was that first available; this has since been replaced by a variant of the drug of finer particle size.

The percentages of patients, with the number of finger-nails and toe-nails recorded from mycology or clinical observation as infected before treatment, are shown in Figs. 1 and 2. Of the patients presenting finger-nail infections 28 (58%) were judged to have dystrophy of all their finger-nails, though, mycologically, the maximum number infected in any patient was eight, and only four (6%) had as many as eight infected. The discrepancy between clinical observation and the mycological findings, though maintained throughout the trial, was less evident in toe-nail infections. Clinically, 48 (73%) of the patients were judged to have all their toe-nails infected, whereas mycologically in only 17 (26%) was this so.

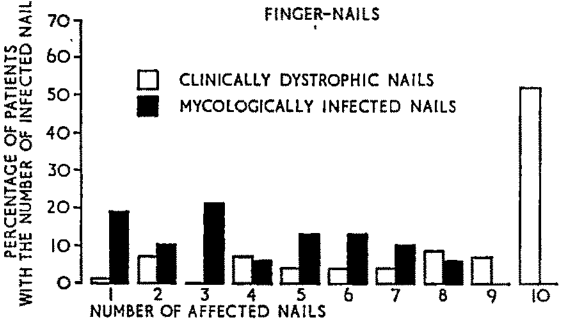


FIG. 1

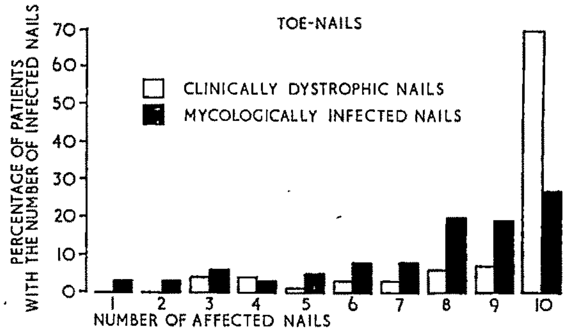


FIG. 2

FIG. 1.—Percentage of patients having one to ten finger-nails infected before treatment. FIG. 2.—Percentage of patients having one to ten toe-nails infected before treatment.

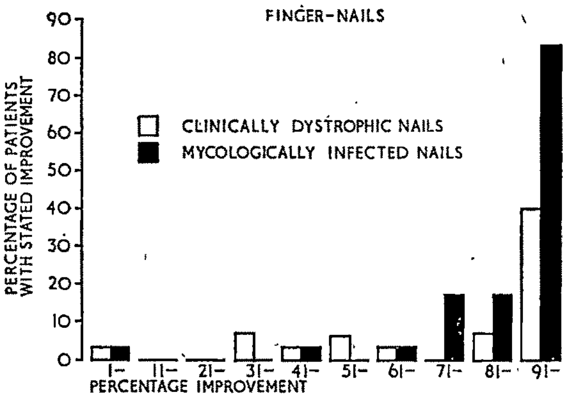


FIG. 3

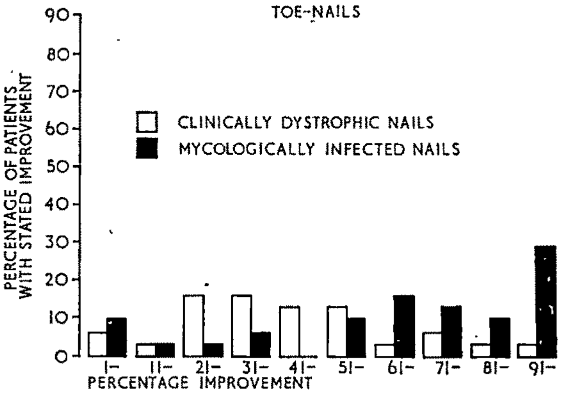


FIG. 4

FIG. 3.—Patients with *T. rubrum* infection of finger-nails treated with a standard dose of griseofulvin for two years; percentage showing improvement, which for each patient was calculated as a percentage of the maximum of nails infected. FIG. 4.—Patients with *T. rubrum* infection of toe-nails treated with a standard dose of griseofulvin for two years; percentage showing improvement, which for each patient was calculated as a percentage of the maximum of nails infected.

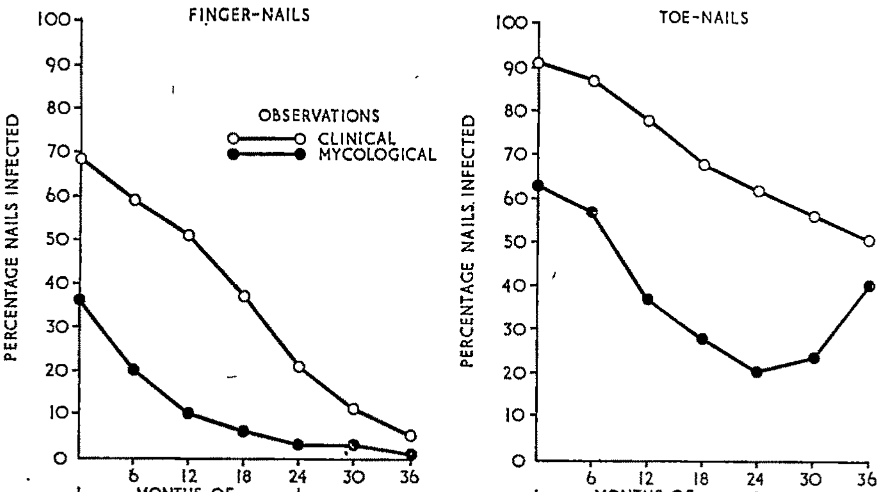


FIG. 5.—Percentage of infected nails in patients with *T. rubrum* infections treated with a standard dose of griseofulvin for 24 months and followed for another 12 months without treatment.

Therapeutic Response to Standard Dose

Response to treatment (Figs. 3 and 4) is given as the percentage of patients showing an improvement, which for each subject has been calculated as a percentage of the maximum number of nails infected. After 24 months' treatment clinical cures were recorded in 12 (40%) patients with finger-nail infections; mycologically, 24 (80%) were cured. With regard to toe-nail infections, while only 1 patient (3%) was thought to be clinically cured, the mycological evidence showed that in 9 (29%) patients cure was effected.

After 24 months, during which time each patient had taken 1 g. of griseofulvin daily for 23 months, treatment was stopped and the patients were kept under observation for another year. It must here be emphasized that in the trial of a treatment "for a relatively rare" condition it takes many months to collect patients, and when after six years we decided to conclude the trial, though 74 patients had been treated for two years, only 53 had been followed for six months after treatment and 36 for the full year. Since the number treated and followed diminished steadily between 6 and 36 months, to determine the effect of treatment and its cessation in a group of patients the percentage of infected nails at each of the different time intervals is shown in Fig. 5.

On both clinical and mycological criteria the numbers of infected finger-nails decrease and show no evidence of relapse during and after treatment. With toe-nail infections the clinical observations reveal a steady improvement throughout, from 91% down to 62% of toe-nails infected at the end of treatment, down to 51% of the nails infected after a further year without treatment. The mycological evidence shows improvement from 63% of toe-nails infected before treatment down to 20% infected after two years' treatment. Six months after treatment was stopped a small rise to 23% of infected nails was recorded, but within a year of stopping treatment 40% of the nails were found to be infected, showing clear mycological evidence of relapse not apparent to the clinician.

Thumb Crutch and Outer Toe Web Infections

During the course of the trial it became apparent that in some patients outer toe web infections were persistent. The percentage of patients having both, one, or no thumb crutches infected and both, one, or no outer toe webs infected, as shown by mycological evidence after different periods of treatment and during the follow-up periods, is illustrated in Fig. 6.

After 12 months' treatment both thumb crutches were clear in over 75% of the patients, after two years 95% of the patients had clear thumb crutches, and there is no evidence of relapse during the year without treatment. With outer toe web infections, however, only 53% of the patients had clear toe webs after two years' treatment, 28% had both webs infected, and 19% had one web infected. A year after the cessation of treatment the proportion of patients with clear toe webs had fallen to 45%, and the number of patients with both their outer toe webs infected had risen 45%. There is therefore a relapse in the smooth-skin infections of the feet which parallels that observed with the toe-nails.

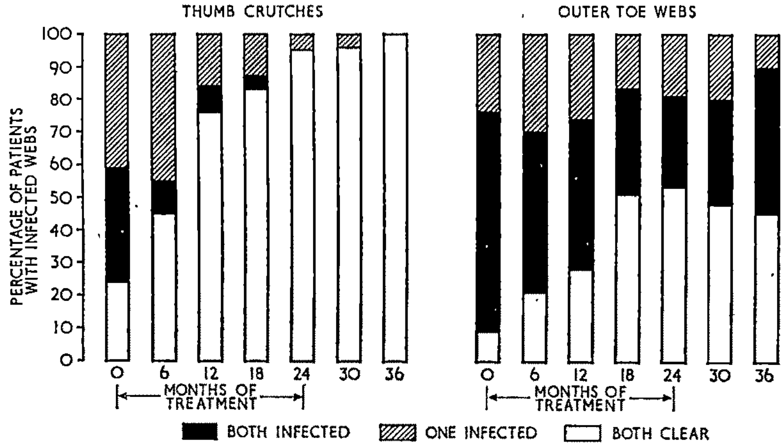


FIG. 6.—Percentage of patients with thumb crutches and outer toe-webs infected by *T. rubrum* as shown by mycological evidence after different periods of therapy with a standard dose of griseofulvin and during a follow-up year without treatment.

Response to Intermittent Griseofulvin Treatment

This smaller group of patients comprised those who were prescribed the standard dose but omitted to take the drug for periods varying from weeks to months during the lengthy period of treatment. The percentage of nails found infected according to clinical and mycological criteria are given in Table II.

TABLE II.—*T. rubrum Response to Intermittent Treatment*

Observations	Months Treated and Followed						
	0	6	12	18	24	30	36
	Percentage of Toe-Nails Infected						
Clinical	76	52	69	64	68	56	64
Mycological	56	43	36	38	38	26	63
	Percentage of Finger-Nails Infected						
Clinical	66	44	25	16	33	14	13
Mycological	43	15	11	14	4	0	1

Clinically, no patient with a toe-nail infection was cured, but 5 out of 10 defaulting patients were cured of their finger-nail infections. Mycologically, three out of eight patients examined after two years' treatment were cleared of toe-nail infections, but one relapsed and had four nails infected after six months without treatment. Another of these patients, who had 10 toe-nails mycologically infected at 12 months, had three infected at 24 months, one at 30 months, and 10 at 36 months. Both these cases presented mycological evidence of relapse in toe-nail infections when treatment was stopped. Mycologically, among five patients with finger-nail infections who were examined after 24 months two had infected nails, but one cleared during the follow-up period and the other was 86% improved.

T. mentagrophytes Infections and Response to Treatment

Of the 22 patients with nail infections due to this fungus only seven did not at some time default in taking the prescribed treatment, and none of these was followed for more than 30 months. As seven of the defaulters were followed for a year after treatment was stopped all the patients with infection due to this fungus are best considered together.

Of the 12 patients treated for two years with finger-nail infections six showed a clinical cure and 10 (83%) were mycologically clear. Thirteen patients with *T. mentagrophytes* infections of their toe-nails were treated for two years, and though no clinical cure was recorded six (46%) were mycologically clear.

The percentage of nails found infected after different periods of treatment is given in Table III. The mycological results are biased in that among 13 patients three with toe-nail infections and one with a finger-nail infection grew worse during the period of treament. The mycological observations on patients with *T. rubrum* infections showed that no patient taking the standard dose of griseofulvin became worse, and among the *T. rubrum*-infected patients treated with an intermittent dose only one patient's toe-nails failed to show improvement.

TABLE III.—*T. mentagrophytes Response to Intermittent Treatment*

Observations	Months Treated and Followed						
	0	6	12	18	24	30	36
	Percentage of Toe-Nails Infected						
Clinical	88·5	75	70	66·5	36	56	49
Mycological	25	22	27	14·5	18	14	13
	Percentage of Finger-Nails Infected						
Clinical	54	28	32	24	22	24	23
Mycological	19	3	12	3	5	13	10

Mixed *T. rubrum* and *T. mentagrophytes* Infections

Six patients had nails infected with both *T. rubrum* and *T. mentagrophytes*. From the nails of another three patients *T. rubrum* was isolated consistently at examinations during the course of treatment, and during the examination at the cessation of treatment *T. mentagrophytes* was found. There were also three patients in whom one of the species of *Trichophyton* was isolated from the nails and the other from the skin.

Before treatment the frequency with which *T. rubrum* was isolated relative to *T. mentagrophytes* from the nails of these patients was 22 to 9; after griseofulvin for a year or more 16 isolates of *T. mentagrophytes* were obtained to 14 of *T. rubrum*. It would therefore appear that *T. mentagrophytes* in nails is less susceptible to griseofulvin than is *T. rubrum*.

Onychomycosis—Fungus Unknown

In 26 patients treated for over six months, while no fungus was isolated, a diagnosis of onychomycosis was confirmed when mycelium was observed in KOH preparations. Of these patients 13 were treated for two years—two with the standard dose and 11 with intermittent dosage—and six were followed for a year after treatment. Despite repeated attempts no fungus was isolated from the nails of these patients. The percentage of nails infected according to clinical and mycological criteria during the course of treatment and follow-up periods is given in Table IV.

TABLE IV.—*Percentage of Toe-nails and Finger-nails Infected with Fungus not Isolated*

Observations	Months Treated and Followed						
	0	6	12	18	24	30	36
				Toe-nails			
Clinical	92	58	70	61	59	54	60
Mycological	30	11	7	15	6	8	0
				Finger-nails			
Clinical	53	59	44	44	17·5	16	32
Mycological	17	14	3	1	1	1	0

The trial described was terminated in 1964. In October 1966 a questionary was sent to 74 patients who had been treated for two years. They were asked if their finger-nails and toe-nails were better or worse, how many were affected, whether they had any irritation or peeling or trouble with the skin of the hands or feet, and whether or not they had consulted a doctor and received treatment for any skin or nail infection.

Only 27 patients returned their forms correctly completed. Of these nine regarded their toe-nail infections as cured, but six of these were known to have had infected toe-nails when they were last seen. Among 18 patients reporting infected toe-nails five recorded a greater number of infected nails than when they were last seen. Another four stated that all their toe-nails were infected, as shown at their last visit to the clinic. From the patients' own descriptions of the state of their toe-nails nine seemed to be unchanged.

Only one patient reported a relapsed finger-nail infection, and he had shown a poor response to treatment throughout the course. Three patients reported peeling skin, four recorded irritation, and four had consulted a doctor.

Toxicity

No patient complained of serious subjective side-effects, but a few reported headaches, which ceased either spontaneously or when the tablets were taken with meals. No change in the red and white blood cell counts was observed in patients under treatment.

Griseofulvin when given to rats in large doses intravenously or intraperitoneally has been reported by Paget and Walpole (1958) to have colchicine-like effects on the seminal epithelium and bone marrow. With high dosage in mice, toxic liver damage occurs (De Matteis and Rimington, 1963), and prolonged intake of griseofulvin leads to the development of hepatoma in the enlarged liver (Hurst and Paget, 1963). Blood and stool porphyrin levels were determined in 84 of the patients in the present trial, and the results have been reported by Rimington *et al.* (1963). Faecal porphyrins were raised in 21 of 50 patients receiving treatment, and in 51 patients in whom erythrocyte porphyrins were determined normal maximum values were exceeded in 20. However, in four out of six patients with onychomycosis who had not been treated with griseofulvin total faecal porphyrins exceeded the normal, and in two blood coproporphyrin levels were slightly raised. Conventional liver-function tests on 10 patients with raised and 10 with normal porphyrin excretion showed no evidence of abnormality.

In vitro Sensitivity of *T. rubrum* and *T. mentagrophytes* to Griseofulvin

Griseofulvin stock solutions in 50% acetone were sterilized by Seitz filtration, and serial dilutions were made in Sabouraud's glucose peptone agar. The concentrations employed to determine the minimum inhibitory concentrations for strains of *T. rubrum* ranged from 0.75 to 4 μg./ml. in 0.25-μg. steps. The inoculum was taken from a freshly grown colony, which when it had attained a diameter of 2 cm. was scraped from the medium, added to 5 ml. of sterile distilled water in a tissue grinder, and after grinding transferred to a sterile container. Each of a series of plates containing griseofulvin, together with control plates, were then inoculated with three 0.02-ml. drops of the inoculum in random order. The cultures were incubated at 25° C. and read after 10 days, and the next highest concentration to that on which growth was recorded was taken as the minimum inhibitory concentration. A total of 57 cultures obtained from patients before treatment and 186 from patients treated for a year or more were screened. The group of pretreatment isolates had a mean M.I.C. of 1.93 μg./ml. (S.D. 0.54), the group from treated patients a mean M.I.C. of 2.17 μg./ml. (S.D. 0.54). Student's *t* test showed no significant difference between the means of the two groups at the 0.1 level. It may be concluded that in patients infected with *T. rubrum* failure to respond to treatment is not due to the fungus becoming resistant to the antibiotic.

The griseofulvin concentrations used to determine the minimum inhibitory concentrations for *T. mentagrophytes* ranged from 2.5 to 16.5 μg./ml. in 1-μg. steps, and cultures were read after seven days' incubation. The 19 isolates obtained from untreated patients had a mean M.I.C. of 4.8 μg./ml. (S.D. 4.68); 98 cultures from patients treated for a year or more had a mean M.I.C. of 7.17 μg./ml. (S.D. 9.37). Student's *t* test showed no significant difference between the means of the two groups at the 0.2 level. In patients infected with *T. mentagrophytes* failure to respond to therapy is not due to the fungus becoming adapted to the antibiotic.

Discussion and Conclusions

In 1961 Ainsworth reported, "More than a hundred papers have been published to show that 1 g. daily of griseofulvin taken orally effectively controls infection in man by diverse dermatophytes in all five continents." This has not been our experience in the study described. Most reports have been a clinician's account of his observations on a small number of patients over a brief period, and, apart from the investigation by Stevenson and Djavahiszwili (1961), even where a clinical diagnosis was confirmed mycologically no consistent mycological investigations appear to have been undertaken.

Alone in the present study have all the nails been repeatedly examined mycologically at regular intervals during and after treatment whether they were dystrophic or not. Stevenson and Djavahiszwili (1961), with 0.5 g. of griseofulvin thrice daily, found that 5 out of 14 patients still had *T. rubrum*-infected toe-nails after 15 months' treatment. The two-year treatment in our trial is the longest one described. Both 1 g. of griseofulvin daily for two years and 1.5 g. daily for 15 months have been inadequate for the elimination of toe-nail infections due to *T. rubrum*. A small group of patients not shown in the results described gave a better response when treated with 1.5 g of griseofulvin daily, but some patients naturally respond better than others. In the follow-up the mycological evidence described showed relapse in toe-nails infected with *T. rubrum* before it was apparent to the clinician (Fig. 5). Among patients who completed questionaries two years later 18 recorded infected toe-nails and 5 (28%) reported a greater number infected than when they were last seen.

Finger-nail infections showed a better response than toe-nails on both mycological and clinical criteria (Fig. 5), and there was no evidence of relapse during the follow-up. Among patients completing questionaries only one described a relapsed finger-nail infection, and he had shown little response to treatment. From the mycological evidence of thumb crutch and outer toe web infections due to *T. rubrum,* the response of smooth-skin infections parallels that of the nails. After two years 95% of the patients had clear thumb crutches, and there is no evidence of relapse during the year without treatment, whereas with outer toe web infections only 53% of the patients had clear toe webs after two years' treatment, and this fell to 45% during the year without treatment.

In no case could a patient's failure to respond to therapy be ascribed to the fungus becoming insensitive to the drug. The rate of growth of finger-nails was unrelated to therapeutic response, as also was the griseofulvin serum levels attained in a limited number of patients.

Mycological observation on patients with nails infected with *T. mentagrophytes* showed that some became worse during the course of treatment; this was not observed in patients with *T. rubrum* infections, and only one patient with a *T. rubrum* infection was not improved. In patients whose nails were infected with both these fungi the frequency with which *T. mentagrophytes* was isolated relative to *T. rubrum* increased during the course of treatment. It may be concluded, therefore, that in nails *T. mentagrophytes* is less likely to be inhibited by oral griseofulvin than *T. rubrum*; in-vitro tests showed that *T. rubrum* has a mean M.I.C. of 2 µg./ml., whereas that for *T. mentagrophytes* was 6.25 µg./ml.

The fact that toe-nail and outer toe web infections did not respond as well as finger-nail and thumb crutch infections may be due to a variety of causes. Gentles (1958) and Gentles *et al.* (1959) have shown that griseofulvin is incorporated in hair, where it presents a barrier to fungal penetration. There seems to be no record of griseofulvin having been recovered from human nails, or of the amounts in finger-nails versus toe-nails. The moisture content of the skin in the toe webs must, however, be higher than that of the thumb crutch, and the effect of sweat in leaching out griseofulvin from the tissues cannot be overlooked. The warm moist feet present a better ecological niche for fungal colonization than the hands, which tend to be drier and cooler, and this alone may account for early relapse in infections of the feet after the cessation of treatment when fungus has not been completely eradicated by the fungistatic antibiotic.

It has been found (Davies, in preparation) that finger-nail is more slowly hydrolysed by KOH than is toe-nail, and appears to be a more compact tissue into which griseofulvin may be incorporated as a barrier to fungal penetration. The fingers have a better blood supply than the feet, and finger-nails may consequently receive more griseofulvin, though while the finger-nails grow more quickly than toe-nails it does not necessarily follow that the concentration of griseofulvin in the tissue is higher. What must be concluded, however, is that insufficient griseofulvin is incorporated in toe-nails with the dosages so far tried. Though the drug has a low toxicity with the dose regimen prescribed in the present study, it has affected blood and stool porphyrin levels. In high dosage it has colchicine-like effects on nuclear division, and any long-term toxic effect must await the test of time. Griseofulvin, however, must remain the treatment of choice for finger-nail infections, especially in women, but should never be prescribed for smooth skin infections, which are resolved with topical treatments, and its use in toe-nail infection is justifiable only when the patient has severe discomfort. Whether dosage with the new finer-particle-sized variant of the drug can be increased sufficiently to cure the chronic toe-nail infection without any deleterious effect remains to be seen.

Summary

Griseofulvin by mouth was used to treat 122 patients with chronic fungal infections of their nails for a minimum of six months; 74 received the drug continuously for two years, and 36 were followed for another year after the cessation of treatment to study relapse. Patients were assessed clinically at six-week intervals and a detailed mycological investigation of all their nails, thumb crutches, and outer toe webs was undertaken before treatment and at six-monthly intervals thereafter. All patients were prescribed 0.5 g. of griseofulvin t.d.s. for the first month, followed by 0.5 g. b.d.; those failing to take the drug consistently were transferred to an intermittent-dose group. Treatment was found to be less effective in infections of the toe-nails and outer toe webs than in those of the finger-nails and thumb crutches, which showed a good response; a significant number of toe-nails and outer toe webs relapsed after treatment was stopped.

The response of patients with infections due to *Trichophyton rubrum* is described in detail, as they comprised the largest group; that of patients infected with *T. mentagrophytes*, mixed infections due to both these fungi and of patients with chronic onychomycosis but from whom no fungus was isolated are only briefly described.

Response to therapy in nails infected with *T. mentagrophytes* is less favourable than in those infected with *T. rubrum,* and in nails infected with both these fungi *T. mentagrophytes* becomes dominant during treatment. In-vitro tests showed that *T. mentagrophytes* was less sensitive to griseofulvin than *T. rubrum.* Failure to respond to treatment could not be correlated with the sensitivity of the fungus isolated from any patient, and there was no evidence of the fungi developing an increased resistance to griseofulvin.

Observations on toxicity are discussed, and it is concluded that while griseofulvin is the treatment of choice for chronic finger-nail infections it should not be prescribed for smooth-skin infections, which are resolved with topical treatments, and its use in toe-nail infections is justifiable only when the patient has severe discomfort.

We are indebted to Miss M. J. Denny and Miss C. Howard for technical assistance; to the Imperial Chemical Industries Ltd. and the Govenors of St. Mary's Hospital for generous financial assistance; and to Mr. E. Hyde, of I.C.I., for his help with punched-card data recording and retrieval.

References

Ainsworth, G. C. (1961). *Nature (Lond.)*, **191**, 12.
Blank, H., Smith, J. G., Roth, F. J., and Zaias, L. (1959). *J. Amer. med. Ass.*, **171**, 2168.
De Matteis, F., and Rimington, C. (1963). *Brit. J. Derm.*, **75**, 91.
Gentles, J. C. (1958). *Nature (Lond.)*, **182**, 476.
—— Barnes, M. J., and Fantes, K. H. (1959). Ibid., **183**, 256.
Hurst, E. W., and Paget, G. E. (1963). *Brit. J. Derm.*, **75**, 105.
Paget, G. E., and Walpole, A. L. (1958). *Nature (Lond.)*, **182**, 1320.
Rimington, C., Morgan, P. N., Nicholls, K., Everall, J. D., and Davies, R. R. (1963). *Lancet*, **2**, 318.
Stevenson, C. J., and Djavahiszwili, N. (1961). Ibid., **1**, 373.
Williams, D. I., Marten, R. H., and Sarkany, I. (1958). Ibid., **2**, 1212.

Importance of Dietary Calcium in the Definition of Hypercalciuria

M. PEACOCK,* M.B., CH.B.; A. HODGKINSON,* D.SC., F.R.I.C.; B. E. C. NORDIN,* M.D., PH.D., M.R.C.P.

Brit. med. J., 1967, 3, 469–471

The relation between a high urinary calcium and renal stone disease was first noted by Flocks in 1939, but the recognition of "idiopathic hypercalciuria" as an entity in its own right dates from 1953, when the condition was described by Albright, Henneman, Benedict, and Forbes. These workers defined a syndrome in which a high urinary calcium was associated with normocalcaemia, a tendency to hypophosphataemia, and renal stone formation, and this syndrome has since been recognized by many other workers in the field (Henneman, Benedict, Forbes, and Dudley, 1958; Harrison, 1959; Litin, Diessner, and Keating, 1961; Parfitt, Higgins, Nassim, Collins, and Hilb, 1964; Edwards and Hodgkinson, 1965).

The cause of the high urinary calcium has never been established. The original workers suggested that it was a renal tubular disorder possibly associated with an ascending pyelonephritis (Albright *et al.*, 1953), but this has never been confirmed. Other workers have subsequently observed a reduced faecal excretion of calcium in idiopathic hypercalciuria (Henneman *et al.*, 1958; Harrison, 1959; Jackson and Dancaster, 1959; Hodgkinson, 1961). Whether this is the cause or the result of the condition is unknown, but Jackson and Dancaster (1959) suggested that the hyperabsorption was secondary to the hypercalciuria. Attempts to lower the urinary calcium by restricting calcium intake have been successful in some cases (Hennemann *et al.*, 1958; Harrison, 1959; Gill and Bartter, 1961) but not in others (Jackson and Dancaster, 1959; Edwards and Hodgkinson, 1965). This discrepancy may signify that some of the patients studied have tubular hypercalciuria or that the restriction of dietary calcium has been inadequate. Dent and Watson (1965), for instance, described the case of a man with hypercalciuria whose urinary calcium was finally reduced to normal when he was instructed to drink distilled water in addition to having a very strict low-calcium diet.

In studying this problem further we have encountered difficulty in defining exactly what is meant by hypercalciuria. Though the definition of Hodgkinson and Pyrah (1958)—a urinary calcium over 250 mg. in females and 300 mg. in males—has been widely adopted and proved useful in practice, we have seen many patients whose urinary calcium on a free diet varies substantially from one day to another. Such patients would be defined as "hypercalciuric" on one occasion and as "normocalciuric" on another. We have therefore found it necessary to examine in more detail the relation between dietary and urinary calcium in an attempt to define more rigorously what is meant by hypercalciuria and to understand its nature.

The present paper deals with the relation between dietary and urinary calcium in normal and stone-forming subjects and presents evidence to suggest that hyperabsorption is more likely to be the cause than the result of idiopathic hypercalciuria.

Clinical Material and Methods

Stone-forming Patients.—The patients consisted of 31 idiopathic male stone-formers, and 21 idiopathic female stone-formers, most of them having been "hypercalciuric" at one time or another according to the definition given above. They were admitted to a metabolic ward and studied on two known calcium intakes: a low intake of 2–5 mg./kg./day and a high intake of 15–20 mg./kg./day. The duration of study on each intake was variable, but was not less than five days. Urine was collected 24-hourly for calcium estimation, and the calcium excretion was expressed as the average of the last three days on a particular regimen.

Controls.—These were of two kinds: observations of our own and data collected from the literature. Our own non-stone cases comprise all the subjects studied by us at two calcium intakes who had no disease involving or affecting calcium metabolism other than simple ageing. There are 13 males in this category and 21 females. In addition, we have collected from the literature data on 31 normal male adults in whom urinary calcium data were available at two intake levels (Steggerda and Mitchell, 1941; Malm, 1958; Jackson and Dancaster, 1959; Clarkson, McDonald, and de Wardener, 1966). Our own control data fell within the same range as the normal data extracted from the literature.

Diets.—The patients were first studied on a low-calcium diet. This was followed by a high-calcium diet which consisted of the previous low-calcium diet supplemented with milk.

Biochemical Methods.—Various biochemical methods were used for the measurement of urinary calcium since the data were collected over a period of 12 years. The main methods were oxalate precipitation followed by permanganate titration, flame photometry by means of the Eppendorf flame photometer, or colorimetry with murexide or cresolphthalein complexone (Technicon Instruments Ltd. Method N 3). There is satisfactory agreement between urine calcium values obtained by these four methods.

Results

The relation between urinary and dietary calcium in the male subjects is shown in Fig. 1. The shaded area represents the normal range as established by us previously from observations in the literature (Nordin and Smith, 1965). It is apparent that in the great majority of stone-formers the urinary calcium on

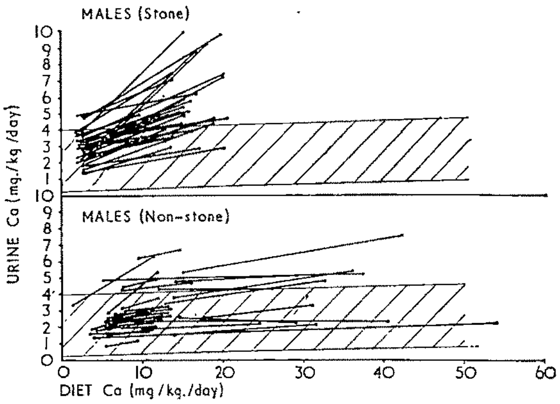


FIG. 1.—Relation between urinary and dietary calcium in male stone-formers (top) and non-stone-formers (below). The shaded area represents the approximate normal range.

---

* Medical Research Council Mineral Metabolism Unit, the General Infirmary, Leeds 1.

a low-calcium diet falls within the normal range. However, when the dietary intake is raised, urinary calcium rises steeply in most cases until at the higher intakes it is generally above or at the upper limit of the normal range. By contrast, the great majority of the male controls fall within or only slightly above the normal range, and, in particular, do not show the steep slope of urinary on dietary calcium which is a feature of the stone-formers.

The corresponding data for females are shown in Fig. 2. In the women there is very much less difference between stone-formers and controls than in the men. A few stone-forming cases lie above the suggested normal range, but the same is true of three of the controls. Some of the stone-forming cases have rather steeper slopes of urinary on dietary calcium than are seen in the control series, but most are within the normal range in this respect.

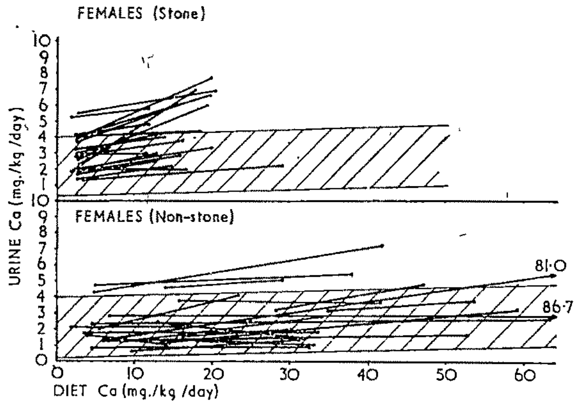


FIG. 2.—Relation between urinary and dietary calcium in female stone-formers (top) and non-stone-formers (below). The shaded area represents the approximate normal range.

These data can also be analysed in other ways. Firstly, the relation between urinary and dietary calcium can be expressed as a slope which denotes the change in urinary calcium for each unit change in dietary calcium. Secondly, this slope of urinary calcium on diet can be extrapolated back to a theoretical zero intake and the result expressed as the intercept of the slope on the urinary calcium axis. The data shown in Figs. 1 and 2 are expressed in these two ways in Figs. 3 and 4 and in the Table.

Relation of Urinary to Dietary Calcium in Stone-forming and Non-stone-forming Individuals

	Non-stone Cases			Stone Cases			*t*	P
	No. of Cases	Mean	S.E.	No. of Cases	Mean	S.E.		
	Mean regression coefficients of urinary on dietary calcium							
Males	44	0·074	0·012	31	0·199	0·020	5·4	<0·001
Females	21	0·029	0·008	21	0·105	0·019	3·8	<0·001
	Mean values of theoretical minimal urinary calcium (mg./kg./day)							
Males	44	2·31	0·19	31	2·37	0·16	0·24	>0·1
Females	21	1·95	0·28	21	2·53	0·22	1·66	>0·1

Fig. 3 shows the slope of urinary on dietary calcium in the stone-forming and non-stone-forming males and females. It is apparent that this slope has a gradient of less than 0.1 in the great majority of control males (mean 0.074) and of more than 0.1 in nearly all the stone-forming males (mean 0.199). This difference is highly significant (see Table). In the females the mean slope in the stone-formers is 0.105 and in the controls 0.029. This difference is also highly significant.

The theoretical urinary calcium values at zero calcium intake are shown in Fig. 4. The mean in the male non-stone-forming cases is 2.31 and in the stone-formers 2.37 mg./kg./day. In the females the corresponding values are 1.95 and 2.53 mg./kg./day. These differences are not significant (see Table).

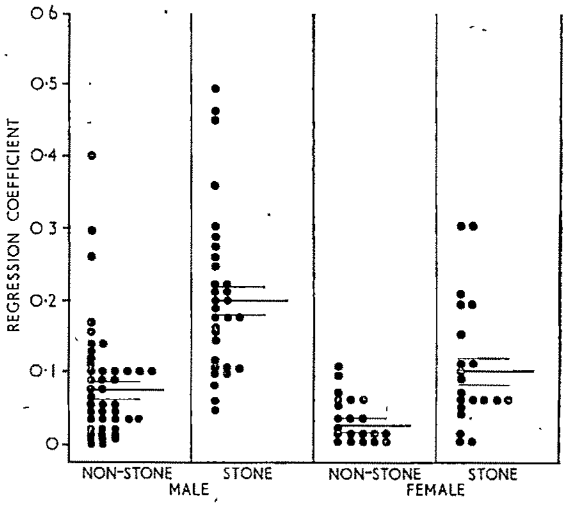


FIG. 3.—Regression coefficients of urinary on dietary calcium in male and female stone-formers compared with non-stone-forming individuals. The horizontal bars represent the means ± one standard error.

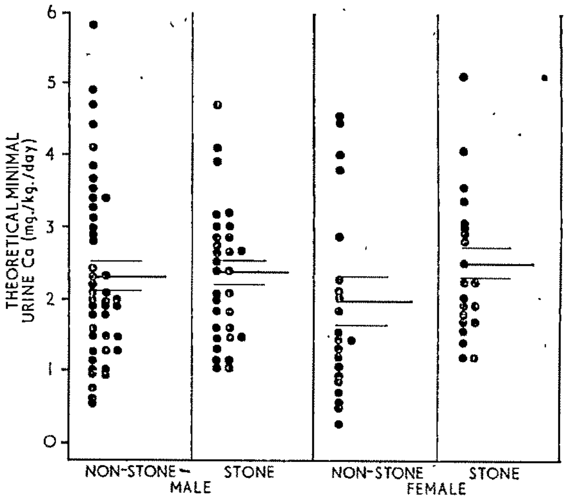


FIG. 4.—Theoretical minimal urinary calcium at zero calcium intake in male and female stone-forming and non-stone-forming individuals. The horizontal bars represent the means ± one standard error.

Discussion

Our data show that hypercalciuria should only be defined in relation to dietary calcium intake. Though the definition of hypercalciuria proposed by Hodgkinson and Pyrah (1958) has been and remains a useful guide, the fact that urinary and dietary calcium are closely related in stone-forming subjects indicates the need to define the dietary intake whenever the urinary calcium is examined in detail. Measurement of urinary calcium at two levels of intake enables patients to be classified into three different categories. Firstly, those in whom urinary calcium is high on a high intake but falls into the normal range on a low intake; these probably represent the majority of the male cases of so-called "idiopathic hypercalciuria." Secondly, those in whom urinary calcium is high on a high intake but remains high on a low intake; this is the general picture with sustained hypercalcaemia, but in the absence of hypercalcaemia probably denotes reduced tubular reabsorption of calcium. Thirdly, those patients whose urinary calcium falls within the normal range at high- and low-calcium intakes and who from this point of view are entirely normal.

We find that the majority of cases of idiopathic hypercalciuria, particularly the males, fall into the first category. Their urinary calcium at very low intakes is normal—that is, less than 4 mg./kg./day—but it rises more steeply than normal as intake is raised, and therefore tends to be high on the average dietary calcium of this country (about 20 mg./kg./day). This close relation between dietary and urinary calcium suggests, but does not prove, that the hypercalciuria is absorptive in origin as Caniggia, Gennari, and Cesari (1965) believe. It is possible to conceive of a renal "leak" which operates only at high intakes of calcium, but this seems to us an improbable explanation of our results.

In women the picture is much the same, though only a minority of the female stone-formers (6 out of 21) have a slope of urinary on dietary calcium above the upper limit of non-stone controls. The difference between the mean slopes is highly significant, whereas the theoretical urine calcium at zero intake does not differ as between the two groups.

It would be of the greatest interest to know whether the hypercalciuria of renal stone disease has the same basis as the hypercalciuria seen in a proportion of apparently normal individuals. It has repeatedly been noted that the urinary calcium of normal subjects is distributed asymmetrically in that there is a "tail" of high values in any normal population, which has been variously estimated at 10–14% of the total (Hodgkinson and Pyrah, 1958). This is probably not attributable to differences in intake, since it is still apparent when intake is taken into account (Knapp, 1947; Watson and Dale, 1966). We have therefore recalculated the data of Knapp (1947) to make them comparable with our own (Fig. 5), and found that the hypercalciuria of her normal individuals is essentially the same as that of our stone-formers. Examination of the "upper limit" in Fig. 5 shows that Knapp's series of 606 subjects must have included a small proportion of "hypercalciuric" individuals in whom the slope of urinary on dietary calcium was much steeper than in the majority. This "hypercalciuria" is not apparent at very low calcium intakes where the distribution of urinary calcium is apparently normal, but as the intake is raised the upper limit rises steeply in much the same way as in our hypercalciuric stone-formers shown in Figs. 1 and 2. We take this to mean that the basis of "idiopathic" hypercalciuria in stone-forming individuals is probably the same as that in normal controls—that is, absorptive in origin. This implies that idiopathic stone-formers are largely drawn from that segment of the population in whom absorption, and therefore urinary excretion of calcium, is above the average.

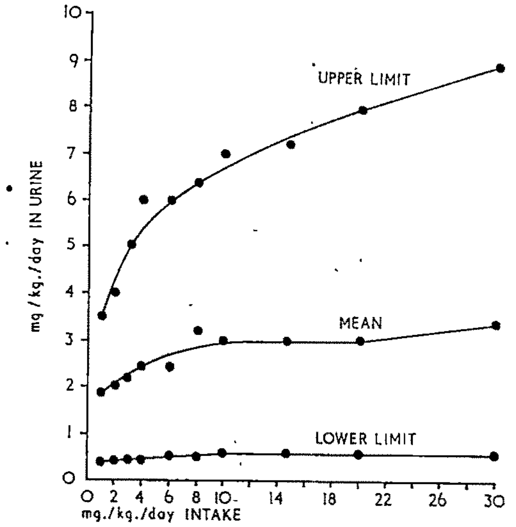


FIG. 5.—Relation between urinary and dietary calcium in normal individuals calculated from the data of Knapp (1947).

Summary

Urinary calcium was determined at two known levels of intake in 31 male and 21 female idiopathic stone-formers, and the results are compared with 13 males and 21 females with no history of stone. In addition, comparable data collected from the literature on 31 normal male adults are included.

At low-calcium intakes there was little difference in the urinary calcium excretion of stone-forming and non-stone-forming individuals, but as the intake was raised the urinary calcium rose more steeply in the stone-formers than in the controls. "Hypercalciuria" was therefore detectable only at moderately high calcium intakes, the characteristic feature of this syndrome being a steep slope of urinary on dietary calcium. This relation of urinary to dietary calcium is similar to that reported by Knapp (1947) in a small proportion of normal individuals.

It is concluded that "hypercalciuria" can only be defined in relation to calcium intake; that "idiopathic hypercalciuria" is generally attributable to an increased calcium absorption; and that the hypercalciuria of idiopathic stone disease is probably of the same nature as that seen in a small proportion of normal individuals.

REFERENCES

Albright, F., Henneman, P., Benedict, P. H., and Forbes, A. P. (1953). *J. clin. Endocr.*, **13**, 860.
Caniggia, A., Gennari, C., and Cesari, L. (1965). *Brit. med. J.*, **1**, 427.
Clarkson, E. M., McDonald, S. J., and de Wardener, H. E. (1966). *Clin. Sci.*, **30**, 425.
Dent, C. E., and Watson, L. (1965). *Brit. med. J.*, **2**, 449.
Edwards, N. A., and Hodgkinson, A. (1965). *Clin. Sci.*, **29**, 143.
Flocks, R. H. (1939). *J. Amer. med. Ass.*, **113**, 1466.
Gill, J. R., and Bartter, F. C. (1961). *J. clin. Invest.*, **40**, 716.
Harrison, A. R. (1959). *Brit. J. Urol.*, **31**, 398.
Henneman, P. H., Benedict, P. H., Forbes, A. P., and Dudley, H. R. (1958). *New Engl. J. Med.*, **259**, 802.
Hodgkinson, A. (1961). *Proc. Ass. clin. Biochem.*, **1**, 52.
—— and Pyrah, L. N. (1958). *Brit. J. Surg.*, **46**, 10.
Jackson, W. P. U., and Dancaster, C. (1959). *J. clin. Endocr.*, **19**, 658.
Knapp, E. L. (1947). *J. clin. Invest.*, **26**, 182.
Litin, R. B., Diessner, G. R., and Keating, F. R. (1961). *J. Urol. (Baltimore)*, **86**, 17.
Malm, O. J. (1958). *Scand. J. clin. Lab. Invest.*, **10**, Suppl. No. 36.
Nordin, B. E. C., and Smith, D. A. (1965). *Diagnostic Procedures in Disorders of Calcium Metabolism.* London.
Parfitt, A. M., Higgins, B. A., Nassim, J. R., Collins, J. A., and Hilb, A. (1964). *Clin. Sci.*, **27**, 463.
Steggerda, F. R., and Mitchell, H. H. (1941). *J. Nutr.*, **21**, 577.
Watson, L., and Dale, N. E. (1966). *Clin. Sci.*, **31**, 77.

Renal Function after Leptospirosis

B. SIMPSON,* M.A., M.B., M.R.C.P.ED.; A. T. COOK,† M.B., M.R.C.P.; A. H. DIMOND,‡ M.A., M.B., M.R.C.P.
M. BROWN,§ M.B., M.R.C.P.; R. N. T. THIN,§ M.B., M.R.C.P.ED.

Brit. med. J., 1967, **3**, 472–473

It is generally assumed that a patient who survives an attack of leptospirosis is left with normal kidneys (Van Thiel, 1948; Gsell, 1952; Ross Russell, 1959), but no long-term follow-up study has been published and certain facts suggest the need for such an investigation. Firstly, the frequency of renal damage in this disease is illustrated by the reports of Penna *et al.* (1963) and de Brito *et al.* (1965) in Brazil; they obtained renal biopsy specimens between the eleventh and forty-fifth days of the illness, and even in patients with minimal impairment of renal function they demonstrated infiltration of the interstitial tissue with lymphocytes and histiocytes, tubular damage, focal thickening of the glomerular basement membrane, and objects resembling leptospirae. Further, leptospiruria is not uncommon and may persist for as long as 11 months (Johnson, 1950); indeed, Spînu *et al.* (1962), who studied an epidemic outbreak of leptospirosis in Vietnam, concluded that in certain circumstances human excreters might be the source of spread. It thus seems possible that leptospirosis might cause chronic renal damage and impairment of renal function, and this paper describes an investigation into this aspect.

Present Investigation

Our patients were soldiers who contracted leptospirosis in South-East Asia, where the disease is an important military problem and caused 333 admissions to hospital in 1954–5 (Levis, 1957). Renal damage provides the main problem in management, though since the introduction of rational conservative therapy for uraemia the main cause of death in the few fatal cases (less than 2% of patients) has been haemorrhage (Trimble, 1957). Thirty serotypes have been incriminated in this group (Alexander *et al.*, 1957), including *Leptospira icterohaemorrhagiae* and *L. canicola,* and there is no correlation between the serotype responsible for the illness and the severity of the renal lesion, jaundice, or meningitis. This finding is in accord with the experience of Continental workers (Gsell, 1952), but differs from the pattern hitherto reported in Britain, where jaundice due to *L. icterohaemorrhagiae* and meningitis due to *L. canicola* are the commonly diagnosed forms of leptospirosis.

Subjects.—Nineteen British and 25 Gurkha soldiers had contracted leptospirosis between 1 and 14 years previously (mean eight years), when aged 18 to 28. Of these, four had developed anuria with a blood urea level of over 350 mg./100 ml. and two required haemodialysis, in eight the blood urea level had exceeded 150 mg./100 ml., and the remainder had normal or slightly impaired renal function with albumin, cells, and granular casts in the urine. The original clinical diagnosis had been confirmed by laboratory and serological findings (Trimble, 1957; Ross Russell, 1959). Most of the patients had been treated with large doses of penicillin by intramuscular injection; this drug shortens the duration of the illness and may produce a Herxheimer type of reaction (Mackay-Dick and Robinson, 1957). The patients were selected solely on grounds of availability and represent aproximately a 30% sample of currently serving soldiers who have had leptospirosis. As no soldier has been medically discharged from the Army because of this disease it is unlikely that our series is biased in favour of the fittest.

Methods.—Each patient was admitted to hospital for assessment. Biochemical methods were as described by Varley (1962). Urine specific gravity was measured at room temperature (15–23° C.) by standard hydrometers. In the urine concentration test dehydration was not prolonged beyond 16 hours.

Results

No patients had symptoms or were anaemic (Hb<13.5 g./100 ml.) and only one was hypertensive (B.P.>130/90 mm. Hg). His B.P. was 115/70 at the time of the attack, but three years later it was 170/120 and the E.C.G. showed hypertensive changes.

Examination of two fresh morning midstream specimens of urine for albumin, glucose, and deposit gave normal results. The blood urea level (mean of two estimations) was in the range 16–35 mg./100 ml. The creatinine clearance, corrected to a body surface area of 1.73 sq. m., was twice estimated over 24 hours in the British soldiers and exceeded 90 ml./min. in all except one. In this patient, who was not hypertensive, the values were 60 and 63 ml./min., but the results of other tests (including kidney length as visualized on a plain *x*-ray film) were normal. Single estimations of the creatinine clearance in eight Gurkha soldiers investigated in one hospital (group A) gave values of over 90 ml./min. Of the 17 assessed elsewhere (group B), seven had values of less than 90 ml./min., but the serum creatinine levels were similar to those of the patients with normal clearances.

All the British patients concentrated urine to a specific gravity of at least 1020 and diluted to a specific gravity of at least 1002, the narrowest range being 1022–1002. The results were similar in the Gurkha patients in group B, but of the eight in group A five did not concentrate to this degree.

A plain *x*-ray film of the renal area was taken in each case and it was possible to measure the length of both kidneys in 12; the overall range was 12–14.5 cm., and in no instance did the difference between the two sides exceed 1 cm. Intravenous pyelograms were performed in four men (including the patient with hypertension) who were reviewed between one and eight years after the attack of leptospirosis; all showed normal renal anatomy and secretion. In two of these patients ^{131}I Hippuran renograms were performed, with normal results.

There was no correlation between the severity of the initial renal lesion and the blood urea level, creatinine clearance, and maximum specific gravity of the urine, nor did the length of the interval betwen the acute attack and reassessment influence these results.

Dr. L. H. Turner, of the London School of Hygiene and Tropical Medicine, examined the sera of 12 British patients, using pools of formolized leptospiral antigens based on the currently accepted arrangement of serogroups and designed to detect all known pathogenic serotypes. Each showed agglutinin titres of 1:30 to 1:100 against at least two, and in some

---

* Major, R.A.M.C.; Queen Alexandra Military Hospital, Millbank, London S.W.1.
† Lieutenant-Colonel, R.A.M.C.; British Military Hospital, Singapore.
‡ Major. R.A.M.C.; British Military Hospital, Hong Kong.
§ Major, R.A.M.C.; British Military Hospital, Terendak, Malaysia.

instances six, serotypes. In only two were the maximum titres against the serotypes responsible for the original infection.

Discussion

Our results suggest that the long-term prognosis after the acute renal lesion of leptospirosis is good. Thus in the British patients all the results of renal function tests were normal except for a slightly reduced creatinine clearance in one man ; as the serum creatinine level and other results in him were normal the significance of this isolated finding is doubtful. Another man developed hypertension, but renal damage did not appear to be the cause. One group of Gurkha patients had normal creatinine clearances but all did not concentrate urine adequately, while in the others these findings were reversed ; since each abnormality was confined to one group it seems likely that these discrepancies reflect incomplete dehydration and incomplete urine collection respectively.

As intravenous pyelograms were performed in only four patients, and renal biopsy in none, we cannot be certain that permanent minor anatomical damage to the kidneys has not occurred ; but as the individual results were not influenced by the severity of the initial renal lesion or the time interval before reassessment it is unlikely that there is an active process present causing progressive destruction of renal tissue.

The finding of leptospiral agglutinins in the sera of the 12 patients examined is of interest, though in only two did the serological pattern parallel that of the original infection. Hart (1967), using the sensitized erythrocyte lysis test, has shown that a small proportion of soldiers serving in jungle areas in South-east Asia develop a rising titre of leptospiral antibodies without clinical evidence of infection, and our patients have served in this area on several occasions since their original illness. It is thus conceivable that they have acquired subclinical infections during this time and that this explains the serological findings. As, however, all our patients showed significant titres of agglutinins, and none of them had a clinical attack, which would be surprising if they were frequently exposed to infection, this explanation may be too facile. Further investigation of this point is required.

Summary

Renal function was studied in 44 soldiers who had contracted leptospirosis in South-east Asia up to 14 years previously. The findings suggest that renal function is now normal, and individual results do not reflect the severity of the initial renal damage or the time interval before reassessment.

The sera of 12 patients were examined for leptospiral agglutinins. All showed significant titres, but in only two were these against the serotype responsible for the original illness. These results may possibly reflect subclinical leptospiral infections contracted during later periods of service in the same area, but the present evidence is insufficient to allow firm conclusions to be drawn.

We wish to thank Dr. Gordon Smith, Director M.R.E., Porton, and Major-General R. J. G. Morrison, Consultant Physician to the Army, for suggesting and encouraging this investigation ; Dr. L. H. Turner for the serological results and advice ; Captain K. Hedges, R.A.M.C., for his help in arranging for the investigation of patients under his care ; and the Director-General, Army Medical Services, for permission to use case records.

Requests for reprints should be sent to Major B. Simpson.

REFERENCES

Alexander, A. D., Evans, L. B., Toussaint, A. J., Marchwicki, R. H., and McCrumb, F. R., jun. (1957). *Amer. J. trop. Med. Hyg.*, **6**, 871.

de Brito, T., *et al.* (1965). Ibid., **14**, 397.

Gsell, O. (1952). *Leptospirosen.* Berne.

Hart, R. J. C. (1967). To be published.

Johnson, D. W. (1950). *Med. J. Aust.*, **2**, 724.

Levis, D. G. (1957). *Proc. roy. Soc. Med.*, **50**, 119.

Mackay-Dick, J., and Robinson, J. F. (1957). *J. roy. Army med. Cps*, **103**, 186.

Penna, D., de Brito, T., Aguiar Pupo, A., Marcondes Machado, M., Ayroza Galvão, P. A., and Soares de Almeida, S. (1963). *Amer. J. trop. Med. Hyg.*, **12**, 896.

Ross Russell, R. W. (1959). *Ann. trop. Med. Parasit.*, **53**, 416.

Spînu, I., Topciu, Vl., Trinh Thi Hang Quy, Vo van Hung, Chau xuan Luong, and Le van Tuyen (1962). *Arch. roum. Path. exp.*, **21**, 763.

Van Theil, P. H. (1948). *The Leptospiroses*, Leiden.

Trimble, A. P. (1957). *Proc. roy. Soc. Med.*, **50**, 125.

Varley, H. (1962). *Practical Clinical Biochemistry*, 3rd ed., pp. 112, 151, 153. London.

Effect of Medical and Surgical Vagotomy on Intrinsic Factor Secretion

J. F. ADAMS,* V.R.D., M.D., F.R.C.P.ED., F.R.C.P.GLASG. ; A. G. COX,*† M.D., F.R.C.S.ED.
ELIZABETH H. KENNEDY,*‡ B.SC. ; J. THOMPSON,*§ M.B., M.R.C.P.GLASG.

Brit. med. J., 1967, 3, 473–476

The recent development of in-vitro techniques for the assay of gastric intrinsic factor has made possible the study of the effects of various pharmacological and surgical manœuvres on this facet of gastric secretory function. Using one such technique, we have studied the effects of pharmacological vagal blockade—" medical vagotomy "—in a group of patients with proved duodenal ulceration, and in some of these have also studied the effects of section of the vagus nerves.

Material and Methods

Twenty-six patients (23 men aged 22–60 and 3 women aged 42–48) with the clinical and radiological features of chronic duodenal ulceration were studied before operation, and further studies were made in 15 of them after operation. Vagotomy and pyloroplasty were performed on six men and one woman and vagotomy and gastrojejunostomy on six men and two women. The augmented histamine test was carried out in 26 cases before operation and in 15 after operation. Medical vagotomy was carried out in 25 cases before operation. The insulin test was done in 15 cases after operation. The choice of pyloroplasty or gastrojejunostomy was determined by a randomization procedure. The completeness of surgical vagotomy was confirmed in all cases by an insulin test.

The augmented histamine test (Kay, 1953) was performed after an overnight fast. Gastric aspiration was maintained by continuous suction. After collection of basal secretion in 15-minute periods for one hour, 100 mg. of mepyramine maleate was injected intramuscularly. Thirty minutes later histamine acid phosphate, 0.04 mg./kg. body weight, was injected subcutaneously and gastric aspiration was continued for a further hour, again in 15-minute collection periods.

---

* Southern General Hospital and University Department of Surgery, Western Infirmary, Glasgow.

† Now Senior Lecturer in Surgery, Royal Postgraduate Medical School, London.

‡ Now Scientific Officer, National Engineering Laboratory, East Kilbride, Lanarkshire.

§ Now Lecturer in Dermatology, University and Western Infirmary, Glasgow.

The medical vagotomy test (Gillespie and Kay, 1961) was carried out on another day. This differed from the standard augmented histamine test in that a combined intramuscular injection of 50 mg. of hexamethonium bromide, and 0.325 mg. of atropine, was given at the beginning of the test.

The insulin test was performed with a standard dose of 20 units of soluble insulin given intravenously after collection of three 15-minute specimens of spontaneous secretions. After the injection gastric aspiration was continued for two hours. Vagotomy was regarded as complete only if the acid concentration failed to rise 20 or more mEq/l. over the maximal basal level.

The volume and *p*H of all specimens of gastric juice were measured. The amount of acid was determined by titration to *p*H 7 with N/10 NaOH, phenol red being used as the indicator. Intrinsic factor assays were performed by the method of Gottlieb *et al.* (1965). Several sera containing antibody to intrinsic factor were used, all being of high potency. When the total binding exceeded 75% of the amount of radioactive cyanocobalamin added (usually 7.5 mμg.) the procedure was repeated with half the normal amount of neutralized gastric juice: if the total binding still exceeded 75% of the amount of radioactive cyanocobalamin added then the procedure was repeated with half the normal amount of neutralized gastric juice and double the normal amount of radioactive cyanocobalamin. For convenience we adopted the convention of expressing intrinsic factor activity in terms of units, one unit being taken as the specific intrinsic factor binding of 1 mμg. of radioactive cyanocobalamin.

The results were analysed by standard statistical methods.

Results

All results are given as hourly values, representing spontaneous secretion ("basal hour"), the augmented histamine response ("augmented histamine hour"), and the response to histamine after medical vagotomy ("medical vagotomy hour").

Effect of Histamine Stimulation

The mean values for volume, acid, intrinsic factor output, and intrinsic factor concentration were all significantly higher ($P<0.01$) in the augmented histamine hour than in the basal hour (Table I).

Correlation between Acid and Intrinsic Factor Output

An insignificant correlation was found between the mean values for acid and intrinsic factor in the basal hours, both before and after operation. However, a significant ($P<0.01$) correlation was found between these two measurements in the augmented histamine hours both before and after operation, and also in the medical vagotomy hour (Table II).

TABLE II.—*Correlation and Regression Equations*

Series	Period	Regression of y (I.F.) on x (Acid)	No. of Patients	r
All patients	Histamine hour ..	$y = 3{\cdot}085x + 60{\cdot}045$	26	0·551
	Medical vagotomy hour . ..	$y = 4{\cdot}773x + 34{\cdot}629$	25	0·585
Surgical group	Preoperative histamine hour ..	$y = 4{\cdot}926x + 25{\cdot}947$	15	0·693
	Medical vagotomy hour	$y = 7{\cdot}419x + 15{\cdot}0965$	14	0·751
	Postoperative histamine hour ..	$y = 7{\cdot}759x + 18{\cdot}652$	15	0·762

Effect of Medical and Surgical Vagotomy

The results are most conveniently considered in two groups. The first relates to the effect of medical vagotomy on the augmented histamine response. The second relates to the effect of surgical vagotomy on basal secretion and the augmented histamine response.

Medical Vagotomy.—The mean values for volume and acid were significantly less ($P<0.01$) in the medical vagotomy hour than in the augmented histamine hour. Differences in the mean values for intrinsic factor output and concentration did not

TABLE III.—*Values for Acid and Intrinsic Factor Secretions After Histamine and After Medical Vagotomy. The Differences Between the Respective Values are Shown as a Percentage of the Value in the Histamine Hour*

Case No.	Augmented Histamine Hour		Medical Vagotomy Hour		Percentage Change	
	Acid (mEq)	I.F. (mμg. Units)	Acid (mEq)	I.F. (mμg. Units)	Acid	I.F.
1	32·6	19,110	13·7	9·564	−58	−50
2	23·6	9,170	14·3	6,698	−39·4	−27
3	19·6	10,351	7·0	4,096	−64·3	−60·4
4	21·8	10,875	14·0	4,326	−35·8	−60·2
5	52·6	16,311	34·2	10,523	−35·0	−35·5
6	41·3	15,524	23·1	12,173	−44·1	−21·6
7	73·6	19,023	44·3	14,827	−39·8	−22·1
8	29·9	12,078	4·5	10,875	−84·9	− 9·3
9	43·2	10,619	20·2	6,919	−53·2	−34·8
10	39·2	18,195	17·6	5,275	−55·1	−71·0
11	28·3	15,000	13·5	5,300	−52·3	−64·7
12	7·3	10,931	4·3	10,174	−41·0	− 6·9
13	48·2	16,593	26·6	17,929	−44·8	+ 8·1
14	21·8	6,233	23·9	11,510	+ 9·6	+84·6
15	24·4	12,765	14·5		−40·5	
16	16·3	11,223	7·7	12,705	−52·7	+13·2
17	20·8	13,984	10·3	7,554	−50·4	−45·9
18	15·0	17,280	13·4	13,937	−10·6	−19·3
19	36·1	35,838	21·1	20,613	−41·5	−42·5
20	56·8	29,796	31·4	30,125	−44·7	+ 1·1
21	43·9	18,589	16·7	13,969	−61·9	−24·8
22	23·9	6,406	20·0	9,466	−16·3	+47·8
23	36·2	12,412	18·8	7,270	−48·0	−41·4
24	57·5	45,021	42·4	38,280	−26·2	−14·9
25	24·8	17,485	21·1	27,381	−14·9	+56·6
26	34·8	14,802	19·8	6,088	−43·1	−58·8
All cases					−42·9	−20·6
All except Case 15					−43·0	−20·6

TABLE I.—*Mean Hourly Values for Volume, Acid, Intrinsic Factor and Intrinsic Factor Concentration*

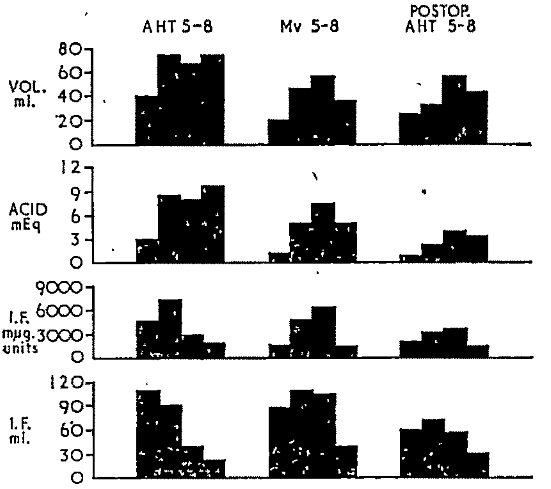
		Basal Hour					Post-Histamine Hour					Medical Vagotomy Hour					Postoperative Basal Hour					Postoperative Post-Histamine Hour				
		No.	Vol. (ml.)	Acid (mEq)	I.F. (mμg. units)	I.F./ml.	No.	Vol. (ml.)	Acid (mEq)	I.F. (mμg. units)	I.F./ml.	No.	Vol. (ml.)	Acid (mEq)	I.F. (mμg. units)	I.F./ml.	No.	Vol. (ml.)	Acid (mEq)	I.F. (mμg. units)	I.F./ml.	No.	Vol. (ml.)	Acid (mEq)	I.F. (mμg. units)	I.F./ml.
All patients	No.	26					26					25														
	Mean		126·84	6·29	3,680	31·16		299·77	33·60	16,370	55·94		181·6	19·36	12,702	71·32										
	S.D.		48·87	3·88	1,783	19·26		98·57	15·44	8·654	24·27		68·93	10·40	8,492	38·33										
	S.E.		9·58	0·76	350	3·78		19·33	3·03	1,697	4·76		13·79	2·08	1,698	7·67										
Surgical patients	No.	15					15					14					12					15				
	Mean		119·47	5·70	3,406	30·96		276·87	31·19	17,957	64·61		175·57	19·82	16,214	93·36		65·92	1·07	1,148	12·88		163·67	10·33	9,883	60·33
	S.D.		49·72	4·00	1,908	22·87		97·34	15·24	10,838	28·22		70·01	9·77	9,653	37·97		33·15	1·37	1,611	14·89		65·67	6·88	7,010	31·63
	S.E.		12·84	1·03	493	5·91		25·13	3·94	2,798	7·29		18·71	2·61	2,580	10·15		9·57	0·40	465	4·30		16·96	1·78	1,810	8·17

achieve significance, though the mean intrinsic factor output was lower and the concentration higher in the medical vagotomy hour. The detailed results (Table III) show the very marked individual variations in response.

Surgical Vagotomy.—The effect of surgery on basal secretion was a significant reduction in mean values for volume, acid, and intrinsic factor ($P<0.01$) and for intrinsic factor concentration ($P<0.05$). The effect of surgery on histamine-stimulated secretion was a significant reduction in mean values for volume, acid ($P<0.01$), and intrinsic factor output ($P<0.05$), but there was no significant change in mean values for intrinsic factor concentration. Patients having gastrojejunostomy did not differ from those in whom pyloroplasty was employed as the drainage procedure. Detailed results (Table IV) again showed very marked individual variation in response. The pattern of response to histamine after operation was similar to that found during medical vagotomy (see Chart).

TABLE IV.—*Values for Acid and Intrinsic Factor for the Hour After Histamine Stimulation, Before and After Operation, and also During Medical Vagotomy. The Differences are Shown as a Percentage of the Value in the Preoperative Histamine Hour*

Case No.	Preoperative Augmented Histamine Hour		Preoperative Medical Vagotomy Hour		Postoperative Augmented Histamine Hour		Percentage Change			
							Acid		I.F.	
	Acid (mEq)	I.F. (mμg. Units)	Acid (mEq)	I.F. (mμg. Units)	Acid (mEq)	I.F. (mμg. Units)	Due to M. Vag.	Due to Op.	Due to M. Vag.	Due to Op.
12	7·3	10,931	4·3	10,174	6·1	5,872	−41·0	−16·4	− 6·9	−47·9
13	48·2	16,593	26·6	17,929	20·9	7,677	−44·8	−56·6	+ 8·1	−53·7
14	21·8	6,233	23·9	11,510	4·1	1,689	+ 9·6	−81·1	+84·6	−39·4
15	24·4	12,765	14·5		12·7	16,770	−40·5	−47·9		+31·3
16	16·3	11,223	7·7	12,705	1·2	1,878	−52·7	−92·6	+13·2	−83·2
17	20·8	13,984	10·3	7,554	4·1	4,175	−50·4	−80·2	−45·9	−70·1
18	15·0	17,280	13·4	13,937	8·2	14,497	−10·6	−45·3	−19·3	−16·1
19	36·1	35,838	21·1	20,613	5·8	3,226	−41·5	−83·9	−42·5	−90·9
20	56·8	29,796	31·4	30,125	24·6	24,871	−44·7	−56·6	+ 1·1	−16·5
21	43·9	18,589	16·7	13,969	19·6	15,961	−61·9	−55·3	−24·8	−14·1
22	23·9	6,406	20·0	9,466	10·8	5,091	−16·3	−54·8	+47·8	−20·5
23	36·2	12,412	18·8	7,270	5·0	4,630	−48·0	−86·1	−41·4	−62·6
24	57·5	45,021	42·4	38,280	14·6	18,166	−26·2	−74·6	−14·9	−59·6
25	24·8	17,485	21·1	27,381	8·7	12,711	−14·9	−64·9	+56·6	−25·0
26	34·8	14,802	19·8	6,088	8·6	11,036	−43·1	−75·2	−58·8	−25 4
All cases •							−37·4	−66·8	−11·5	−44·9
All except case 15							−37·5	−67·9	−11·5	−48·7



Secretory patterns in cases studied before and after surgery. The figures 5–8 signify the four 15-minute periods after the injection of histamine, 1–4 being the four 15-minute periods before the injection.

Comparison of Effects of Medical and Surgical Vagotomy.—Comparison of the mean hourly values after medical vagotomy and after histamine stimulation in the postoperative period showed that the mean values for volume and intrinsic factor did not differ significantly ($P>0.05$) but that the mean values for acid and intrinsic factor concentration were significantly less ($P<0.01$ and <0.05 respectively) after operation than after medical vagotomy.

Discussion

The object of this study was to determine and compare the effects of medical and surgical vagotomy on gastric secretory function with particular emphasis on intrinsic factor secretion, and discussion of the results is limited to these points.

During the course of the study Bitsch *et al.* (1966) published their findings on the effects of surgical vagotomy on gastric secretory function, and comparison of the two sets of results is desirable. The mean values for volume, acid, intrinsic factor, and intrinsic factor concentration found by us are less than those of Bitsch *et al.*, but the data given in their paper do not permit calculation of the significance of these differences. The results can be compared, however, by taking the difference between the values obtained in the histamine hour before and after operation and expressing the difference as a percentage of the preoperative value. Bitsch *et al.* observed a volume reduction of 46.7%, an acid reduction of 62.5%, and a reduction in intrinsic factor output of 43.8% (not 34% as printed in their paper). The corresponding values in the present study are 40.8% for volume, 66.8% for acid, and 44.9% for intrinsic factor. These results are clearly in close agreement and confirm that surgical vagotomy and a drainage procedure effect a significant reduction in the output of gastric juice, acid, and intrinsic factor in response to histamine.

The type of drainage procedure employed does not appear to be important. In our series both groups responded in a similar manner and no significant differences were found between them in regard to volume, acid, or intrinsic factor output after operation. This suggests, but does not prove, that vagotomy is the effective agent.

The effect of medical vagotomy differs sharply from that of surgical vagotomy. The effect of medical vagotomy was a significant reduction in volume and acid output after histamine stimulation, as was expected (Gillespie and Kay, 1961), but an insignificant change in intrinsic factor output. This finding is of interest in relation to the mechanisms which control intrinsic factor secretion. Hoedemaeker *et al.* (1964) have produced evidence from immunological and autoradiographic studies that the site of secretion is the parietal cell, and this view is supported by the close correlation between amounts of acid and intrinsic factor secreted (Ardeman, 1965; Irvine, 1965; Rødbro, *et al.*, 1965). The pattern of acid and that of intrinsic factor secretion differ, however, the difference being most obvious on continued histamine stimulation when the output of acid remains high and that of intrinsic factor falls off rapidly after an initial rise (Irvine, 1966; Lawrie and Anderson, 1967). This indicates either that the two secretions come from different cells or that they come from the same cell, in which case the secretion of acid is by a process of true stimulation and that of intrinsic factor is one of release or "washout." The importance of vagal control is clearly shown by the effect of surgical vagotomy as found by Bitsch *et al.* (1966) and confirmed here.

That medical vagotomy did not have a quantitatively significant effect on the histamine-stimulated output of intrinsic factor was therefore unexpected but is not necessarily evidence against the concept of vagal control of intrinsic factor secretion. The pattern of intrinsic factor secretion is affected by medical vagotomy in the same way as by surgical vagotomy, suggesting that both procedures exert an effect on the controlling mechanisms even if the effect is quantitatively insignificant with one but not with the other. There are two possible explanations. First the vagal component of acid secretion may be more dominant than the vagal control of intrinsic factor secretion, and since medical vagotomy is less complete than surgical vagotomy the quantitative effect will be correspondingly less. Other influences on intrinsic factor secretion, such as intragastric reflexes, may be more important than the vagal component. Secondly, the medical vagotomy differs from surgical vagotomy in that it fails to block histamine-stimulated washout effect while having a blocking effect on the pattern of active secretion stimulated by histamine.

Summary

The effect of medical and surgical vagotomy on intrinsic factor secretion was studied in patients with duodenal ulceration.

Surgical vagotomy brought a significant reduction in both basal and histamine-stimulated output, but medical vagotomy did not significantly affect histamine-stimulated output. The pattern of intrinsic factor secretion in response to histamine was affected in the same manner by medical and surgical vagotomy.

The results suggest either that the vagal component in the control of intrinsic factor secretion is less dominant than the vagal component in acid secretion or that medical vagotomy differs from surgical vagotomy, the former failing to block a washout type of pattern and the latter doing so.

We are grateful to Professor A. W. Kay for advice and encouragement, to Professor T. Ferguson Rodger for facilities in his department, and to Merck Sharp & Dohme Ltd. for supplies of radioactive cyanocobalamin. We acknowledge with thanks a grant from the Secretary of State for Scotland on the advice of the Advisory Committee on Medical Research.

REFERENCES

Ardeman, S. (1965). *Proc. roy. Soc. Med.*, **58**, 916.
Bitsch, V., Christiansen, P. M., Faber, V., and Rødbro, P. (1966). *Lancet*, **1**, 1288.
Gillespie, I. E., and Kay, A. W. (1961). *Brit. med. J.*, **1**, 1557.
Gottlieb, C., Lau, K-S., Wasserman, L. R., and Herbert, V. (1965). *Blood*, **25**, 875.
Hoedemaeker, P. J., Abels, J., Wachters, J. J., Arends, A., and Nieweg, H. O. (1964). *Lab. Invest.*, **13**, 1394.
Irvine, W. J. (1965). *New Engl. J. Med.*, **273**, 432.
—— (1966). *Clin. exp. Immunol.*, **1**, 99.
Kay, A. W. (1953). *Brit. med. J.*, **2**, 77.
Lawrie, J. H., and Anderson, N. M. (1967). *Lancet*, **1**, 68.
Rødbro, P., Christiansen, P. M., and Schwartz, M. (1965). Ibid., **2**, 1200.

Medical Memoranda

Hydatidiform Mole and Coexistent Foetus, both with Triploid Chromosome Constitution

Brit. med. J., 1967, **3**, 476–478

Triploid chromosome complement in man has been described in abortions and also in three living subjects, all of whom were mosaics (Böök and Santesson, 1960 ; Penrose and Delhanty, 1961 ; Delhanty *et al.*, 1961 ; Carr, 1963, 1965 ; Ellis *et al.*, 1963 ; Ferrier *et al.*, 1964 ; Thiede and Salm, 1964 ; Aspillaga *et al.*, 1964 ; Szulman, 1965).

Atkin and Klinger (1962) and Szulman (1965) have reported a case of mole with an associated foetus in which triploidy was found in the molar tissue. Makino *et al.* (1964) found triploid chromosome complements in three cases of early abortion, where the chorionic villi were swollen and oedematous, forming small vesicles as in hydatidiform mole. Carr (1965) in his later series described a similar case. In none of these molar or molar-like gestations were the clinical features reported.

This paper describes the finding of triploid chromosome complement in a hydatidiform mole and its associated abnormal foetus, the mother showing antepartum and postpartum clinical features of molar pregnancy.

CASE REPORT

A 22-year-old woman developed severe pre-eclampsia at 17 weeks of gestation in her first pregnancy. She had palpitations, severe dyspnoea, and pain in the right iliac fossa when referred to the Royal Women's Hospital seven weeks later. The haemoglobin had fallen from 13 to 7.1 g./100 ml., though vaginal bleeding had not occurred. The blood pressure was 170/110 and the urine contained 20 g. of protein per litre. The right lower abdomen was tender, but no mass was felt apart from the uterus, which reached to the level of the umbilicus. *X*-ray examination showed a foetal skeleton commensurate with 18 rather than 24 weeks of development ; the plasma uric acid was 4.7 mg./100 ml. ; urinary oestriol 1.5 mg./24 hours, and urinary chorionic gonadotrophin 300–400 i.u./ml.

After treatment with sedation and hypotensive drugs artificial rupture of the membranes was performed and 300 ml. of amniotic

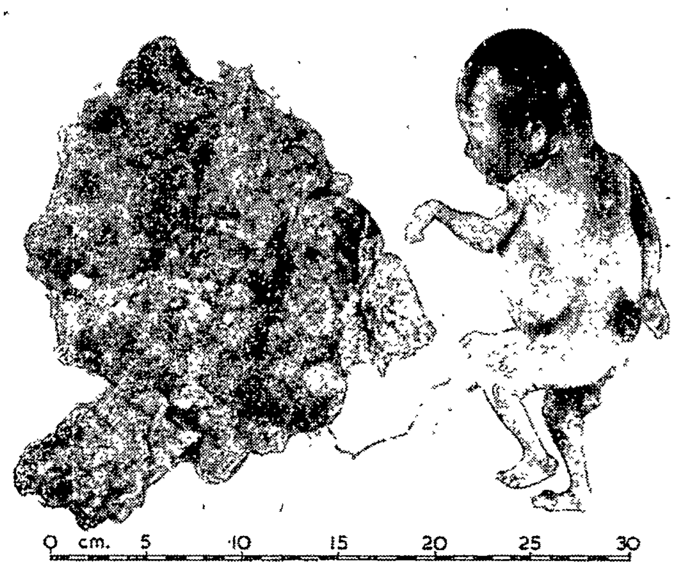


FIG. 1.—Malformed foetus together with placenta showing diffuse macroscopic molar degeneration.

fluid was obtained. As vaginal bleeding then occurred, a blood transfusion was begun. An oxytocic infusion was given, and after a five-hour labour the patient aborted the conceptus shown in Fig. 1, and within 10 minutes became cyanosed and acutely dyspnoeic. Crepitations were heard throughout the lungs, and chest *x*-ray examination (Fig. 2) showed consolidation extending from the left hilum and congestive changes at both bases. The patient responded to treatment with oxygen and aminophylline, and within six days the lung fields were clinically and radiographically clear, the urine was free of protein, and the blood pressure had subsided to 140/85. The patient had remained well when seen six months later.

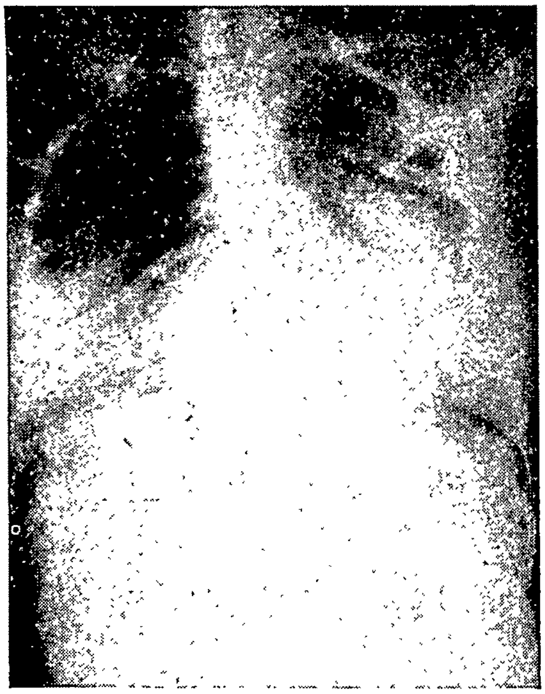


FIG. 2.—Chest *x*-ray film two hours after delivery, showing consolidation in both lung fields.

The molar condition of the placenta was presumably the cause of the patient's pre-eclampsia. The abdominal pain and fall in haemoglobin are explained by retromolar haemorrhage. The acute heart failure after delivery may have been the result of molar emboli caused by the oxytocic infusion. Hendrickse *et al.* (1965) reported 25 cases of acute dyspnoea complicating trophoblastic tumours, and three patients in their series had benign hydatidiform mole. We have seen only one other patient with acute heart failure and hydatidiform mole, and she also had a mole with associated foetus.

The abortus is of particular interest because the molar condition of the single placenta was diffuse and the female foetus abnormal, both on macroscopic inspection and on chromosomal analysis.

PATHOLOGY REPORT

The placenta was 15 cm. in diameter and the cord 30 cm. in length. Throughout the placenta numerous vesicles were visible, the majority being 0.5–1 cm. in diameter and some as large as 4 cm. When incised the vesicles released clear fluid. Apart from the obvious vesicles, closer examination with the dissecting microscope showed a mixture of swollen and relatively normal villi. The cord and membranes were normal.

The foetus was female, weighing 350 g., crown–heel length 27 cm., crown–rump length 17 cm. It showed bruising and oedema of the scalp tissues, effusions in the serous cavities, and a lumbar meningomyelocele 2 cm. in diameter. On dissection the brain was found to be grossly abnormal, with complete absence of corpus callosum and septum pellucidum, and hyperplasia of the cerebellum. Underlying the meningomyelocele, the vertebral column showed posterior spina bifida involving the lower four lumbar vertebrae. The left kidney was enlarged and polycystic with no normal renal tissue identifiable, and measured 3 by 2 by 4 cm. The right kidney contained several small cysts in the medullary zone.

Microscopical examination of the placenta (Fig. 3) showed swollen, oedematous, poorly vascularized villi. Some of the larger villi were cystic, with a thin wall of stromal tissue and a lining of flattened cells next to the cavity. Other villi were swollen and oedematous but contained dilated vessels. Some of the vessels in supporting villi appeared thickened. The remaining smaller villi were like those seen in full-term placentae. Trophoblastic proliferation was present over some of the villi, but was not pronounced.

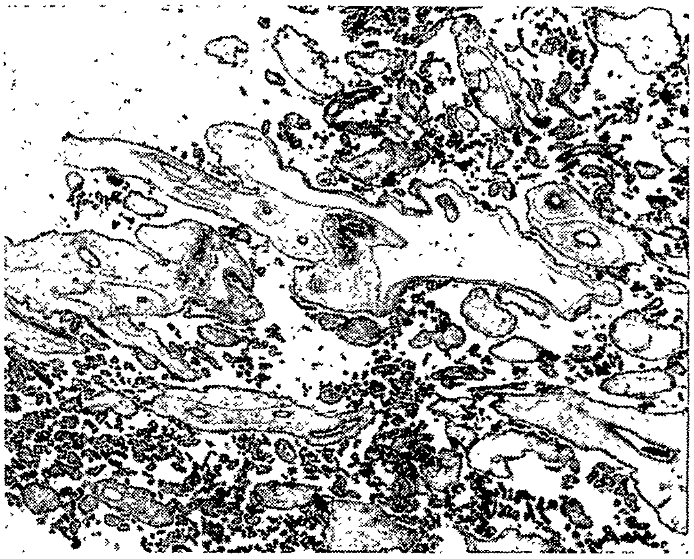


FIG. 3.—Section of placenta showing a mixture of hydropic and relatively normal villi. (H. and E. ×9.)

The left polycystic kidney showed scattered collections of glomeruli and tubules, and cysts which seemed to be of tubular origin. The few cysts in the right kidney were of similar origin.

CYTOGENETIC STUDIES

Cultures of foetal peripheral blood, thymus, and cord were set up and also vesicular tissue from the mole.

Suitable metaphase plates for counting and detailed analysis were obtained from all tissues, though the yield from the molar tissue was low. A modal count of 69 chromosomes was found (Table I) and karyotyping showed a triploid constitution (3A 3X) (Fig. 4). In many of the karyotypes and particularly in the larger groups two of each trio appeared morphologically similar, suggesting a common origin, as was observed in triploidy by Ferrier *et al.* (1964).

TABLE I.—*Chromosome Number Distribution in Foetal and Molar Tissues*

Tissue	Chromosome Number					No. of Cells Counted	Sex Chromosomes
	47	67	68	69	70		
Peripheral blood ..	1	1	1	29	2	34	XXX
Thymus	—	—	—	29	1	30	XXX
Cord	—	—	—	30	—	30	XXX
Mole	—	—	—	8	—	8	XXX

TABLE II.—*Distribution of Sex Chromatin in Foetal and Molar Tissues*

Tissue	No. of Sex Chromatin Masses			No. of Cells Counted
	0	1	2	
Mole stroma	39	54	7	200
„ trophoblast ..	40	50	10	200
Amnion	35	58	7	200
Cord	34	56	10	200
Striated muscle ..	27	62	11	200
Cardiac „	36	56	8	200
Kidney	35	58	9	200
Lung	41	51	8	200
Liver	36	54	10	100
Brain	27	62	11	200
Adrenal	30	59	11	100
Skin	22	62	16	300
Cord cultures	54	30	6	300
Mole „	70	28	2	300

The reported incidence of sex chromatin in triploid tissues has been variable; therefore counts were made on various foetal tissues, the mole, and cultured cells (Table II). Since some of the foetal tissues were not as well preserved as others, only characteristic chromatin masses on the nuclear membrane were scored, thus lowering the tissue incidence of single and double chromatin masses. The occurrence of sex chromatin was nevertheless shown to be remarkably consistent in molar and foetal tissues, with a lower incidence in the cultured tissues from cord and mole.

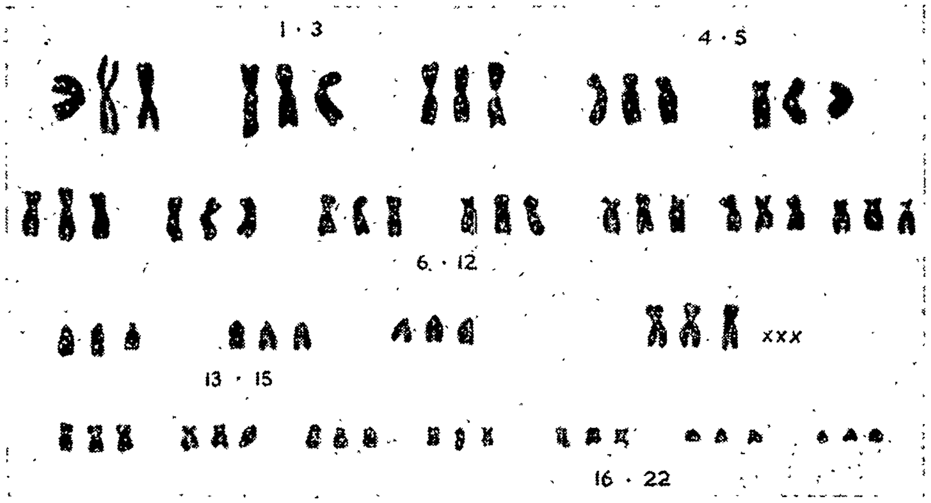


FIG. 4.—Triploid karyotype with XXX sex chromosome constitution.

DISCUSSION

Of 82 cases of mole with coexistent foetus abstracted from the literature 52 were associated with a single placenta and 30 were cases of dizygotic twins in which the molar tissue was separate from the normal placenta associated with the foetus (Beischer, 1966). There were eight abnormal foetuses among those associated with a single placenta, and in two spina bifida with meningomyelocele was described along with other malformations. The case reported above falls into this group of abnormal pregnancies and shows an associated chromosomal abnormality.

Fig. 5 shows a female foetus with meningomyelocele and its associated single molar placenta. This specimen was obtained by hysterotomy performed because of severe pre-eclampsia at 16 weeks of gestation and was reported in a previous paper (Beischer, 1961, Case 8). Because of the similarities between this case and the one reported here, we have carried out sex chromatin studies on both foetal and molar tissues; nuclei containing two sex chromatin masses were found in the stromal cells of the mole with single masses in the trophoblast and several types of foetal tissues. It is therefore probable that a triploid cell line was present in the mole with an XXX sex chromosome constitution. Atkin and Klinger (1962) mention developmental abnormalities in their case of foetus with single molar placenta, where they found a triploid chromosome constitution in the mole and double sex chromatin masses in some of the nuclei of the foetal tissues.

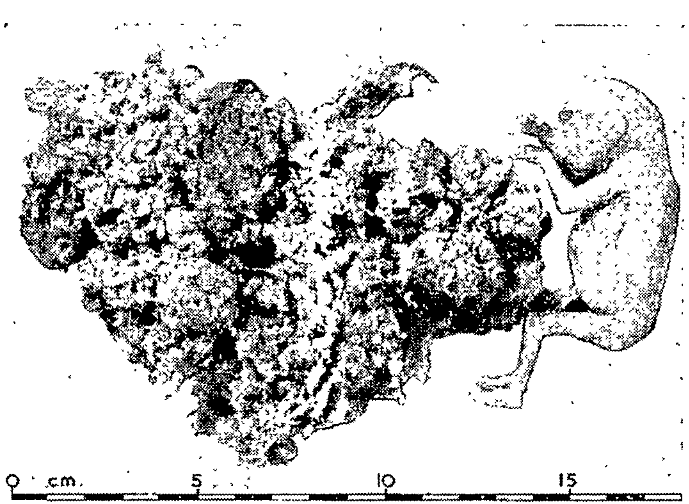


FIG. 5.—Abnormal female foetus with a single placenta showing complete macroscopic molar degeneration.

There is, therefore, accumulating evidence that certain molar pregnancies are associated with chromosomal abnormalities, and at present triploidy is most frequently reported. Where a single molar placenta is associated with a foetus the latter is often abnormal, and developmental defects of the central nervous system are not uncommon.

We wish to thank Miss S. Searle for technical assistance and Miss M. L. Johnson for the photographs.

N. A. BEISCHER, M.B., M.G.O., F.R.C.S.ED., F.R.A.C.S., M.R.C.O.G.,
Department of Obstetrics and Gynaecology, University of Melbourne.
D. W. FORTUNE, M.B., M.R.C.P.ED., M.C.PATH., M.C.P.A.,
Cytopathologist, Royal Women's Hospital, Melbourne.
M. G. FITZGERALD, B.SC.,
Cytogeneticist, Royal Children's Hospital, Melbourne.

REFERENCES

Aspillaga, M. J., Schlegel, R. J., Neu, R., and Gardner, L. I. (1964). *J. Pediat.*, **65**, 1098.
Atkin, N. B., and Klinger, H. P. (1962). *Lancet*, **2**, 727.
Beischer, N. A. (1961). *J. Obstet. Gynaec. Brit. Emp.*, **68**, 231.
—— (1966). *Aust. N.Z. J. Obstet. Gynaec.*, **6**, 127.
Böök, J. A., and Santesson, B. (1960). *Lancet*, **1**, 858.
Carr, D. H. (1963). Ibid., **2**, 603.
—— (1965). *Obstet. and Gynec.*, **26**, 308.
Delhanty, J. D. A., Ellis, J. R., and Rowley, P. T. (1961). *Lancet*, **1**, 1286.
Ellis, J. R., Marshall, R., Normand, I. C. S., and Penrose, L. S. (1963). *Nature (Lond.)*, **198**, 411.
Ferrier, P., Ferrier, S., Stalder, G., Bühler, E., Bamatter, F., and Klein, D. (1964). *Lancet*, **1**, 80.
Hendrickse, J. P. de V., Willis, A. J. P., and Evans, K. T. (1965). *J. Obstet. Gynaec. Brit. Cwlth*, **72**, 376.
Makino, S., Sasaki, M. S., and Fukuschima, T. (1964). *Lancet*, **2**, 1273.
Penrose, L. S., and Delhanty, J. D. A. (1961). Ibid., **1**, 1261.
Szulman, A. E. (1965). *New Engl. J. Med.*, **272**, 811.
Thiede, H. A., and Salm, S. B. (1964). *Amer. J. Obstet. Gynec.*, **90**, 205.

Current Practice

GROWING POINTS

Autoimmune Disease—II*

G. L. ASHERSON,† D.M., M.R.C.P.

The first part of this article described the way in which autoimmune responses—namely, autoantibodies, delayed hypersensitivity, and sometimes tissue damage—could be produced in animals. These autoimmune responses occur when (*a*) the animal is exposed to antigens similar to but not identical with self; (*b*) the animal is exposed to its own body constituents, together with an adjuvant such as Freund's complete adjuvant; and (*c*) spontaneously in New Zealand black mice. The tissue damage seen is regarded as autoimmune in nature because

(1) It is provoked by the injection of the appropriate organ, preferably in Freund's complete adjuvant, which increases and modifies immune responses. Well-characterized antigens such as thyroglobulin are able to cause autoimmune disease.

(2) It can be prevented by treatment with cortisone and folic-acid antagonists under conditions which limit immune responses, and by antigen under conditions which limit delayed hypersensitivity.

(3) The histology of the affected organ, showing infiltration with lymphocytes and histiocytes, is characteristic of delayed hypersensitivity.

(4) In the case of allergic encephalomyelitis the lesions can be transferred to normal recipients by spleen cells.

(5) Circulating autoantibodies can be demonstrated.

It is possible to cause autoantibody formation in animals, however, without producing tissue damage. For instance, rats injected with carbon tetrachloride produce autoantibodies against their own livers which are not thought to damage the liver.

It is easy to recognize disease produced by the injection of antigen as autoimmune. In man, allergic encephalomyelitis sometimes follows the injection of rabbit spinal cord used in the treatment of suspected rabies. The post-cardiotomy and post-myocardial-infarction syndromes sometimes follow damage to the heart, and the autoimmune response is probably responsible for the clinical picture. Ligation of the vas deferens by making available or altering testicular antigen causes the formation of autoantibody to sperm. These are probably responsible for infertility in some patients.

In most cases, however, the agent causing an autoimmune response is unknown, and this makes it difficult to determine whether the autoimmune response causes tissue damage or whether tissue damage gives rise to an autoimmune response. There are three possibilities:

(A) The initiating agent causes an immune response which is responsible for the main features of the disease. An example is human encephalomyelitis produced by rabbit spinal cord. If the tissue damage caused by the autoimmune response leads to further damaging autoimmune responses the disease will be self-perpetuating.

(B) The initiating agent causes tissue damage leading to an autoimmune response which is responsible for the main features of the disease. The post-cardiotomy syndrome is a possible example. Here again the autoimmune response may be self-perpetuating.

(C) The initiating agent causes the tissue damage and is responsible directly for the clinical and pathological changes of the disease. The autoimmune response is a result of the tissue damage, or is a direct effect of the initiating agent but is unimportant in pathogenesis. The formation of autoantibodies to pancreas seen in obstruction of the pancreatic duct is a possible example.

Because it is often uncertain whether an autoimmune process is the result or cause of disease, the term putative autoimmune disease is used in this article. There are certain common features of putative autoimmune diseases. These are:

(i) Raised serum gammaglobulins, which offer indirect evidence of immunological activity because antibodies are gammaglobulins.

(ii) Direct evidence of an autoimmune response, as shown by autoantibody and delayed hypersensitivity.

(iii) Tissue lesions characterized by infiltration with lymphocytes, histiocytes, and plasma cells.

(iv) Genetic incidence of the disease, and clinical and serological association with other autoimmune diseases, in either the patient or his family.

(v) Association with enlargement of the thymus or thymic tumour or both.

(vi) Ameliorating effect of corticosteroids and cytotoxic drugs.

(vii) Production of similar disease of an autoimmune aetiology in animals.

The occurrence of these features in a disease provides evidence that it resembles other putative autoimmune diseases.

Diseases in which Autoimmune Reactions may be Provoked by Micro-organisms

Rheumatic Fever.—This disease is always associated with group A beta-haemolytic streptococcal infection. These organisms have an antigen similar to human heart. Autoantibodies which react with streptococcal extracts, and can be absorbed by the human heart, may be found by gel-precipitation techniques in acute rheumatic fever. They also occur in acute glomerulonephritis and less frequently in uncomplicated streptococcal pharyngitis. The autoantibodies probably arise because of exposure to streptococcal antigen resembling human heart. The cause of tissue damage is less clear. Patients with rheumatic heart disease who undergo cardiac surgery have an increased incidence of post-cardiotomy syndrome, compared with patients with congenital heart disease. This syndrome is characterized by precordial pain, fever, and pericardial effusion. There are autoantibodies against heart, and the response to steroids is good. The raised incidence in subjects with past rheumatic fever may be related to the fact that they have already produced an autoimmune response to heart tissue.

Acute Glomerulonephritis.—This is associated with certain strains of group A beta-haemolytic streptococci. The type-12 nephritogenic strain has antigens similar to those of renal glomeruli. Acute glomerulonephritis is one of the few diseases (systemic lupus erythematosus is another) in which the level of serum complement is low. A low serum-complement level provides some evidence of complement-fixing antigen-antibody reactions *in vivo*. Serum complement is often raised when there is tissue damage, and not all immune reactions fix complement. Hence the finding of normal serum complement is not evidence against the presence of immunological disease.

---

* The first part of this article appeared in last week's issue (p. 417).

† Reader in Immunology, Department of Bacteriology, the London Hospital Medical College, London E.1.

Renal Disease.—Renal damage is a common cause of death in systemic lupus erythematosus, and it is often suggested that various forms of glomerulonephritis are immunological in nature. There are several different methods of producing immunological renal disease:

(*a*) Masugi nephritis, caused by the injection of antikidney serum. For a long time this was the chief evidence that renal disease might be immunological.

(*b*) Immune response to foreign antigens adhering to the glomeruli. Certain bacterial antigens adhere to the glomeruli, and immune responses against them may cause renal damage.

(*c*) Injection of kidney tissue in Freund's complete adjuvant. This may be an example of an autoimmune response against the kidney.

(*d*) Circulating antigen-antibody complexes. When antibody is mixed with an excess of antigen soluble antigen-antibody complexes are formed. These complexes are often able to bind (fix) complement and to cause renal damage. Their presence in the circulation is usually associated with a low serum-complement level, and they may be responsible for the renal damage in systemic lupus erythematosus.

The demonstration of gammaglobulin bound to the tissues by immunofluorescence is often taken as evidence of local combination of antibody and antigen. The presumption is strengthened by the demonstration of complement in the lesion by immunofluorescence. Nevertheless, bound gammaglobulin is seen in the glomeruli in certain experimental diseases of non-immunological nature, and this evidence requires careful assessment in renal disease.

Ulcerative Colitis.—In about 10% of these patients autoantibodies to colon can be demonstrated by immunofluorescence. Autoantibodies can also be demonstrated by haemagglutination, using red cells coated with polysaccharide derived from colonic tissue. These autoantibodies react with an antigen which occurs in sterile human and rat colon, and in certain strains of *Esch. coli.* The suggestion is that these autoantibodies arise because the human body is stimulated by bacterial antigens similar to but not identical with its own tissue components. But it is not certain that autoantibody production is an important part of the disease, and it is possible that immune reactions to bacterial residues in the tissues has a more central role. In some cases food allergy, particularly to milk, is important; and in controlled trials withdrawal of milk has been shown to diminish the frequency of relapse.

Coeliac Disease.—Antibodies to gluten show a high frequency and titre in patients with coeliac disease. There is no evidence that this is an autoimmune disease, but it may be an immune reaction to foreign antigens. Autoantibodies to gut occur in pernicious anaemia and ulcerative colitis, and in both of these the incidence of carcinoma of the affected organ is raised. In coeliac disease the incidence of lymphosarcoma of the small intestine is raised (but this is still low).

Glandular Fever.—Autoantibodies against formed elements of the blood are sometimes found, and they may be responsible for haemolytic anaemia and thrombocytopenia. The virus has not been isolated, and we do not know whether it shares antigens with human tissue.

Primary Atypical Pneumonia.—This is due to *Mycoplasma pneumoniae.* Cold agglutinins (which are autoantibodies directed against the I antigen of human erythrocytes) are often found, and they may present clinically as Raynaud's phenomenon or haemolytic anaemia and jaundice on exposure to cold. A raised titre of antibodies to *M. pneumoniae* is sometimes found in the Stevens–Johnson syndrome.

Hashimoto's Thyroiditis Group of Diseases

This group of diseases includes Hashimoto's thyroiditis, pernicious anaemia, and non-tuberculous Addison's disease of the adrenal. Certain forms of hypoparathyroidism and diabetes may ultimately be shown to belong to this group. The diseases have several common features:

(I) Autoantibodies occur which react with the affected organ, and can be demonstrated by complement fixation and immunofluorescence. Autoantibody against cell secretions—thyroglobulin and intrinsic factor—occur in Hashimoto's thyroiditis and pernicious anaemia.

(II) Patients with one disease commonly have autoantibodies characteristic of the other diseases of the group. These autoantibodies are called organ-specific, because they react with antigen from one organ only. In contrast, the autoantibodies in systemic lupus erythematosus react with widely distributed nuclear and cytoplasmic antigens. These non-organ-specific antibodies are rare in the Hashimoto's thyroiditis group of diseases.

(III) Patients sometimes have more than one disease in the group.

(IV) The patients give a family history of their own disease and of other diseases in the group.

These diseases are clinically important, because they may present insidiously and simulate psychological disorders.

Nearly all patients with Hashimoto's thyroiditis have autoantibodies against thyroid by at least one test, and the diagnosis is usually wrong if the tanned-cell-haemagglutination test for thyroglobulin, the complement-fixation reaction for antibody against cytoplasmic antigen, the immunofluorescent test for antibody against thyroglobulin, the second colloid antigen (CA2), and the cytoplasmic antigen are all negative. Low titres of antibody against thyroglobulin by the tanned-cell test are not uncommon, being shown in about 15% of women over the age of 50. Like many other autoantibodies which occur in a few apparently normal people, the incidence is much higher in women than in men. The complement-fixation reaction is rarely positive in the absence of disease. The immunofluorescent and complement-fixation tests for cytoplasmic antigen run in parallel. The immunofluorescent test is a little more sensitive (90% of patients with Hashimoto's thyroiditis give positive results), but there is a higher incidence of borderline positive results (0–15%) in apparently healthy subjects.

In the differential diagnosis of carcinoma of the thyroid and Hashimoto's thyroiditis the absence of autoantibodies is strong evidence against Hashimoto's thyroiditis. The converse is not true, and the presence of autoantibodies does not exclude carcinoma.

Tissue damage in these diseases is probably due to autoimmune processes. This is suggested by the histology of the affected organ, which is infiltrated with lymphocytes and histocytes, and the finding of autoantibodies. Cytotoxic antibodies to thyroid cells in tissue culture are almost invariably present in active Hashimoto's thyroiditis. The process which initiates autoantibody formation is unknown. The classical view was that the thyroid antigens were secluded and therefore unable to induce tolerance, but recently thyroglobulin has been demonstrated in the circulation. Perhaps its levels are too low or too variable for the maintenance of tolerance.

Graves's Disease.—Patients with Graves's disease have a thyroid-stimulating factor which behaves differently from thyrotrophic hormone, and is known as the long-acting thyroid stimulator or L.A.T.S. Recently it has been shown that L.A.T.S. is a gammaglobulin, which presumably acts by combining with the thyroid gland and stimulating the action of thyrotrophic hormone. The implication is that the hypersecretion in Graves's disease is due to an autoantibody. The thymus is usually enlarged in Graves's disease, and contains germinal centres, which are morphological evidence of antibody production. They are not found in the normal thymus. Similar changes are seen in myasthenia gravis and systemic lupus erythematosus, and in a few cases of Hashimoto's thyroiditis that have been examined. The incidence of autoantibodies to thyroid, as detected by conventional tests, is raised in Graves's disease. There is, however, a particularly high incidence of autoantibodies to thyroglobulin in exophthalmic goitre.

Pernicious Anaemia.—Autoantibodies against intrinsic factor are a distinctive feature of this disease, and they do not occur in patients with uncomplicated gastritis. They are detected by their effect on the electrophoretic mobility of radioactive-B_{12} intrinsic-factor complexes. Autoantibodies against the secretory cells of the stomach can be detected by complement-fixation and immunofluorescence in 50 to 90% of patients with pernicious anaemia. As in ulcerative colitis, the incidence of carcinoma of the affected organ is raised. The incidence of antibodies to stomach is increased in chronic gastritis (diagnosed by biopsy) and idiopathic iron-deficiency anaemia. Antibodies against stomach are not reported in infantile pernicious anaemia. These patients have normal acid secretion, and infantile pernicious anaemia is a distinct disease from the adult form.

Myasthenia Gravis and the Role of the Thymus

Autoantibodies against muscle have been demonstrated in myasthenia gravis. The techniques used for their detection include complement fixation, immunofluorescence, and tanned-cell haemagglutination. Autoantibodies are also produced against an antigen in the thymus, and occasionally against nuclei. Myasthenia gravis is sometimes associated with other putative autoimmune diseases, such as Graves's disease. Lymphorrhages (accumulations of lymphocytes) similar to those seen in thyrotoxicosis, Hashimoto's thyroiditis, and Addison's disease are found in the muscles. In this disease the relationship between the autoantibodies and the characteristic neuromuscular block is unknown.

The thymus is often enlarged, and contains germinal centres which provide morphological evidence of antibody production. In some cases there is a thymic tumour, and these patients characteristically have high titres of autoantibodies and respond poorly to thymectomy. Thymic tumours also associated with aplastic anaemia, dermatomyositis, polymyositis, granulomatous myocarditis, hyperglobulinaemic purpura, and hypogammaglobulinaemia. The question arises whether autoimmunity is important in any of these diseases.

The role of the thymus in disease is still obscure. In early post-natal life cells leave the thymus to populate the lymphoid system, and the thymus produces a hormone which favours the development of immunologically competent cells. The thymus is required in adult life for the rapid restoration of immunological function after damage to the lymphoid system by *x*-rays and other agents. The presence of germinal centres in the thymus in myasthenia gravis presumably reflects antibody production which may be directed against autoantigens.

Diabetes Mellitus

The possibility of autoimmune mechanisms in diabetes mellitus is under discussion. The most suggestive evidence is the association of Hashimoto's thyroiditis, Addison's disease, and sometimes hypoparathyroidism with diabetes (Schmidt's syndrome). Antibodies against insulin are commonly found in treated diabetics. They may be directed against human insulin, and arise as a result of stimulation with foreign insulin. They are sometimes responsible for insulin resistance.

Systemic Lupus Erythematosus and Related Diseases

Systemic lupus erythematosus is characterized clinically by multisystem involvement. The increase in gammaglobulin suggests increased antibody production. The wide range of autoantibodies characteristically react with widely distributed antigen, and these are described as non-organ-specific; the incidence of organ-specific autoantibodies of the type seen in the Hashimoto thyroiditis group of diseases is little altered.

The antibodies against nuclei (antinuclear factor) are usually detected by immunofluorescence. This test is nearly always positive in systemic lupus erythematosus, and diagnosis of the disease is nearly always wrong when the antinuclear-factor test is negative. The antinuclear-factor test, unlike the L.E.-cell test, is usually positive even when the disease is clinically inactive. The L.E.-cell test also detects antibodies against nuclei. It is positive much less frequently than is the antinuclear factor test, but there are very occasional patients with positive L.E. and negative antinuclear-factor tests.

Antibodies against cytoplasm are also found, and are detected by complement fixation—the autoimmune complement-fixation reaction. There is sometimes a biologically false-positive test for syphilis. Rheumatoid factor (which behaves like an antibody to altered gammaglobulin) occurs in about a third of patients. Autoantibodies against formed blood elements and coagulation factors may cause haemolytic anaemia, thrombocytopenia and bleeding disorders, and some cases of apparent idiopathic thrombocytopenia and thrombotic thrombocytopenic purpura develop features of systemic lupus erythematosus.

Patients with systemic lupus erythematosus have an unusual tendency to give drug and blood-transfusion reactions, and relapses may be provoked by drug reactions. In children the anticonvulsant drugs may precipitate an illness resembling systemic lupus erythematosus; the prognosis of this drug-induced disease is apparently better than that of the "idiopathic" disease. There is evidence that when patients with systemic lupus erythematosus are injected with antigens which do not cause autoantibody formation in normal subjects they produce a range of autoantibodies.

The histology of the thymus in systemic lupus erythematosus is of considerable interest. Lymphoid infiltrates and germinal centres are found, but few observations are available, because corticosteroids and terminal illness cause involution of the thymus.

The incidence of hypergammaglobulinaemia, antinuclear factor, and diseases of the systemic lupus erythematosus group is slightly raised in the relatives of patients with systemic lupus erythematosus, and in a few families the incidence of related disease is very high. The familial association with hypogammaglobulinaemia is an intriguing finding.

The aetiology of systemic lupus erythematosus is unknown, although New Zealand black mice provide a good natural model of the disease. Because of the many different autoantibodies found, this disease can be described as a disorder or breakdown of immune tolerance, but it is not clear whether this is due to exposure to altered antigens or to a defect in the antibody-producing system.

Rheumatoid Arthritis.—Rheumatoid factor, which behaves like an antibody to altered gammaglobulin (and some of the allotypes of gammaglobulin), is found in most patients with chronic rheumatoid arthritis showing joint erosions on radiological examination and nodules. It is often absent in the first year of the disease, and it is found in about 5% of normal subjects. Rheumatoid factor can be produced in animals by immunizing with antigen-antibody complexes; by infection, which probably acts by producing antibody–antigen complexes *in vivo*; and by immunization with altered gammaglobulin. Rheumatoid factor is often found in subacute bacterial endocarditis, where it has been suggested as a diagnostic aid, and in a range of diseases—including infectious hepatitis, cirrhosis of the liver, sarcoid, scleroderma, and pulmonary fibrosis. In most diseases, other than rheumatoid arthritis, the latex-fixation test (based on human gammaglobulin) is more often positive than the Rose-Waaler reaction (based on rabbit gammaglobulin).

Antinuclear factor and positive L.E. tests are found in some cases of rheumatoid arthritis. Systemic lupus erythematosus rarely develops in these patients, but they tend to have somewhat more severe disease with a raised incidence of arthritis.

Though the arteritis involves digital and visceral vessels, and the peripheral neuropathy is attributed to it, renal damage is rare. The affected joints in rheumatoid arthritis show infiltration with lymphocytes, histiocytes, and sometimes plasma-cells, and the formation of lymphoid follicles. Pannus is formed and there is erosion of cartilage. These changes can all be produced by implanting particulate (insoluble) antigens into the joints of animals; streptolysin S of the streptococcus has a similar effect. These findings raise the question of whether the human disease is due to the presence of antigenic material in the joints, and there is current interest in the possible role of mycoplasma and other micro-organisms.

Sjögren's Disease presents as failure of secretion by the lacrimal and salivary glands, and it is often associated with rheumatoid arthritis. It is of considerable immunological interest, because organ-specific antibodies against intralobular salivary-gland ducts can be demonstrated by immunofluorescence, while non-organ-specific antibodies, which react with nuclear and cytoplasmic cell components, often occur. In some patients the clinical picture merges with that of systemic lupus erythematosus.

Dermatomyositis.—Some types of dermatomyositis may belong to the systemic lupus erythematosus group of diseases. Antinuclear factor is sometimes found, and the disease may develop features of systemic lupus erythematosus. In adults there is a frequent association with carcinoma.

Miscellaneous Conditions

Liver Disease.—Patients with infectious hepatitis often have antibodies against altered gammaglobulin (positive latex test) and complement-fixing antibodies against cytoplasm. This is an example of autoantibody formation caused by infection.

Cirrhosis of the liver and infiltration of the liver with lymphocytes is sometimes associated with minor manifestations of systemic lupus erythematosus, such as rashes and haemolytic anaemia. Many of the patients have positive L.E.-cell tests, and antinuclear factor, antibody against smooth muscle, and complement-fixing antibodies against cytoplasm are found. This disease, which is called lupoid hepatitis, responds to some extent to cortisone.

Primary biliary cirrhosis presents as jaundice simulating that of extrahepatic biliary obstruction. The vast majority of these patients have positive autoimmune complement-fixation reactions, often to very high titres. The antibody reacts with a mitochondrial antigen: this is useful in differential diagnosis, because antibodies against mitochondria are rare in extrahepatic biliary obstruction.

Multiple Sclerosis.—The ease with which encephalomyelitis can be produced in animals by immunization with brain in Freund's complete adjuvant has led to the suggestion that multiple sclerosis may be an autoimmune disease. The gammaglobulin in the cerebrospinal fluid, which is responsible for the positive colloidal-gold reaction, is raised. Recently autoantibodies have been demonstrated which damage myelinated cells in tissue culture; but similar antibodies occur in motor-neurone disease, and these particular autoantibodies may be the result rather than the cause of tissue damage.

Carcinomatous Neuropathy.—Carcinoma, especially oat-cell carcinoma of the bronchus, is often associated with neuropathy which is not due to local metastases. Antibodies against the nerve bodies of posterior-root ganglia and other cells are found in sensory carcinomatous neuropathy. Tumours sometimes secrete material which is not produced by the normal cells from which they are derived. The question arises whether the tumours associated with certain forms of carcinomatous neuropathy have an antigen similar to brain tissue and so cause autoimmune disease.

Peripheral Neuritis.—Autoantibodies against nervous tissues are found in about a quarter of patients with the Guillain-Barré syndrome of peripheral neuritis associated with high protein content but low cell count in the cerebrospinal fluid.

Pemphigus is characterized by Nikolsky's sign—that is, the stratum corneum can be easily separated from the underlying epidermis—which is the result of damage to the prickle-cell layer. Autoantibodies against these latter cells can be demonstrated by immunofluorescence.

Aphthous Ulcer.—Autoantibodies against buccal mucosa have been demonstrated by complement fixation and immunofluorescence.

Conclusion

Immunologists at the turn of the century were aware of the damaging effect of immune reactions, and they considered the possibility of autoimmune disease. Interest in autoimmune disease revived with the identification of autoimmune haemolytic anaemia and the detection of autoantibodies adhering to red cells with the help of antihuman gammaglobulin serum (Coombs test). Burnet's concept of immune tolerance indicated a special mechanism whereby animals do not produce antibodies against their own tissue components, and this implied that altered physiology might lead to autoimmune reactions and disease. Two sets of observations were historically important. Firstly, the discovery of the L.E. test and the demonstration of antibodies against nuclei in systemic lupus erythematosus; this provided an example of a multisystem disease associated with multiple autoantibody production. Secondly, the production of various autoimmune diseases, including encephalomyelitis and thyroiditis, by immunization with the corresponding organ in Freund's complete adjuvant, and the demonstration of autoantibodies in Hashimoto's disease.

Early interest was focused on the following factors:

(1) Were the antibodies found in putative human autoimmune disease true antibodies? In all cases investigated autoantibodies have been shown to have the physicochemical properties of antibodies, and they are found by methods used to detect antibodies. Rheumatoid factor was originally considered to be an exception because it is a macroglobulin; but it is now known that many antibodies, especially those produced shortly after immunization or in response to particulate antigen, are macroglobulins.

(2) Were the antibodies indeed autoantibodies and not isoantibodies reacting with antigens produced in some but not all humans, and not in the patient from whom the antibody was taken? With the exception of some of the rheumatoid factors, the initial view that an antibody was an autoantibody has proved to be correct.

(3) Is autoantibody or autoreactive delayed hypersensitivity responsible for tissue damage? Methods are not yet available to answer this question. It seems likely that in some situations both circulating antibody *and* cellular factors are important..

(4) Are autoimmune responses the cause or merely the result of tissue damage?

Despite the inability to answer the last two questions, and the unsatisfactory situation in which putative autoimmune disease is virtually synonymous with the discovery of an autoimmune system, current research interest is now centring on the mechanism of production of autoimmune responses.

Three of the lines of approach are (*a*) the role of antigens similar but not identical with self; (*b*) the role of micro-organisms, including mycoplasma and viruses; and (*c*) the role of the hydrolytic enzymes in the intracellular organelles called lysosomes, which are able to degrade normal tissue components.

REFERENCES

Asherson, G. L., *Abstr. Wld Med.*, 1965.
Glynn, L. E., and Holbrow, E. J., *Autoimmune Disease*, 1965. Oxford.
Humphrey, J. H., and White, R. G., *Immunology for Students of Medicine*, 2nd edition, 1964. Oxford.

ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Fumes from Soldering

Q.—*What are the hazards of inhaling the fumes given off in the process of soldering?*

A.—Soldering processes include soft soldering and brazing (hard soldering and silver soldering). Brazing[1] is defined as "the making of a joint between pieces of metal, in which molten filler metal is drawn by capillary attraction into the space between the closely adjacent surfaces of the parts to be joined. In general, the melting point of the filler metal is above 500° C. and below that of the metal to be joined." Soldering is "a joining process similar to brazing but in which the filler metal melts at a temperature below 500° C."

Toxic fumes and gases are generated from the constituents of the filler metals, the fluxes, and the coatings on the metal surfaces. Generally speaking, hazards are likely to occur from poor technique and the overheating of the filler metal. The most common chemical contaminants of the toxic fumes and gases generated from different soldering processes are zinc, lead, cadmium, and beryllium from the filler metals and coatings on metal surfaces, and fluorine compounds, zinc chloride, rosin, methylated spirits, and isopropyl alcohol from the fluxes.

REFERENCE

[1] *Health and Safety in Welding and Allied Processes*, 1965, 2nd edition, edited by P. J. R. Challen. Institute of Welding, London.

Chrome Ulcer of Nasal Septum

Q.—*Is it safe for a man with a healed perforated chrome ulcer of the nasal septum to return to work involving contact with chrome salts?*

A.—There is no reason why a man with a healed perforated chrome ulcer of the nasal septum should not return to work involving contact with chrome salts. However, a chrome ulcer of the nasal septum indicates that an employee has been exposed to unduly high atmospheric concentrations of chrome salts, and the situation should be investigated by air sampling and analysis so that preventive measures can be instituted.

The threshold limit value[1] for chromic acid and chromates (as C_2O_3) is 0.1 mg./m.^{3} (milligrammes per cubic metre).

REFERENCE

[1] *Threshold Limit Values*, 1966. American Conference of Governmental Industrial Hygienists, 1966. Pittsburgh.

Aetiology of Osteogenesis Imperfecta

Q.—*A healthy woman with one normal child has had a stillborn infant with severe osteogenesis imperfecta. What are the risks of future infants being affected by this disorder?*

A.—When neither parent has any evidence of osteogenesis imperfecta the risks of future infants being affected are small.

Osteogenesis imperfecta congenita has occurred on several occasions as an exceptionally severe manifestation in families with dominant osteogenesis imperfecta.[1] Most cases, however, are sporadic and are probably caused by fresh dominant mutations. In Seedorff's Danish series[1] one patient was born to a parent with osteogenesis imperfecta tarda and 6 were sporadic with 19 unaffected sibs. In Smårs's series for Sweden,[2] of the 22 cases born to unaffected parents 17 were sporadic and had in all 46 unaffected sibs, but the other 5 occurred in two non-consanguineous families, 3 in a sibship of 7, and the other 2 in a sibship of 2. In a third series of 15 consecutive cases from one hospital[3] one mother had blue sclerae and deafness and another mother blue sclerae alone, but it appears that no sib was affected. The total number of sibs, however, was not stated.

In addition to the families of Smårs there are a few convincing case reports of individual families with normal parents having two children or dizygotic twins affected by osteogenesis imperfecta congenita.[4 5] Other reports are not fully documented, and do not exclude a diagnosis of congenital recessive hypophosphatasia.

REFERENCES

[1] Seedorff, K. S., *Osteogenesis Imperfecta*, 1949. Copenhagen.
[2] Smårs, G., *Osteogenesis Imperfecta in Sweden*, 1961. Stockholm.
[3] Freda, V. J., Vosburgh, G. J., and Di Liberti, C., *Obstet. and Gynec.*, 1961, 18, 535.
[4] Goldfarb, A. A., and Ford, D., *J. Pediat.*, 1954, 44, 264.
[5] Zeitoun, M. M., Ibrahim, A. H., and Kassem, A. S., *Arch. Dis. Childh.*, 1963, 38, 289.

Inhalation of Starch Dust

Q.—*Is there any hazard from the inhalation of starch dust over a long period?*

A.—There is no evidence that the inhalation of starch dust over a long period gives rise to any health hazard.

Pox Scars

Q.—*Is there any effective treatment for scars resulting from smallpox or chickenpox?*

A.—Scarring results from destructive damage to the skin affecting not only the full thickness of the epidermis, including the accessory glands and hair follicles, but also of the corium. These changes are irreversible.

Scarring from chicken-pox or smallpox tends to produce slight superficial atrophy with depigmentation, which tends to become more conspicuous during the summer with tanning of the adjacent normal skin. It is rarely possible to improve such superficial scars by excision followed by grafting of normal skin. It is advisable to cover the whole affected area with some screening applications before exposure to intense sunlight. That will prevent disproportionate tanning of the normal skin and burning of the depigmented scars.

Hypertrophic and keloid scars can be flattened by infiltration with a 1% solution of triamcinolone, repeated if necessary at intervals of two to three weeks until the lesion is flush with the normal skin. It is then possible to camouflage any discoloration of the scar with proprietary applications like Covermark. This is usually more acceptable also for depigmented depressed scars than staining with potassium permanganate solution (1:8,000). Scars tend to become less conspicuous with the passage of time.

Treatment of Alopecia

Q.—*A preparation of live E. coli was recommended years ago in the treatment of intractable alopecia areata or even totalis. Was this preparation of use?*

A.—It is not surprising that in conditions for which specific treatment is not available, and which pursue an unpredictable natural course, widely different treatments have been claimed to be of value. There is no acceptable evidence that preparations of *E. coli*, live or dead, are beneficial in alopecia areata or totalis.

Ultrasonic Treatment for Varicose Ulcer

Q.—*Have ultrasonic rays any place in the treatment of a refractory ulcer?*

A.—Ultrasonic rays have a reputed ability to fragment local fibrous tissue. Their particular place is therefore in the management of the woody plaque type of induration in the lower leg that results from local "venous" fat necrosis and periphlebitis. This type of induration often effloresces into the full-blown venous ulcer lesion. Even so, results from this type of therapy have not been particularly rewarding. Compression, preferably over "Molefoam" pads, still forms the linchpin of management.

For the refractory ulcer lesion—presumably refractory to compression treatment—bed-rest in hospital and elevation of the limb are the proper answer. Antibiotic creams of all types are to be avoided. The ulcer should be repeatedly dressed with equal parts of eusol and liquid paraffin. This rapidly clears local sloughs and allows a rich granulation bed to form, for which small pinch grafts from the abdomen make a good cover.

Congenital Ichthyosis

Q.—*A patient who has congenital ichthyosis has noticed that whenever she has a course of tetracycline her skin stops scaling. Is there any explanation for this?*

A.—It would be relevant to know whether the patient has ichthyosis vulgaris or bullous ichthyosiform erythroderma. Both conditions are congenital and incurable, but, though they may have much in common clinically, secondary infection, with often inconspicuous pustules and bullae, is a feature only of bullous ichthyosiform erythroderma. The latter condition may benefit significantly from systemic treatment with antibiotics. Swabs from moist lesions, especially bullae and flexures, should identify the infecting micro-organisms.

Book Reviews

Urology

Encyclopedia of Urology. Vol. XI/1. Tumours I, by Arthur Jacobs and Eric Riches, Organic Diseases, by Leslie N. Pyrah. (Pp. 286+xii; illustrated. DM.128.) Berlin, Heidelberg, and New York: Springer. 1967.

Volume XI/1, the latest to appear in this important international work, deals with tumours of the kidney, ureter, and bladder, and also with a miscellaneous collection of unrelated urological conditions grouped under the heading of "organic diseases."

There have doubtless been good reasons for breaking the sequence on tumours and leaving the remainder to a future section (volume XI/2), but one effect which may well appeal to British readers has been to allow the whole of the present text to appear in English. Furthermore, notwithstanding the eminence of the contributors, the interpolation of additional material contrives to make this volume one of the most valuable and interesting in the series.

Writing on tumours of the kidney and ureter Sir Eric Riches ranges over their incidence and classification and refers to current aspects of aetiology. His exceptional clinical and surgical experience, supplemented by radiological and pathological studies at the Middlesex Hospital, provides an appropriate background for a critical review of treatment and prognosis. The importance of radiology in the detection of early tumours is suitably stressed and amply illustrated by photographs of surgical specimens superimposed on the *x*-ray films. Among the techniques discussed are nephrotomography and aortography but, though selective arteriography is mentioned, most of the illustrations depict the earlier translumbar technique. Of particular interest are the sections dealing with the grading and staging of parenchymal tumours in relation to prognosis, and details of a 10-year follow-up study are included. The excellence of the supporting microphotographs merits special commendation.

Tumours of the bladder, a subject of perennial interest to all urologists, are ably dealt with by Arthur Jacobs, whose facile style and wide acquaintance with the problems involved contribute to a well-balanced account. He is assisted by Professor Symington and his colleagues in a description of the pathology of the wide variety of neoplastic lesions which may affect the organ. Particular emphasis is again laid on the grading and staging of epithelial tumours as a guide to the selection of appropriate treatment, and the merits of surgery and radiotherapy are fully discussed. No mention is made of the instillation of cytotoxic agents, nor of recent work on chromosome analysis as a possible guide to tumour staging, but perhaps in each instance their present value is difficult to assess.

The remainder of the volume affords full scope for the peripatetic philosophy of Professor Pyrah with subjects ranging in descending order from infarction of the kidney to torsion of the testicle. Movable kidney, positional change of the bladder, foreign bodies, priapism, Peyronie's disease, and scrotal swellings are all matters on which urologists will welcome his expert guidance. Indeed his far-reaching and discriminating descriptions will be recognized as filling a gap which notably exists in many of the standard textbooks.

Throughout the volume, as in the case of its predecessors, a high technical standard of production is sustained. The wide range and quality of the contents redounds to the credit of British urology and should ensure pride of place in the library of all interested in the specialty.

J. D. FERGUSSON.

Misery in our Midst

Sans Everything. A Case to Answer. Presented by Barbara Robb on behalf of A.E.G.I.S (Pp. 148+xvi. 18s.) London: Thomas Nelson. 1967.

The small volume *Sans Everything* packs between its covers a horrifying story of the grim conditions in which many old people exist in hospital. The material for the book is a record of reports made to A.E.G.I.S. This association for Aid for the Elderly in Government Institutions has as its aim to shame the Government and people into doing something about the cruelty and neglect which is the lot of many of our aged citizens.

The first section of the book, "The Case," consists of a number of letters from nurses and social workers whose consciences have led them to protest, and an account of the life of an old lady in a mental hospital as observed by the authors. Some of the evidence suggests that the observers have failed to understand the way facts are distorted by patients suffering from mental disorder and the way relatives may project their own guilty feelings on to the institution. There is no attempt in the report to assess the frequency of callousness in the hospital service and little to assess its causes.

In spite of these deficiencies the authors succeed in stimulating the conscience of the reader and the book has undoubtedly drawn public attention to the problem. The danger is that the lack of facts may enable it to be too easily dismissed, for those who have worked with the aged know that there is some truth in the accusations. Most voluntary and hospital workers will know of geriatric institutions where the doctors bring nothing of modern medicine to the care of their patients, and where the nurses are more concerned about their authority and their concept of discipline than about understanding and kindness.

The second section of the book, "Some Answers," deals with the way in which the black spots might be eradicated. Priority is rightly given to a medical solution, because an unhealthy hospital cannot be cured until the medical staff have been converted, and the doctors are in the best position to teach new attitudes to the other staff. The administration of the psycho-geriatric service in Severalls Hospital, Colchester, is described with reference to admission procedure, month-in month-out system, day care, boarding out, and community support. Such a procedure is practised in the most progressive of the geriatric and psycho-geriatric departments in this country, but there are too few of them.

Mrs. Barbara Robb and Mr. P. G. M. Thomson then give details of their "Project 70," which is a self-financing scheme in which they propose that new townships should be built on huge, undeveloped estates of certain carefully chosen mental hospitals, and that the revenue from the family flats and houses of these self-contained communities and their shops, offices, and other premises could finance new accommodation for the elderly patients now in hospital. This is an attractive scheme, but its success would depend upon trained personnel, and these do not exist at present. A.E.G.I.S., however, urges the following measures should be taken at once to remedy this:

(1) Provision of courses for young registrars to train as consultants.

(2) Provision of training course for geriatric nurses and recognition of their status and the establishment of a register, such as already exists for midwifery. The inclusion of more training in the care of the elderly in nurses' general training.

(3) The organization of voluntary help.

(4) The adoption of such methods as are used at Severalls and other progressive departments.

In another chapter Professor Brian Abel Smith discusses an administrative solution, that of a "Hospital Commissioner." While he accepts that the National Health Service has already improved the situation, he argues that in hospitals where interpersonal relationships, staffing, buildings, and amenities are poor in quality and quantity these bad conditions and attitudes perpetuate themselves. He suggests that "new recruits, whether medical, nursing, or domestic, either accept the institution as it is or find a job elsewhere. Very few stay to fight for what they know is right. The vast majority protest only by leaving. Those who cannot leave are the patients with nowhere else to go." Professor Abel Smith's suggestion that a hospital commissioner should be appointed who can enforce better standards in the hospital service is unrealistic, and would not have been suggested had the author attempted a more detailed diagnosis of the trouble. It is well known throughout the British medical service, and indeed in medical services in other countries in the Western world, that geriatrics is not attractive to medical or nursing recruits, except for a dedicated minority. To commence a series of disciplinary actions would aggravate the problem by making geriatrics even less attractive and driving the staff into closer defensive attitudes. What is required is an investigation into the causes of the inferior status of geriatrics so that these may be changed. Some of the special troubles include the desperate state of the buildings in which old people are nursed, the low level of medical and nurse staffing, the poor co-operation that so often exists between the hospitals and the welfare services, and the failure to separate mentally and physically ill old people and treat them in appropriate hospitals. These disorders, and others, are clearly described in the book, but the opportunity to present constructive reforms is not taken.

Change will come about only if the public conscience is effectively aroused. Dr. M. D. Enoch, postgraduate clinical tutor at the University of Birmingham and consultant psychiatrist to the Shrewsbury Hospital Group, in the last chapter of the book, "Ready for the Scrap Heap," summarizes the situation: "The elderly, increasing in numbers year by year, are a group of people who do not fit into the materialistic plan of this present affluent society. From the politicians' point of view they must be seen as a group who do not constitute any form of pressure group. The greater number of them anyway would not be able to creep to the polling booths. A great number of them cannot even write an awkward letter of protest to the press or anybody else, and anyway they have their pride. It might be said that we have provided for them, but can we really expect them to choose the role of public beggars ? "

It is surely impossible for anyone who reads this book not to feel some personal responsibility for the sufferings of the defenceless which it describes.

E. WOODFORD-WILLIAMS.

Nucleic Acid Research

Progress in Nucleic Acid Research and Molecular Biology. Vol. 5. Edited by J. N. Davidson and Waldo E. Cohn. (Pp. 450+xvii; illustrated. £6 8s.) New York and London: Academic Press. 1966.

In 1960 appeared the last three volumes of *The Nucleic Acids: Chemistry and Biology*, edited by Chargaff and Davidson. Progress in this field was so rapid that it was widely welcomed when the present authors published in 1963 the first two volumes of their series *Progress in Nucleic Acid Research.* The fifth volume, which carries the additional and fashionable label "Molecular Biology," again fully demonstrates the enormous progress in this area of endeavour, and it will be gratefully received by those who are unable to follow the very numerous single publications in many journals.

The editors have assembled contributions particularly about unusual or altered nucleosides. These are sometimes referred to as "minor" nucleosides, but this qualification is used only in the quantitative sense, and, as the editors point out, it does not in any way indicate a lack of importance. There are chapters on pseudouridine, which was discovered as recently as 1957 and is found in the transfer R.N.A. of many organisms, and an exhaustive discussion of the D-arabinosyl nucleosides, which are associated with sponges and metabolized by bacteria. The relative lack in animal cells of a deaminase acting on arabinonucleosides has permitted the demonstration of the considerable effect of such compounds on, for example, leukaemic cells in culture. This toxicity manifests itself primarily in an inhibition of D.N.A. synthesis.

There are now known numerous nucleoside antibiotics. They include purine nucleosides such as puromycine, pyrimidine nucleosides, and compounds such as septacidin, which contain a carbohydrate moiety linked glycosylically to adenine, and other related molecules. One chapter records the effects of some chemical mutagens and carcinogens on nucleic acids. Nucleoproteins are attacked by mustard gas by way of alkylation of their guanine moiety. A great deal is known now about chemical carcinogens alkylating nucleic acids in vivo. Collagen is unique among proteins for its high content of hydroxyproline and hydroxylysine. In view of recent work on methylation of nucleic acid by alkylating reagents it seems reasonable to postulate the possible existence of lysine and proline hydroxylases acting in a similar fashion on proline and lysine in the preformed polymer.

The discovery of D.N.A. in the chloroplasts of algae and higher plants has produced evidence that there is D.N.A. in mitochondria of animal cells. It is thought that the cell contains various kinds of autonomous organelles with their own genetic D.N.A. One chapter is devoted to chloroplast D.N.A. and to the extranuclear D.N.A. in *Chlorella,* which provides evidence for the existence in cells of "metabolic D.N.A." in addition to the "genetic D.N.A." Another review deals with the different ways in which hormones affect the metabolism of all types of R.N.A., and thereby control utilization of R.N.A. for protein synthesis. The recombination of D.N.A. molecules is discussed thoroughly. It is of fundamental importance for the understanding of D.N.A. genetics. It seems likely that genetic or molecular recombination is based on the interaction of complementary polynucleotides, and it is concluded that freely recombining D.N.A. molecules must be assembled from nonrepetitive short lengths.

This volume is full of interest not only for the molecular biologist—for whom the numerous references will be invaluable—but will also appeal to a much wider circle of biologists, and in fact to all those who are concerned with the living cell.

H. LEHMANN.

Advice for First Aiders

First Aid in the Factory. 3rd edition. By Lord Taylor, B.Sc., M.D., F.R.C.P. (Pp. 150+ix; illustrated. 12s. 6d.) London: Longmans, Green. 1967.

The first aid described by Lord Taylor for the guidance of factory workers is well conceived and includes a good deal of treatment that, though simple, is in fact definitive. He makes a good case for this interpretation and is careful to remind his readers that they must know when to stop.

The sections on wounds and bleeding are admirably clear and sensible, but it is regrettable that although the author refers to its "mythology" his loose use of the word "shock" is less likely to clarify the subject than would entirely abandoning the word. After the introductory remarks about splintage it is disappointing to find how much of it is recommended for use on the upper limb and more disappointing to find that inflatable splints are not even mentioned. It is hard to see the justification for devoting space to a detailed description of the obsolete methods of ventilating the lungs artificially. There is no mention of the airways that have been recommended for use with artificial ventilation ; if this is because they are not favoured, the reasons for this would have been worth reading.

In spite of the critical note of the foregoing, the points mentioned occur in a large amount of admirable advice. At the present rate, the fourth edition will soon be due and it could usefully contain references to injection injuries, overbreathing tetany, and thumping the sternum and raising the legs to restore the heartbeat.

P. S. LONDON.

Tropical Diseases

Tropical Diseases. 2nd edition. Supplement to *The Principles and Practice of Medicine.* 8th edition. By Frederick J. Wright, M.A., M.D.Cantab., F.R.C.P.Ed., F.R.C.P.Lond., D.T.M.&H.Eng., and James P. Baird, M.D., F.R.C.P.Ed., F.R.C.P.Lond. (Pp. 176+viii; illustrated. 10s. 6d.) Edinburgh and London: E. & S. Livingstone. 1967.

The supplement to *The Principles and Practice of Medicine* will be useful only to persons who already own or intend to buy this textbook of medicine, since such important tropical diseases as malaria and amoebiasis are deliberately left out.

The text is 171 pages long and contains sections on diseases due to protozoa ; diseases due to bacteria, spirochaetes, and spirilla ; diseases due to viruses and rickettsiae ; diseases due to helminths ; diseases due to fungi ; micellaneous conditions ; and anaemia in the tropics. The text is clearly and concisely written, with the sections on treatment remarkably up to date. In view of the diminishing importance of yaws possibly less space need be devoted to this subject in the future, while the beneficial effect of niridazole in the treatment of guinea-worm infection should be mentioned. Most pathologists would not accept malaria as an aetiological agent in cirrhosis of the liver.

It may be wiser in future editions of the main textbook of medicine to include the contents of this supplement in it rather than to produce it as a separate and incomplete entity.

H. M. GILLES.

Mental Health

Mental Health and Contemporary Thought. Vol. 2 of Report of World Federation for Mental Health. Edited by Kenneth Soddy and Robert H. Ahrenfeldt. (Pp. 362+xxix. 55s.) London: Tavistock. 1967.

Mental Health in the Service of the Community. Vol. 3 of Report of World Federation for Mental Health. Edited by Kenneth Soddy and Robert H. Ahrenfeldt. (Pp. 306+xxvii. 45s.) London: Tavistock. 1967.

These two volumes are numbers 2 and 3[1] of a report of a conference held in 1961 by a study group of the World Federation of Mental Health. It surveyed the field of mental health from the point of view of various disciplines. Accordingly, though psychiatrists predominated, anthropology, social psychology, education, and personnel research were also represented.

---

[1] For review of Vol. 1 see *Brit. med. J.*, 1966, 1, 407.

As might be expected, a wide range of topics are discussed. Volume 2 deals with problems brought about by changes in social structure; individual aggressiveness and war; the definition of "mental health" and professional training and education for workers in this field. Volume 3 is concerned with the recognition of mental disorders, the setting up of psychiatric services, and future research.

The approach has to balance breadth of vision with depth of focus, knowing that whatever balance is struck it will not please everybody. In these volumes an enormous number of interesting issues are raised, but they are discussed with a ponderous superficiality which makes frustrating reading. Though the original contributions to the conference may well have been stimulating, their impact has been muffled by the mists of time and an editorial style which tends to start paragraphs with redundant phrases such as "it appears to have become much more generally accepted that" or "it can hardly be doubted that." Each volume has a useful and extensive bibliography to the subjects covered in all three books.

For their comprehensiveness these volumes will be of value to readers interested in mental health, but they are unlikely to inspire many enthusiastic new recruits. They should be compulsory reading for future editors of multidisciplinary conferences.

J. L. T. BIRLEY.

Books Received

Review is not precluded by notice here of books recently received.

Historic Derivations of Modern Psychiatry. Edited by Iago Galdston, M.D. (Pp. 241+xiv; illustrated. £5 0s. 6d.) London: McGraw-Hill. 1967.

Social Work with the Mentally Subnormal. By Joan Todd. (Pp. 86. 15s.) London: Routledge & Kegan Paul. 1967.

Principles and Practice of Obstetric Analgesia and Anesthesia. Vol. 1. Fundamental Considerations. By John J. Bonica, M.D. (Pp. 837+xvi; illustrated. £9 15s.) Oxford: Blackwell. 1967.

Principles of Clinical Electrocardiography. 6th edition. By Mervin J. Goldman, M.D. (Pp. 394; illustrated. 45s.) Oxford: Blackwell. 1967.

Notes on Medical Virology. By Morag C. Timbury, M.D., Ph.D., M.C.Path. (Pp. 106+vii; illustrated. 10s. 6d.) Edinburgh and London: E. & S. Livingstone. 1967.

Outline of Orthopaedics. 6th edition. By John Crawford Adams, M.D., M.S., F.R.C.S. (Pp. 467+vii; illustrated. 40s.) Edinburgh and London: E. & S. Livingstone. 1967.

Principles and Methods of Social Psychology. By Edwin P. Hollander. (Pp. 520+xxiii. 64s.) London: Oxford University Press. 1967.

Pathology of Laboratory Rats and Mice. Edited by Ernest Cotchin, D.Sc., F.R.C.V.S., F.C.Path., and Francis J. C. Roe, D.M.(Oxon.), D.Sc., F.C.Path. (Pp. 848+xxiii; illustrated. £7 15s.) Oxford: Blackwell. 1967.

Radio-Diagnostic en Rhumatologie. By Stanislas de Sèze, Micheline Phankim-Koupernik, et les médecins du Centre de Rhumatologie Viggo Petersen. (Pp. 479; illustrated. No price given.) Paris: Expansion Scientifique Française. 1967.

Clinical Psychopathology. Signs and Symptoms in Psychiatry. By Frank Fish, M.B., M.R.C.P., M.R.C.P.Ed., D.P.M. (Pp. 120+vii. 30s.) Bristol: John Wright. 1967.

Laboratory Diagnostic Procedures in the Rheumatic Diseases. Edited by Alan S. Cohen, M.D. (Pp. 363+xii; illustrated. £5.) London: J. & A. Churchill. 1967.

A Primer of Pathology. 2nd edition. By F. A. Ward, L.R.C.P.I., M.C.Path. (Pp. 116+viii. 22s. 6d.) London: Butterworth. 1967.

Aspects of Drug Addiction. By Martin Silberman. (Pp. 112. 7s. 6d.) London: Royal London Prisoners' Aid Society. 1967.

Communicating with the Patient. By P. Ley, B.A., Dip.Psych., and M. S. Spelman, M.B., Ch.B., D.P.M., M.D. (Pp. 128. 37s. 6d.) London: Staples. 1967.

Phase Contrast and Interference Microscopy for Cell Biologists. By K. F. A. Ross, D.Phil. (Oxon.). (Pp. 238+xxi; illustrated. 70s.) London: Edward Arnold. 1967.

Surgery for Nurses. 11th edition. By James Moroney. (Pp. 803+xii; illustrated. 45s.) Edinburgh and London: E. & S. Livingstone. 1967.

Penguin Science Survey 1967. The Biology of Sex. Edited by Anthony Allison. (Pp. 288; illustrated. 12s. 6d.) Harmondsworth, Middlesex: Penguin. 1967.

Introducing Biology. By James F. Riley. (Pp. 154; illustrated. 4s. 6d.) Harmondsworth, Middlesex: Penguin. 1967.

Fonctions Endocriniennes de l'Ovaire. Vol. 2. Symposium, directed by M. F. Jayle. (Pp. 212–634; illustrated. No price given.) Paris: Gauthier-Villars. 1967.

Recent Research on Gonadotrophic Hormones. Edited by E. Trevor Bell, B.Sc., Ph.D., and John A. Loraine, D.Sc., M.B., Ph.D., F.R.C.P.Ed. (Pp. 345+ix; illustrated. 70s.) Edinburgh and London: E. & S. Livingstone. 1967.

Vascular Histochemistry. By C. W. M. Adams, M.A., M.D.(Camb.), D.Sc.(Lond.), M.R.C.P. (Lond.), M.C.Path. (Pp. 448; illustrated. £6.) Lloyd-Luke. 1967.

Practical Paediatric Problems. 2nd edition. By James H. Hutchison, O.B.E., M.D.(Glasg.), F.R.S.E., F.R.C.P.(Lond.), F.R.C.P.(Ed.), F.R.C.P.(Glasg.). (Pp. 559+xv; illustrated. 55s.) London: Lloyd-Luke. 1967.

Vision and the Eye. By M. H. Pirenne, Dr.Sc., Ph.D., M.A. (Pp. 224+xvi; illustrated. 50s. Paper 25s.) London: Chapman and Hall. 1967.

Pränatale Erkrankungen des Menschen. By Professor O. Thalhammer. (Pp. 442+ix; illustrated. DM. 78.) Stuttgart: Georg Thieme. 1967.

Narkose. Eine Einführung. By Dr. Ludwig Stöcker. (Pp. 243+viii; illustrated. DM. 9.) Stuttgart: Georg Thieme. 1967.

Les Mouvements Conjugués Oculaires et leurs Diverses Modalités d'Atteinte. By Jean de Recondo. (Pp. 113+viii; illustrated. 30 F.) Paris: Masson. 1967.

The State of Psychiatry. Essays and Addresses. By Sir Aubrey Lewis. (Pp. 310+ix. 63s.) London: Routledge & Kegan Paul. 1967.

Inquiries in Psychiatry. Clinical and Social Investigations. By Sir Aubrey Lewis. (Pp. 335+vii. 63s.) London: Routledge & Kegan Paul. 1967.

Physiology in Industry. 2nd edition. By Lucien Brouha, M.D., D.Sc. With a chapter by John A. Zapp, jun., Ph.D. (Pp. 164+xii; illustrated. 27s. 6d.) Oxford: Pergamon. 1967.

Doctors' Strike. Medical Care and Conflict in Saskatchewan. By Robin F. Badgley and Samuel Wolfe. (Pp. 201+xiii. $6.50.) New York: Atherton Press. 1967.

A Textbook for Medical Assistants. By M. Murray Lawton, M.D., and Donald F. Foy, B.S., M.S. (Pp. 465+xii; illustrated. 66s.) London: Henry Kimpton. 1967.

Handbook of Orthopaedic Surgery. 7th edition. By Alfred R. Shands, jun., B.A., M.D., F.A.C.S., and R. Beverly Raney, Sr., B.A., M.D., F.A.C.S. (Pp. 572+xii; illustrated. 90s.) London: Henry Kimpton. 1967.

Médecine et Biochimie. Problèmes d'Actualité. By Alfred Gajdos. (Pp. 360; illustrated. 54 F.) Paris: Masson. 1967.

Physiologie et Physiopathologie de la Plongée en Apnée. By J. H. Corriol. (Pp. 106; illustrated. 28 F.) Paris: Masson. 1967.

Le Moignon de l'Amputation a l'Appareillage. By J.-E. Lescœur. (Pp. 109+viii; illustrated. 34 F.) Paris: Masson. 1967.

Atlas d'Endoscopie Bronchologique. Aspects Normaux et Pathologiques. By Jean Ioannou. (Pp. 64+vi; illustrated. 60 F.) Paris: Masson. 1967.

Heures Internationales dans la Lutte Contre la Tuberculose. 2nd series. By Étienne Bernard. (Pp. 73. 25 F.) Paris: Masson. 1967.

Psychiatrie. Ein Lehrbuch für Studierende und Ärzte. By Kurt Kolle. (Pp. 348+xi; illustrated. DM. 29.80.) Stuttgart: Georg Thieme. 1967.

The Innocent Murmur. A Problem in Clinical Practice. Edited by Cesar A. Caceres, M.D., and Lowell W. Perry, M.D. (Pp. 300+xvi; illustrated. 97s. 6d.) London: J. & A. Churchill. 1967.

The Gamma Globulins. By Charles A. Janeway, M.D., Fred S. Rosen, M.D., Ezio Merler, Ph.D., and Chester A. Alper, M.D. (Pp. 148+xi; illustrated. 50s.) London: J. & A. Churchill. 1967.

The Mother, Anxiety, and Death. The Catastrophic Death Complex. By Joseph C. Rheingold, M.D., Ph.D. (Pp. 271+xi. 67s. 6d.) London: J. & A. Churchill. 1967.

Atlas of Intestinal Stomas. By Rupert B. Turnbull, jun., M.D., F.A.C.S., and Frank L. Weakley, M.D. (Pp. 207+xii; illustrated. £8 1s. 6d.) London: Henry Kimpton. 1967.

Research into Hydrocephalus and Spina Bifida. Spastics Society Medical Education and Information Unit. (Pp. 139; illustrated. 15s.) London: William Heinemann. 1967.

The Year Book of Urology. 1966–1967. Edited by John T. Grayhack, M.D. (Pp. 445; illustrated. 68s.) London: Lloyd-Luke. 1967.

Middle Articles

MEDICAL HISTORY

International Congress of Medicine 1867 and Some of the Personalities Involved

W. H. McMENEMEY,* D.M., F.R.C.P., F.C.PATH.

Brit. med. J., 1967, 3, 487–489

The International Medical Congress of 1867, the first of its kind, was held in Paris from Friday 16 August to Wednesday 28 August. The idea to hold such a gathering to coincide with the Paris exhibition was advanced by Professor Henri Gintrac, of Bordeaux, during the third annual French medical convention held in that city in the year 1865. Though the project was warmly received in France the *British Medical Journal* (1867, 1, 610) feared that the organizers were leaving much undone if they wished it to be truly international: they had, for instance, omitted to invite societies, colleges, and "distinguished personages," so that "the few Englishmen who attend will probably be chiefly excursionists, representing themselves." It is possible, however, that some of the invitations were left in the hands of "the foreign delegates" appointed by the Congress Bureau—Dr. Hermann Beiget, Berlin graduate and physician to the Metropolitan Free Hospital in London, having been one of them. Thus while the only learned societies in the United Kingdom to be represented were the British Medical Association and the Medical Society of London there were no fewer than 18 from the United States. Belgium, France, Holland, Prussia, and Russia were each allocated an honorary member, while Portugal had two: the individual selected for France was the minister of public instruction. Most of these countries and also Bavaria sent a government delegate. Six vice-presidencies went to France and six to other countries, but this time the United Kingdom was represented, in fact by Mr. Victor de Méric, a Glasgow graduate of French origin and fashionable genitourinary surgeon, of 17 Brook Street, London W.1, who found himself in the distinguished company of the great Professor Virchow and Baron Larrey,[1] surgeon to the Emperor Napoleon III. He had done his best to advertise the congress among British doctors and in the columns of the *Lancet,* whose correspondent he was.

Visitors from Overseas

The reputation of La Manche was such as to deter many who otherwise were prepared to follow their portmanteaux on the boat and through *la douane* and the vicissitudes of the railroad journeys: but there were enticements, including a 50% reduction on the ordinary tariff, generously offered by the Compagnie du Nord, thanks to the kind offices of M. de Rothschild, director, and M. Cousin, "chef d'exploitation." Even so, there were "far more Cossaques than English present." At the Congress, de Méric recognized half a dozen London men, and there could have been a few from the country; but he was saddened to find that no one from Great Britain had been chosen to speak in the section on tuberculosis. In fact, there were 72 "adherents" from the United Kingdom, including Lionel Beale, Burney Yeo, Morell Mackenzie, and 25-year-old Robert Cowie, of Lerwick, one-time surgeon at the Fort Charlotte gaol, and then Medical Officer of Health to the Sumburgh Head and Whalsey Skerries Lighthouse, who proposed to address them on the subject of "prolonged menstruation in the Shetland Islands, and its relation to longevity." Dr. Cowie's name, however, appears on a list of authors who had not made the *acte d'adhésion* because their *mémoirs* had not complied with the conditions of the programme.

The only active participants from the British Isles were in fact Victor de Méric, Charles Drysdale, of the Metropolitan Free Hospital, and John Z. Laurence, of 30 Devonshire Street, surgeon at St. Bartholomew's Hospital, Chatham, and at the Southwark Eye Hospital, who presented a case of traumatic aneurysm in the orbit cured by ligation of the common carotid artery. Dr. Edward Tilt, a graduate of Paris and consulting physician to the Farringdon General Dispensary and Lying-In Chārity, an authority on female hygiene, was to have read a paper, but in his unavoidable absence it was presented by Dr. Ball, an Englishman naturalized and practising in Paris, and one of the secretaries of the congress. The ruling of *le Bureau* that "long papers will be deposited in the Acts of the Congress" could be interpreted either as an incentive to authors or perhaps as a deterrent.

There were 60 adherents from the United States, seven from Canada, one from the State of Kentucky, and one from the State of California.[2] There were 333 "founder" members, all Frenchmen, and 300 student tickets were issued, so the total number crowding into the amphitheatre of the School of Medicine sometimes amounted to 1,200 (one report says over 1,500). The flags of many nations decorated the hall, the bare walls of which were clothed with green baize and golden fringes. The "hemicycle" reserved for special dignitaries exhibited "a grand display of red velvet." The president and officials sat in gilt armchairs, but the congressists had to put up with hard benches. As one reporter declared, it was after all but a huge schoolroom. It appears to have been an intensely hot one too.

Patrons

Professor Jean Baptiste Bouillaud, of the Faculté de Paris and consulting physician to the Emperor, presided and Dr. Jaccoud was the general secretary. Others who patronized the congress were Professors Rokitansky, Wertheim, Friedreich,

---

* Professor of Pathology, Institute of Neurology, London W.C.1; Pathologist, Maida Vale Hospital for Nervous Diseases, London W.9.

[1] Baron Félix-Hippolyte Larrey was the same age as the Emperor, having been born in the year 1808. His distinguished father, Baron Dominique Jean Larrey (1766–1842) had been surgeon-in-chief of the Grande Armée and a personal friend of Napoleon Bonaparte.

[2] Although these states were listed separately they were admitted to the Union in 1792 and 1850 respectively.

Dr. Robert Cowie · Ernest Hart · Prof. Jaccoud · Victor de Méric · Dr. Ph. Ricord · Dr A. Robin

Some of the participants in the Congress.

Fallot, Robin, Broca, Tardieu, Vidal, Hughes Bennett, and William Stokes, and Dr. Inman, of Liverpool, but how many of them actually attended and paid their 20 francs it is not possible to say.

In his inaugural address the president spoke of his city with considerable warmth, even going so far as to quote from Casimir Delavigne—"La France, c'est Paris, et Paris c'est le monde." He welcomed them all, and without wishing to be profane believed their congress could be regarded as a *concile médical oecuménique.* People, he said, were travelling more and frontiers and physical barriers, including the Atlantic ocean, were counting for less and less. He reminded them that there had been an isolated medical congress in Paris in the year 1845.

Evidently the atmosphere at first was formal and frigid, but after the first few sessions it became less stiff. The congress was conducted entirely in French, and this was the reason why Dr. Cowie's paper was declined. Mr. de Méric seems to have spoken well and made a good impression. It was he who presented the report of the Harveian Society on the prevention of venereal disease, the committee, consisting of Tilbury Fox, Henry Maudsley, Victor Bazire, Beigel, Drysdale, and himself, having being set up after the passing of the Contagious Diseases (Amending) Act of 1866. Nevertheless de Méric, one-time Jacksonian Prize essayist, in a speech on the control of "une maison de tolérance de Londres," did not find favour with the reporter of the *British Medical Journal,* who doubted if "this very meritorious specialist and syphilographer" appreciated the sentiments of his adopted country. No respectable doctor could allow himself to be the servant of a brothel-keeper for purposes of allowing women to continue in sin.

Incidents

In general the meetings seem to have been quiet and amicable, but there were a few incidents. The first was when Dr. van Lohe, of Amsterdam, complained that the presentations thus far had been but a series of pathological lectures, and he demanded that the meeting forthwith proceed to a discussion of the many practical problems concerned with tuberculosis. But he was overruled by the president, who said that the programme had been sent out well in advance for all to see and that they would keep strictly to it. Another incident occurred when Professor Palasciano, of Naples, boasted that the legal status of members of the medical profession had vastly improved since Italy had become a free country. No longer were they bound, as in other European countries including France, to inform on their patients when, in the course of their professional duties, they learned that they were treating lawbreakers. This evidently upset the president and other Frenchmen too, but the Italians were left in no doubt that any French doctor would rather himself break the law than inform on his patient. An anxious Professor Bouillaud closed the proceedings as soon as he could, pointing out that such questions as they were discussing could not be raised in open meeting without the express permission of the French Government, and such permission would almost surely not be given.

The most dramatic incident, however, was when a tall grey-headed gentleman stood up and proclaimed in a loud voice, "Je suis médecin, syphilisé, et je me porte bien." This arose in the course of a most heated argument between Dr. Auzias-Turenne, who was recommending repeated inoculation as a means of rendering a prostitute resistant to the disease, and Professor Ricord, the chairman of the meeting and a vice-president of the congress, who was utterly opposed to the idea. The chairman, who "boiled with indignation," chided Dr. Auzias-Turenne for not having, like others, experimented on himself if he had faith in his claim. M. Crocq, of Brussels, apparently in an attempt to quieten the meeting, asked facetiously if it was expected of him, the official delegate of his country, to return and advise his government to syphilize all Belgians. A much applauded moment seems to have been when Dr. Lombard, of Geneva, in a discussion on the effects of climate on health, ended by shouting, "Death to malaria !"

Perhaps the most eagerly awaited of the speakers was Dr. Brown-Séquard, who was due to discuss the early signs of cerebral disease ; but, alas for his many admirers, the sudden illness and death from a ruptured aneurysm of the basilar artery of his young former colleague and fellow Mauritian Victor Bazire, assistant physician at the National Hospital for Epilepsy and Paralysis, had called him to London.

Social Occasions

Between two and three hundred attended the banquet which was held at the Grand Hotel, Professor Virchow being placed on the president's right. One of the speakers was Dr. Ernest Hart, editor of the *British Medical Journal,* who hoped that one day such a congress would be held in London. In the course of the evening the president broke the news of the death that morning of Professor Alfred Armand Louis Marie Velpeau, who with great distinction had held the chair of clinical surgery in Paris for 32 years. The request that the Congress should attend at his funeral was "carried by universal acclamation." The death of this man, who was regarded as the king of French surgeons, so soon after that of the great Armand Trousseau (23 June), cast a gloom over the whole congress.

Social occasions seem to have been few, but Dr. Marion Sims, who in the summer of 1862 had left New York and the hospital he had founded, on the *Great Eastern* with a return ticket, laid on "brilliant hospitality" at his handsome residence in the rue du Faubourg St. Honoré which, said one reporter, redounded greatly to the credit of America. In his short time in Paris his gynaecological prowess had brought him wealthy patients and important friends, including the Duchess of Hamilton, the Empress Eugénie, and the Emperor himself. He was in fact a familiar figure in Paris society and at Baden-Baden, and had even enjoyed the entrée to St. Cloud.

Success and Failure

According to the many accounts of this congress it proved a success if only for the reason that the French organizers had brought together men of different nations. But this success was deemed to be due entirely to the guests, because many of the leaders of French medicine did not attend and hospital officials were *en vacances.* It failed because the programme was rigid and did not provide sufficient time for discussion and because it was intelligible only to those fluent in the French language. This must have been the reason for the regrettable and "too absolute silence maintained by a number of the most distinguished of our countrymen" (*Brit. med. J.*, 1867, 2, 259). It failed most of all because apart from the banquet there was no opportunity for doctors to meet each other outside the amphitheatre. No reading-room, lounge, or refreshment room had been provided ; nor was there an official reception. There was, in fact, "an entire absence of hospitality, or even of public courtesies" (*Brit. med. J.*, 1867, 2, 254): this particular censure may well have been provoked by the unfortunate mismanagement of a banquet intended for medical journalists, to which the editors of almost all the principal journals "were forgotten to be invited." We are told that several Paris journalists, presumably also overlooked, regarded the congress as a comparative failure.

Nevertheless the topics seem to have been well chosen, and some of them, like the control of venereal disease, pointed a way which led eventually to the formation of the World Health Organization. Other subjects to engage the attention of members were postoperative accidents and the acclimatization of Europeans in the tropics.

An early report in the *Lancet,* as if to upbraid its readers for failing to support the congress, dwells on the amenities of Paris, adding "neither are English taverns wanting." But unfortunately this first of international medical gatherings was held near the time of the Annual Meeting of the British Medical Association and that of the British Association, which together attracted most of the doctors given to travel, and it is certain that Dublin and Dundee provided all necessary entertainment as well as good scientific fare.

Marion Sims, a native of South Carolina and a naturally happy man, was distressed by the Civil War, and it was during these sad years that his love for Europe matured. Thereafter he led a somewhat restless life between the two continents, spending the greater part on this side of the Atlantic, where, as he was prepared to admit, the wealthy patients were more likely to be found.

Victor de Méric, when he returned to London, would have been pleased to find that the correspondent of the *Edinburgh Medical Journal,* who seems to have been Professor J. Hughes Bennett, had praised him for his part in the scientific meetings. As surgeon at the Royal Free, German, and French Hospitals he seems to have been a busy man. He was also a corresponding member of the Imperial Medical Society of Lyons. He later moved from 17 to 52 Brook Street, and was eventually joined in practice by his son, who had qualified in 1871. He died in 1876 at the age of 65, and the obituary notice in the *British Medical Journal* described him as a genial man and an honourable character.

Robert Cowie published his paper, which in effect had been his graduation thesis, in response to the request of a Danish doctor who had read an abstract of it in *L'Union Médicale* and was interested in the subject. It was therefore incorporated in a short history and account of the Shetland Islands published by Cowie in 1871. It includes a description of an epidemic of "epilepsy" in women churchgoers some fifty years earlier on days when the weather was warm and the preacher "pathetic." The distressing fits, often accompanied by dismal cries and fixation of the eyes, were attributed to superpolarity of the nervous system resulting from religious fervour. When, however, the ingenious minister announced a new form of treatment for this distemper, to consist of immersion in the fresh-water loch facing the kirk, no further case occurred.

Cowie, a tall, powerful man, had received his medical training in Aberdeen and Edinburgh, and had joined his father in practice shortly before the latter's death in 1866. He was well liked by everybody and held many public appointments, including that of Inspector of Lemon Juice for the Northern District of Scotland and honorary surgeon to the 1st Orkney and Shetland Rifles. A few days after revising the second edition of his charming little book he developed symptoms of acute inflammation of the bowels, and 26 hours later, on 1 May 1874, died, greatly lamented, at the early age of 32. Through this tragic death the island crofters lost a fine friend and the profession a geographically isolated member who had been ready to play his humble part in representing his colleagues at the First International Congress of Medicine.

The photograph of Victor de Méric was supplied by the Royal College of Surgeons of England. We are indebted to Mr. E. J. F. Clausen, Shetland Islands, for supplying the picture of Dr. Robert Cowie.

IS THERE AN ALTERNATIVE?

A suggestion that is frequently made is that a quinquennial system of finance for the Health Service would greatly increase financial flexibility. This system has now been in operation for the universities for almost 80 years, and in his article below Mr. Alexander McWilliam discusses some aspects of its history and working.

Yearly or Quinquennial Grants?

A. McWILLIAM,* B.A., A.I.M.T.A.

Brit. med. J., 1967, 3, 489–491

An earlier article in this series examined the suggestion of taking medicine out of politics by creating a public corporation.[1] Keeping universities out of politics has been a matter of concern since they first received State support, and a unique system of grants-in-aid has been evolved to achieve this aim. In fact the University Grants Committee has been described[2] as "one of the most felicitous constitutional inventions of this century" and "characteristic British solution to a problem which many have thought to be logically insoluble, namely the combination of the benefits of State support for this branch of higher education with the benefits of an orderly freedom on behalf of the institutions subsidized."

Evolution of System

The Scottish universities were the first to receive support from public funds through Parliament. In 1831 they were placed on an annual parliamentary vote, and Parliament itself considered and decided academic issues. London was the first English university to receive grants, and was followed by the Welsh university colleges. From the start there were misgivings about State support for universities. The Treasury[3] held that

---

* Finance Officer, University of Durham.

"universities, as representing the highest intellect of the nation, should not be dependent on its politics. . . . The normal condition of a flourishing university should be one of independence and stability." In 1889 Parliament voted a total of £15,000 for the twelve university colleges of England and Scotland, while both the principle of State support and the national importance of the universities were accepted. At the same time a committee was formed to advise on how the grant should be distributed, the Treasury recommending that a review should be made every five years. This interval was regarded as sufficiently long to enable the university colleges to plan their finances, while allowing the committee and Parliament to take account of changes in the colleges' circumstances.

From the outset relations between the committee and the colleges were good: the colleges relied upon the impartiality of the committee, and the Treasury accepted the committee's recommendations for the distribution of the grant. The committee became a permanent advisory committee whose members were or had been university teachers, and M.P.s and active civil servants—who initially had been in the majority—were excluded. A practice of informal visits to universities grew up during which discussions were held with university staff and students as well as with their governing bodies. Within the total grant voted by Parliament on the committee's advice, the committee's recommended distribution to universities was not questioned. The grant received by each university was a block grant to be expended entirely at the university's discretion ; and the amount of the grant was fixed on a quinquennial basis.

University Grants Committee

The University Grants Committee was constituted in 1919, its principal terms of reference being "to inquire into the financial needs of university education in Great Britain ; to advise the Government as to the application of any grants made by Parliament towards meeting them." The 23 members of the Committee are appointed by the Secretary of State for Education and Science. The Chairman's is a full-time salaried post, and there are two part-time Deputy-Chairmen ; the 20 other members give part-time service. Academics have a majority: of the 18 members of the Committee (excluding the Chairman, the Deputy-Chairmen, and two members who assist only on questions connected with academic salaries), 13 are members of university staffs ; two members are engaged in other educational fields, and three in industry. Appointments are made for terms of five years, but members are often asked to serve a second term to provide continuity of experience.

The total grants in aid of universities for which the Committee is responsible now exceed £200m. There are two types of grants for which it is responsible—non-recurrent and recurrent grants.

Non-recurrent Grants

Non-recurrent grants are those given for specific purposes—for example, for buildings, furniture and equipment for new buildings, purchase of land and property, and architects' and other professional fees. The major expenditure relates to buildings—£42m. out of total non-recurrent grants of £69m. in 1966–7.

The universities tell the Committee of their individual building requirements and the priority they attach to them, together with estimates of cost. These are then examined by the Committee before it makes its recommendations to the Government. The next stage is that the Government considers these recommendations in the light of the general economic situation and determines the total available for building grants.

Normally the Committee will accept each university's view about the priorities in its own programme, provided it conforms with the Committee's general criteria. Nevertheless, the allocation for this type of grant is not a sum to be used at the university's discretion and if it cannot agree a detailed programme with the Committee the latter may transfer the allocation to another university's project.

Immediately after the second world war the allocation of non-recurrent grants was fixed year by year. This gave both the Committee and the universities only very short notice of their permitted programme. To plan a building both efficiently and economically requires time, and, moreover, the activities for which it is designed must be organized ; staff must be appointed, students admitted, equipment ordered and installed, and finance made available for these expenses. More recently, however, allocations have been determined for some years ahead—for example, at present they have been approved up to 1969–70. Thus, since the average time to complete a major building project is about two years, universities know reasonably accurately what new buildings will be brought into operation up to the end of the 1967–72 quinquennium.

Recurrent Grants

Recurrent grants to the universities are fixed for five years at a time, and on average amount to about 70% of current university expenditure. (The balance is met from a variety of sources —such as income from fees, endowments and benefactions, and grants from research councils.) Recurrent grant is a general contribution to university revenue, and except for relatively small grants earmarked to particular studies which the U.G.C. wishes to encourage (for example, business studies, Middle Eastern, Oriental, and African studies) is entirely at the disposal of the recipient university for teaching and research. The settlement for each university takes into account its expected development through the quinquennium, and is not re-examined unless Government policy is changed, such as the accelerated expansion which followed the Robbins report. Supplementary grants may be made to meet major increases in costs, such as approved increases in academic salary scales ; but in general each university has to make allowance for increased costs in determining its own budget. And certainly a university would not be able to have its grant reviewed simply because it had underestimated its financial needs.

The process for determining quinquennial grants starts with the visits paid to all universities by the U.G.C. during each quinquennium. The Committee meets various groups of staff and in this way it obtains first-hand knowledge of feelings and opinions in each institution. Conversely, the Committee also has an opportunity to explain its views of national needs and policies to the universities.

Each university subsequently submits estimates for the next quinquennium, distinguishing between existing commitments (the cost of which must not outrun its assured income) and proposed new developments. After considering and adjusting these the Committee then presents a case to the Government showing for each year of the quinquennium the amounts required both for existing commitments and for new developments, but not showing the requirements of individual universities. When the total amount decided by the Government is known the U.G.C. then has to consider its allocation to the universities. In notifying the universities about their grants the Committee normally also tells them about the general considerations which have influenced the allocation of the total sum. The convention is established that no major departure from the development programmes which have been discussed with the Committee should be made without consultation ; but there is no detailed control over the internal disposition of the grants in each university.

Universities are subject to a number of financial restraints: expenditure on academic salaries, which constitutes about half of the total recurrent expenditure, is controlled, since national salary scales are fixed by the Government ; the proportion of senior to junior posts is governed by agreed conventions ; and staff–student ratios in each faculty are important to the U.G.C.'s consideration of the quinquennial grant. Nevertheless there is a wide area within which each university is autonomous.

Advantages of Quinquennial System

Though the general pattern of its expenditure is determined in consultation with the U.G.C., the individual university decides the details of its annual budget without reference to any outside body. It alone is responsible for deciding where and when new posts should be established; what funds should be allocated to each academic department for teaching and research; how much should be devoted to the library; the relative merits of providing a theatre, or a sports hall, or supporting the local radio station. It can also decide whether to restrict expenditure now to provide for additional expenditure later, since the quinquennial system permits unspent balances to be carried forward from one year to another. Apart from the flexibility in planning that this method confers, it also militates against the ill-considered expenditure which sometimes results when funds are voted on an annual basis and unspent balances are cancelled at the end of each year of account. A spending department has little incentive to economy if it cannot expect to benefit from its savings; it may indeed fear that under-expenditure in one year may lead to its estimates for a later one being reduced to the same level. Consequently effort which might be more profitably applied is directed to making expenditure fit the estimate for an arbitrary period. Universities do not suffer this artificial constraint, and for the most part allow similar freedom internally—so that each academic department is free to carry forward unspent balances of the funds allocated to it for teaching and research purposes.

Over a period of nearly 80 years this system of finance has proved itself to be valuable both to the Government and to the universities. The quinquennial block grant, without any supplementation except for proved increased costs (and by no means all of these), is both an incentive to economy and a firm basis for forward planning. Universities were able to respond to the Government's request for rapid expansion of university places (following the Robbins report) because their development plans had been formulated already and policy decisions had already been taken—hence an acceleration of the programme was only a question mainly of administration. Finally, no evidence given to the Public Accounts Committee when the latter considered Parliament's control of university expenditure suggested a preferred alternative method of finance.

REFERENCES

[1] Wiseman, J., *Brit. med. J.*, 1967, 2, 102.
[2] Special report from the Committee of Public Accounts on Parliament and Control of University Expenditure (para. 10, Appendix 15) H.M.S.O 1967.
[3] Report of the U.G.C. on University Development 1957–62 (para. 521), Cmnd. 2267. 1964.

CONFERENCES AND MEETINGS

Dialysis and Transplantation

[FROM A SPECIAL CORRESPONDENT]

A change in emphasis in the regular dialysis programme seems inevitable following the meeting of the European Dialysis and Transplant Association in Paris (24–25 June) and the combined symposium with the Transplantation Society which followed it. At present the majority of effort in Britain and on the Continent is directed to hospital dialysis, but the demands on staff are enormous. In 81 centres answering the European Dialysis and Transplant Association questionary 621 patients were receiving regular haemodialysis; on average every 10 patients occupied the full-time services of six nurses and three doctors. The future role of the hospital unit as a training centre for home haemodialysis and a support for the transplantation centre was delineated during the conferences.

Home Haemodialysis

W. **DRUKKER** (Amsterdam) reported that six European centres were already operating home haemodialysis schemes and others were about to start. Other workers, including S. **SHALDON** and R. A. **BAILLOD** (London) and D. D. **HILTON** (Birmingham), reported success with this technique, showing that both mortality and morbidity were lower than in the hospital, while staff time was also reduced. An important element in the success of home haemodialysis has been the elimination of routine blood transfusion. P. J. **VERROUST** and R. E. **CROCKETT** (London) reported experience totalling 67 patient-years without transfusion except to replace acute blood loss or to relieve symptoms, which became incapacitating when the erythrocyte packed-cell volume had fallen to about 15%. Over 90% of their patients had been found to maintain an acceptable packed cell volume without regular "topping up," provided blood sampling was kept to a minimum and the Kiil dialyser was efficiently washed out.

The arteriovenous shunt remains one of the bugbears of regular dialysis. G. J. A. **CLUNIE** (Edinburgh) had found that nearly all infections of the shunt were due to staphylococci, the majority originating in the nares or other carrier sites of the patient. Prophylactic antibiotics did not prevent infection, but hexachlorophene bathing and local treatment of the nares had proved moderately effective. The use of streptokinase to free clotted cannulae was reported by D. C. **ANDERSON** (Edinburgh) and C.-M. **KJELLSTRAND** (Lund); when followed by anticoagulant therapy it prolonged the life of half the cannulae by more than a month. Prednisone was given to prevent systemic reactions. The possibility of a new shunt site in the upper thigh was opened up by a technique described by J. **HOELTZENBEIN** (Münster), who had used an all-Silastic prosthesis.

An alternative to the arteriovenous shunt, applicable only to hospital dialysis, is the Cimino–Brescia arteriovenous fistula, which permits repeated needling for arterialized venous blood. Many workers reported finding this method preferable to the arteriovenous shunt, and it had proved particularly helpful before transplantation, when freedom from local infection is all-important. Blood flow through the dialyser averaged over 200 ml./minute with a pump, and haemodynamic effects at other times had usually not been found to be serious.

Technique of Dialysis

A policy of increasing protein intake to 50–80 g. per day while extending dialysis time to 30–40 hours per week in three or four sessions met with general approval. The burden on patients of these long dialysing times should be diminished soon by the availability of more efficient dialysers. L. **GRIMSRUD** (Seattle) reported successful clinical trials with his foam support dialyser, which should cut dialysis time by about a third.

L. W. **FLEMING** (Dundee) showed that hypermagnesaemia develops when patients are dialysed against fluid with a "physiological" level of magnesium, though normal plasma levels can be restored if magnesium is withheld from the bath water. With his colleagues he had found a concomitant improvement in nerve conduction time, but M. **KAYE** (Montreal) thought that hypermagnesaemia protected against clinical neuropathy as well as preventing metastatic calcification.

H. G. **SIEBERTH** (Cologne) showed that twice-weekly dialysis did not completely correct the acid–base abnormalities of the patient with chronic uraemia, but left him with a permanent dysequilibrium between blood and cerebrospinal-fluid bicarbonate causing inadequate respiratory compensation for acidosis. One of the complications of correcting acidosis is that for pharmaceutical convenience dialysis solutions usually contain acetate or lactate in place of bicarbonate. H. A. Lee (Manchester) had found that this sometimes led to a rise in plasma lactate during peritoneal dialysis and thought that this might account for some unexplained convulsions during or after dialysis.

M. E. Rubini (Los Angeles) found that the daily rise in plasma urea and creatinine after regular dialysis decreased on successive days in a manner not wholly explained by redistribution between compartments. A. Scholz (Berlin) and N. Deane (New York) using carbon-14 labelled urea showed that the main factor in the case of urea is probably a reduction in extrarenal removal that accompanies the fall in plasma urea.

Transplantation

The value of integrating regular dialysis and transplantation was demonstrated by J. Vantelon from the results of the Necker unit in Paris. He could not, however, confirm previous claims that prolonged dialysis improved the chance of graft tolerance. W. Drukker (Amsterdam) showed that half of the patients receiving a graft in Europe had to wait for over four months on dialysis before reaching the head of the queue—and pointed out, moreover, that the delay was getting longer. A high standard of dialysis was required to keep the patient fit for a major operation over this period, and at present there was an appreciable mortality in the waiting period. J. Traeger (Lyons) suggested how to shorten the queue by selecting the most favourable patients. If all potential recipients were studied by ABO and leucocyte grouping a little less than half were shown to have a reasonable chance of a suitable match from a random cadaver donor or could expect to find a compatible matched donor within a few months. The remainder had a poorer chance, or had to wait longer for a suitable graft, and should be selected for long-term home haemodialysis.

The success of such a scheme depends on the predictive accuracy of leucocyte grouping. J. Dausset (Paris) reported a highly significant correlation between compatibility in leucocyte groups and long-term survival of grafts. Nevertheless, a few rejections had occurred despite perfect matching of known antigens, and hence some tissue groups had yet to be identified. S. D. Nelson (Belfast) reported no correlation between the results of the mixed lymphocyte culture test and the outcome of transplants at Boston. The normal lymphocyte transfer test did show some correlation, but since the results of this took between two and three days to obtain its use in cadaver grafting was limited—and the technique also carried a risk of transmitting hepatitis.

Even with no selection except by ABO blood-grouping, the results of cadaver grafting are improving. In the collected European series F. M. Parsons (Leeds) reported that 89 of 164 were still functioning after a median time of six months. The results from the world transplant registry, discussed by J. Crosnier (Paris), were even more encouraging. V. C. Marshall described series from Melbourne with 20 survivors out of 24 patients who had received grafts within the last 30 months. Still more impressive results with live related donors were reported by T. E. Starzl (Denver), who had a 95% survival at almost one year in patients receiving antilymphocyte globulin in addition to conventional immunosuppressive therapy.

Apart from antilymphocyte globulin there have been no technical breakthroughs to account for these steadily improving results, which must be attributed to more adequate preparation by dialysis, better surgery, and growing experience in aftercare. The value of local therapy to the graft or its lymph drainage area, suggested by the transplant registry results, received further support from studies by S. Kountz (Stanford) and A. Kirpatovsky (Moscow). Moreover, the early diagnosis of rejection is finding more secure foundation; S. Kountz had found that in most crises a fall in estimated renal plasma flow preceded all other signs of rejection, while E. S. Spencer (Aarhus) showed the value of quantitative estimation of urinary lymphocyte excretion.

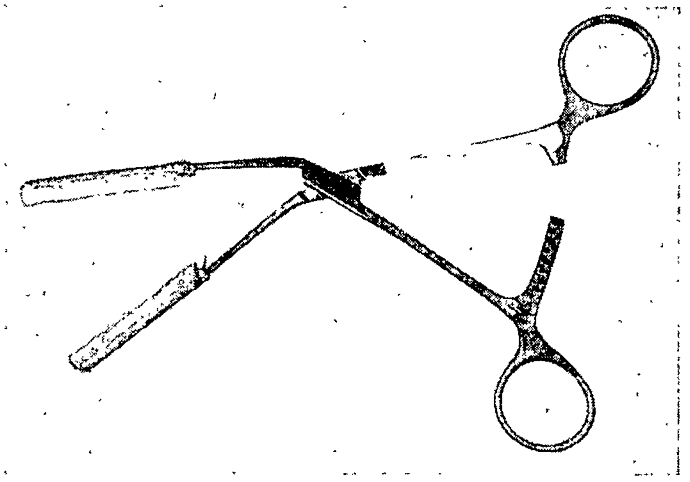
Kidney Preservation

The advent of the kidney bank still seems a long way off, but some progress with the dimethyl sulphoxide freezing technique was reported by P. B. Clark (Leeds), and the development of biochemical tests to predict viability by J. B. Dossetor (Montreal) should speed progress. Shorter term preservation of 24–28 hours is now being achieved by several workers, including J. R. Ackerman (London) and W. F. Hendry (Glasgow), using various combinations of hypothermia, hyperbaric oxygen, low-flow perfusion, and metabolic inhibition. By permitting planned daytime operations and the leisurely collection of waiting recipients on outpatient dialysis, this should be a major stimulus to the development of the dialysis–transplant unit.

NEW APPLIANCES

Modified Brown Clamp for Atraumatic Vascular Occlusion

Professor R. Y. Calne, of Cambridge, writes: In 1961 Brown described a vascular clamp utilizing sponge rubber in an attempt to duplicate the atraumatic effect of controlling a vessel between the index finger and thumb. The rubber was tied to the blades of the clamp with ligatures.



I saw this clamp being used by Dr. T. E. Starzl in Denver during renal transplantation, and have had a slightly modified Brown clamp (see illustration) in use for the past three years. I have found it extremely valuable in controlling delicate vessels. It is particularly well suited for clamping the external iliac vein during anastomosis of the renal vein in kidney transplantation.

It is atraumatic and light, being approximately the same weight as a Babcock clamp, and has a wide ratchet. The sponge-rubber pads are glued to tubular bootlace cloth with Evo-stik, and the cloth is slid over the metal blades and held in place with thread ligatures which do not distort the rubber.

The instrument was made for me by Messrs. Heaton Grogan & Co., Ltd., of 21 Bowling Green Lane, Clerkenwell, London E.C.1, and may be obtained from surgical instrument suppliers.

Reference

Brown, L. (1961). *Arch. Surg.*, **83**, 645.

Correspondence

Letters to the Editor should not exceed 500 words.

The "Pill" and Deep Venous Thrombosis

SIR,—A preliminary report was published by the M.R.C. Subcommittee for the study of the relations between oral contraceptives and thrombo-embolic disease (6 May, p. 335). It is striking that in this communication no statement is given regarding the criteria for the diagnosis of deep venous thrombosis. In our and others' experience the clinical diagnosis of venous thrombosis is extremely difficult and unreliable.

In a series of 512 cases, in which the diagnosis of deep venous thrombosis had been made by experienced surgeons, subsequent phlebography revealed a completely normal venous system of the lower extremity in 233 cases—that is, in 46%. Our experience from phlebographic examination performed in the acute stage of disorders of the leg with classical signs of deep venous thrombosis also showed faulty diagnosis in about 50% of the cases. From these results we concluded that a scientifically tenable diagnosis of deep venous thrombosis cannot be made without the proof of phlebography in every single case. It is hardly probable that diagnoses made by 29 practitioners are more accurate than those made by surgeons with profound experience of thrombo-embolic disease. With these observations in mind the otherwise admirable work by the committee certainly must be interpreted most critically.

Also in previously published reports of cases of venous thrombosis in women having taken oral contraceptives the final proof of correct diagnosis by phlebography is lacking but for a few exceptional cases. Moreover, studies of the coagulation pattern in patients taking oral contraceptives failed to reveal any basis for the assumption that these drugs might induce thromboembolic disease.—We are, etc.,

KNUT HÆGER.
INGA MARIE NILSSON.
BERTIL ROBERTSON.

Department of Surgery
and the Coagulation Laboratory,
Allmänna Sjukhuset,
Malmö S, Sweden.

Overinflation of the Lungs of Coal Miners

SIR,—In their article "Overinflation of the Lungs in Coal Miners" (1 July, p. 10), Dr. Colin Ogilvie and others suggest that the pulmonary function in a group of miners with unexplained dyspnoea is "compatible with some of the reported pathological features of focal emphysema, due to coal dust." This conclusion is open to an alternative interpretation.

The miners they studied (Group 1) were selected on the basis of excessive dyspnoea alone, and may, therefore, not form a homogeneous group with respect to its aetiology. If this is the case, conclusions drawn from the mean results are likely to be misleading. Analysis of the authors' data reveals that the lung function of the five miners with "signs of bronchitis" but no radiological pneumoconiosis resembles that of other men with bronchitis uncomplicated by emphysema.[1] The six miners with radiological simple pneumoconiosis but no "signs of bronchitis" have, on average, less impairment of function. This is a likely consequence of both the factors which lead men to apply for compensation[2] and the known features of the condition.[3]

	V.C. (l.)	F.R.C. (l.)	R.V. (l.)	T.L.C. (l.)	M.V.V. (l./min.)
A	2·18	5·54	4·88	7·06	39·2
B	2·92	3·90	3·18	6·12	75·0
C	4·1	3·9	2·1	6·3	—

Mean values
A—5 men having "signs of bronchitis" without pneumoconiosis.
B—6 men having pneumoconiosis without "signs of bronchitis."
C—Average values for normal men having the ages and heights of Group B[4].

The findings in these two sub-groups of Ogilvie's cases are summarized in the Table, together with average normal values for the second group, which we believe to be more appropriate than those quoted by the authors. The values for the remaining six coal miners who have both pneumoconiosis and signs of bronchitis (two subjects) or neither of these conditions (four subjects) lie mostly within the limits of the other two groups.

Inspection of the Table suggests that the abnormal residual volumes (R.V.) and vital capacities (V.C.) in the coal miners with pneumoconiosis but no "signs of bronchitis" are due to the remarkably low expiratory reserve volumes—that is, F.R.C.-R.V. This result may be due to mild chronic bronchitis, not accompanied by physical signs, but in view of the normal functional residual capacities (F.R.C.) failure to expire fully from F.R.C. to R.V. is an alternative explanation; this should not be overlooked in patients with a possible "compensation neurosis."

We do not rule out that radiological signs of pneumoconiosis may be obscured by focal emphysema. However, this is unlikely in view of the recent finding that the degree of focal emphysema is positively correlated with both *x*-ray category of simple pneumoconiosis and the content of coal dust in the lungs at postmortem.[5]

In summary, it seems that the "unexplained dyspnoea" of the miners in this series may be explained in most instances by impairment of function due to chronic non-specific lung disease, while in the remainder psychological factors may contribute to the symptoms. No good case appears to have been made for co-existence of focal emphysema, the detection of which during life is likely to require application of the refined methods for analysing lung-gas distribution now available.—We are, etc.,

G. B. FIELD.
J. E. COTES.

M.R.C. Pneumoconiosis Unit,
Llandough Hospital,
Penarth, Glam.

REFERENCES

[1] Fletcher, C. M., Hugh-Jones, P., McNicol, M. W., and Pride, N. B., *Quart. J. Med.*, 1963, **32**, 33.
[2] Carpenter, R. G., Cochrane, A. L., Gilson, J. C., and Higgins, I. T. T., *Brit. J. industr. Med.*, 1956, **13**, 166.
[3] Gilson, J. C., Hugh-Jones, P., Oldham, P. D., and Meade, F., *Lung Function in Coalworkers' Pneumoconiosis, Medical Research Council Special Report Series No. 290*, 1955.
[4] Cotes, J. E., *Lung Function, Assessment and Application in Medicine*, 1965. Oxford.
[5] Rossiter, C. E., Rivers, D., Bergman, I., Casswell, C., and Nagelschmidt, Gr., *Inhaled Particles and Vapours*, 1967, **2**, 419, ed. C. N. Davies. Oxford.

SIR,—The article in your issue (1 July, p. 10) by Dr. C. Ogilvie, Dr. K. Brown, and Dr. W. E. Kearn is a most valuable contribution. Industrial physicians and radiologists have long been aware of the fact that some workers occupationally exposed to inhalation of non-silicious dusts, of coal in particular, may suffer from severe disabling symptoms of pulmonary insufficiency without clinical (radiographic) evidence of pneumoconiosis. Now for the first time Dr. Ogilvie and his colleagues have documented this in a fair number of coal miners with exact pulmonary function studies.

In their discussion the authors concentrate attention on explaining both the latency of dust lesions in the radiograms as well as the presence of pulmonary insufficiency by the same factor, namely overinflation—that is, emphysema in the lungs. Referring to my letter to the editor on the same subject (28 May, 1966, p. 1356), they mention the possibility I suggested of emphysema attenuating the shadows cast in radiograms by dust in the lungs. Regarding the origins of overinflation and emphysema, the authors resort to the theory that the dust lesions are of a particular kind and distribution which produces a special type of so-called "focal emphysema."

Of course the authors have no proof of attenuation of shadows of dust lesions in their radiograms in the over-inflated lungs of these coal miners. Nor do they have proof for the assumption that the severe pulmonary insufficiency symptoms were caused by the overinflation emphysema which they describe. What they did demonstrate, however, is the fact that in coal miners long exposed to inhalation of coal dust symptoms of severe pulmonary insufficiency may be present even in the absence of radiographic evidence of dust lesions in the lungs. This fact presents a problem which is not solved by assumptions regarding the nature of overinflation (emphysema) and its shadow-attenuating effect on the radiograms. The problem only gets lost in the vast complexities of the larger problem of emphysema, which still remains unsolved even after the stupendous amount of research, study, and discussions in dozens of symposia recently held here and abroad. In the present state of hopeless confusion about this subject emphysema and pulmonary insufficiency are considered synchronous events and even conterminous conditions. In fact, there seems to be now little awareness of what the real problem is regarding the nature and origin of pulmonary insufficiency resulting from long exposure to inhalation of dust which fails to be removed from the vast internal surface of the ultimate structures of the lungs.

My comments are concerned mainly with this problem. I proposed a new concept of the "visceral function of the lungs." I described this in a series of publications over the past three decades.[1-3] In my theory this vital function consists in activities by which the alveolar structures constantly recreate the vast and most delicate yet completely mobile internal surface membrane, adapting it constantly to the momentary requirements of the function of the lungs as a whole. Although this new concept is still largely theoretical, it can be said that it has already gained abundant substantiation in the recently evolved new chapter of pulmonary physiology. This has revealed the vital role of the highly active alveolar membrane, which constantly secretes and constantly spreads a new surfactant semifluid film over the vast internal lung surface. In this new concept overinflation and emphysema are interpreted as merely incidental phenomena of dysfunction of the lung's ultimate structures in response to loss of internal lung surface, which can be caused by a great variety of factors, including encumbrances of the delicate lung surface by dust which fails to be removed (failure of self-cleansing) owing to dysfunction of affected structures.

Considering the rapid progress made in this new field of pulmonary physiology[4-6] we may now look forward with confidence to the time when our knowledge about the functions of the alveolar structures and the vast internal surface membrane will enable us to make reasonable assumptions about the nature and origin of pulmonary insufficiency caused by excessive deposits of dust on the internal lung surface interfering with its functions, even though the presence of the dust cannot be demonstrated in radiograms.—I am, etc.,

ISRAEL RAPPAPORT.

New York, N.Y.,
U.S.A.

REFERENCES

[1] Miller, J. A., and Rappaport, I., *Ann. intern. Med.*, 1938, **11**, 1644.
[2] —— *Dis. Chest*, 1954, **25**, 1.
[3] —— and Mayer, E., *Lancet*, 1960, **2**, 1217.
[4] Pattle, R. E., *Physiol. Rev.*, 1965, **45**, 48.
[5] —— *Nature (Lond.)*, 1955, **175**, 1125.
[6] —— *Arch. environm. Hlth.*, 1967, **14**, 70.

Tests for Lead Poisoning

SIR,—In the report of the investigation of lead poisoning in Bradford (1 July, p. 56) in which seven children and two adults were investigated in hospital, and two of the children died, no mention is made of blood lead, nor urinary lead, nor urinary coproporphyrin, nor urinary δ-aminolaevulinic acid. This is surprising, as these are the four best tests for lead exposure and lead poisoning.[1]

Blood lead and urinary lead are specialist analyses. The Occupational Hygiene Service attached to the Nuffield Department of Occupational Health, Clinical Sciences Building, York Place, Manchester 13, does some 5,000 such estimations annually for hospitals and industry. The service provides the special heparinized syringes for taking the blood samples and the deleaded urinary containers required; the samples are returned by post.

This excellent service should be used to the full by all responsible for the investigation of children and adults where a diagnosis of lead poisoning is remotely possible, and for the control of lead absorption in industry. Since the reliability of the result and the cost of analysis are related to the number of samples analysed, it is normally desirable to use one specialist laboratory.—I am, etc.,

M. K. WILLIAMS.

London School of Hygiene
and Tropical Medicine,
London W.C.1.

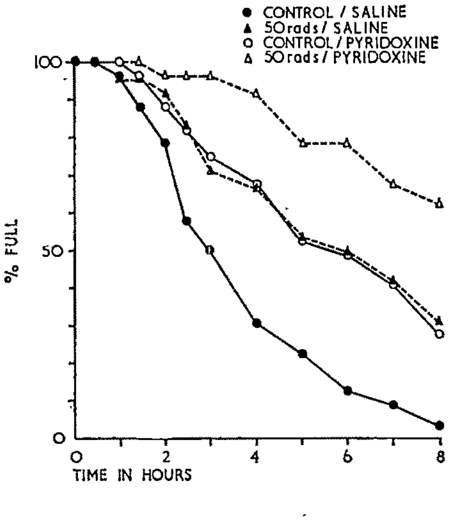
REFERENCE

[1] *Lancet*, 1966, **1**, 1307.

Treatment of Radiation Sickness

SIR,—As the investigation of the usefulness of pyridoxine hydrochloride in radiation sickness by Dr. H. Mattie and others (22 July, p. 215) does not provide a conclusive answer, the following unpublished experiment, performed some years ago, may be of interest.

Rats cannot vomit, but relatively low doses of radiation produce a delay in gastric emptying. The phenomenon can be investigated by allowing rats to feed themselves with a thick paste of a commercial barium meal preparation before irradiation and then following the emptying of the stomach by means of serial radiographs.[1] The technique can be readily adapted to study the effects of radioprotectors and sensitizers[2] and pyridoxine has been tested in this way. Six litters of four adult albino rats were used. After feeding a standard quantity of barium meal two rats of each litter were injected intraperitoneally with 50 mg. of pyridoxine hydrochloride in 1 ml. of saline and the other two were given a similar injection of 1 ml. of physiological saline. Immediately following the injections one of the two rats given pyridoxine and one of the rats given saline were irradiated with 50 rads of *x* rays. The other two rats were mock-irradiated so that separate comparisons could be made of the effects of the radiation and the pyridoxine.



The accompanying graph illustrates the rate at which the stomach emptied during the eight hours after irradiation. Pyridoxine by itself, in the dosage used, delayed gastric emptying as much as 50 rads of *x* rays, and when the two were combined the gastric delay was greater than with either alone. Thus pyridoxine did not counteract the effects of radiation on gastric movement in the rat.

Radiation-induced delay in gastric emptying is presumably an unpleasant experience for the rats, as they subsequently develop an aversion to the barium meal eaten immediately prior to the irradiation.[3] It seems reasonable to assume that the gastric delay is the counterpart of radiation-induced nausea and vomiting in man. If so, this experiment suggests that pyridoxine is not likely to counteract this particular effect of radiation. Pyridoxine may have actions on other symptoms of radiation sickness, but if so these have still to be proved.—I am, etc.,

E. V. HULSE.

Medical Research Council,
Radiological Research Unit,
Harwell, Didcot, Berks.

REFERENCES

[1] Hulse, E. V., *Brit. J. exp. Path.*, 1957, 38, 498.
[2] —— *Brit. J. Pharmacol. Chemother.*, 1958, 13, 260.
[3] —— and Mizon, L. G., *Int. J. Radiat. Biol.*, in press.

Carcinogenic Properties of Ortho-dianisidine

SIR,—The letter on carcinogenic properties of ortho-dianisidine (22 July, p. 238) and your leading article on carcinogenic hazards (same issue, p. 189) draw attention to the possible risks in using ortho-dianisidine and also ortho-tolidine in the clinical routine laboratory.

Unfortunately, we are not given firm advice. Should we discontinue the use of these reagents? In this laboratory, for example, we are using ortho-tolidine for the testing for occult blood in stools, and for estimating blood sugar in the automatic analyser and also in emergencies by a hand method. This amounts to 9,385 estimations a year. The advantage of the ortho-tolidine method for estimating blood sugar is that one measures the true glucose and no other reducing substances. To give up these techniques means going back to the times when one estimated overall reducing substances.

Is it safe to continue with techniques employing ortho-tolidine—naturally with precautions such as using automatic pipettes—when this substance is dispensed?—I am, etc.,

H. LEHMANN.

Biochemical Section,
The John Beckett Clinical Laboratories,
Addenbrooke's Hospital,
Cambridge.

Trismus Following Inferior Dental Nerve Block

SIR,—It would be interesting to know if the condition described by Drs. H. C. Killey and L. W. Kay (15 July, p. 173) really is occurring more frequently, or are more patients reaching them because of their efficacious treatment? Certainly in the case of a patient I saw some years ago I felt that the length of treatment could be a factor, since his dentist had worked for over two hours. Longer treatment times are nowadays quite common with premedication and sedation techniques preceding local or regional anaesthesia.

Having recently studied 10 routine dissections and carried out two special dissections, I am very aware that both large and small vessels are readily available for puncture where a needle may be inserted to block the inferior dental nerve. In consequence, I shall never give another inferior dental block injection without an aspirating syringe.

It seems difficult to believe that this progressive trismus in three or four days can be due to "organization of a band of fibrous tissue"—maybe it is hydrostasis, and aspiration under general anaesthesia in one of their patients might be very interesting.

Several authors have described this complication,[1-3] but the most fascinating article is that by John Campbell.[4] This is a careful account and discussion by an astute dentist of his own affliction: "At the end of the sixth week the first signs of remission came. . . . I reacted philosophically to the incident." Little wonder that Killey and Kay get so many of these cases—even John Campbell might have taken "the dreary road to the south."—I am, etc.,

WARREN HARVEY.

Glasgow Dental Hospital
and School,
University of Glasgow.

REFERENCES

[1] Nevin, M., *Problems in Dental Local Anaesthesia*, 1952. London.

[2] Chaikin, L., and Rubin, B., *J. Amer. dent. Ass.*, 1956, **53**, 672.

[3] Jorgensen, N. B., and Hayden, J., *Premedication, Local and General Anaesthesia in Dentistry*, 1967. London.

[4] Campbell, J., *Dent. Rec.*, 1954, **74**, 180.

Investigating Hypertension

SIR,—May we comment on the letter (29 July, p. 306) in which Wing Commander P. W. Robertson refers to our paper on aortography in the investigation of hypertension ?[1]

We remain quite unashamed that we should attempt to assess the chances of ultimate benefit to the individual when deciding whether or not to perform an investigation on a patient. Far from being a "novel approach" or a "curious parameter" we regard this as an essential of ethical practice.

It is a truism that accurate diagnosis should precede treatment, but clinical medicine is full of situations where to pursue diagnosis to its ultimate detail, though intellectually satisfying, may expose the patient to some risk without altering the correct treatment in the least. In any case, before adopting an attitude of academic superiority it is important to ensure that the investigation advocated is capable of supplying the required answer. In these particular circumstances the relevant questions are:

(1) Has this patient a vascular lesion conceivably the cause of the hypertension ?

(2) Is that lesion in fact the cause of the hypertension or the result of it or merely coincidental ?

(3) Will appropriate surgical treatment of that lesion result in relief of the hypertension ?

Aortography is inherently incapable of answering more than the first question, and without a reliable means of obtaining answers to the others' aortographic findings are of very limited value. The coexistence of a narrow renal artery and hypertension has become a classical chicken-and-egg dilemma. Unfortunately, the various attempts to solve the dilemma such as divided renal function studies, angiotensin infusion, and estimations of blood levels of renin or angiotensin have not proved reliable, and surgery must be advocated or withheld on largely empirical grounds. In these circumstances, and considering the availability and efficiency of drug treatment, we cannot think it proper to subject every hypertensive requiring treatment to aortography as Dr. Robertson appears to advocate. In Dr. Robertson's recent paper,[2] to which he refers, there is no attempt at proof of an aetiological relationship between the vascular abnormalities demonstrated and the coexisting hypertension of the patients studied.

The manifest differences between bronchial carcinoma and surgically correctable hypertension, particularly in terms of relative frequency, morbidity of the appropriate investigations, and the availability and likelihood of success of non-surgical treatment, make Dr. Robertson's analogy between investigating the two conditions peculiarly inappropriate.

Dr. Robertson chides us for drawing conclusions from a highly selected series. We reported on every patient who had undergone aortography for the investigation of hypertension at a London teaching hospital. The series which Dr. Robertson quoted in his support[3] had a male-to-female ratio of nine to one, and two-thirds of the patients were Service personnel.

We would not wish to advocate diagnostic nihilism but merely recognition of the limitations and potential dangers of a particularly diagnostic technique. Our aim was and is to warn against the uncritical submission of large numbers of patients to aortography in the hope that this will provide a diagnostic answer that it is incapable of doing.—We are, etc.,

M. J. CHAMBERLAIN.

Department of Experimental
Pathology,
The Medical School,
Birmingham 15.

J. A. GLEESON.

Westminster Hospital,
London S.W.1.

REFERENCES

[1] Chamberlain, M. J., and Gleeson, J. A., *Lancet*, 1965, **1**, 619.

[2] Robertson, P. W., Hull, D. H., Klidjian, A., and Dyson, M. L., *Amer. Heart J.*, 1967, **73**, 296.

[3] Robertson, P. W., Klidjian, A., Hull, D. H., Hilton, D. D., and Dyson, M. L., *Lancet*, 1962, **2**, 567.

Elusive Popliteal Pulse

SIR,—As one familiar with vascular surgery from the beginning I was interested to read your leading article (5 August, p. 326) suggesting that the best way of feeling for the popliteal pulse is to have the patient in the prone position. With this I agree, but think that further advantage is to be gained by passively flexing the knee-joint. You mentioned this for the supine position but not for the prone.

In extension the tissues of the popliteal fossa are tense, whereas in passive flexion they are relaxed and the artery is then more easily palpable. At the same time the palpating index or middle finger of one hand, if placed over the artery and pressed down by the index or middle finger of the other hand, is more sensitive to pulsations than if pressed down by muscle action of its own side. This means that it is best for the leg to be held in flexion by an assistant, but it can be maintained in that position by supporting the foot and ankle against the examiner's shoulder.

Yet another reliable observation is to watch from the side the foot of the uppermost leg when the patient sits with his knees crossed ; it has to be a severely impaired pulse before oscillation is completely eliminated. This, admittedly, is qualitative rather than quantitative.—I am, etc.,

F. A. R. STAMMERS.

Birmingham Regional
Hospital Board,
Birmingham 16.

SIR,—With reference to your leading article (5 August, p. 326) may I suggest a visual method ?

The subject sits in a chair, crosses one knee over the other with the popliteal space being examined applied to the opposite patella. He then relaxes, thus compressing the popliteal artery by the weight of the leg.

Distinct movements of the foot, synchronous with the pulse, can be seen (like miniature knee jerks) if the popliteal artery is pulsating.—I am, etc.,

West Runton,
Norfolk.

LUCY TURNER.

SIR,—I have found the following technique most satisfactory in enabling the students to display to themselves pulsation of the popliteal artery or its absence. The supine patient's knee is supported slightly flexed by one hand in the popliteal fossa. The other hand presses the patella downwards and backwards, causing some reflex contraction of quadriceps and relaxation of the antagonistic hamstrings. The pulse, if present, is always palpable in this way.—I am, etc.,

AUSTIN T. CARTY.

Mater Misericordiae Hospital,
Dublin 7.

Chemical Treatment of Skin Cancer

SIR,—I was rather concerned to read in your leading article "Chemical Treatment of Skin Cancer" (15 July, p. 125) that "5-fluorouracil . . . is not suitable for the treatment of basal cell carcinomas, let alone squamous carcinomas." This statement gives a misleading impression, since Dr. E. Klein and his co-workers in the paper you quoted[1] made this statement in connexion with the routine clinical management of solitary basal cell carcinoma. They go on to state that this may not be true as regards the management of neoplastic lesions in which standard therapeutic methods are complicated by the large areas of skin involved, such as multiple superficial basal cell carcinomas or extensive solar or arsenical keratoses.

During the past 12 months I have been using 5% 5-fluorouracil ointment initially in the treatment of superficial recurrences of basal cell carcinomas previously treated by irradiation, and more recently as the primary treatment of carefully selected superficial basal cell and intra-epidermal carcinomas.

It is, of course, much too early to assess the long-term success rate of such treatment, but so far the results have been quite impressive and a number of significant facts have emerged from the trial:

Proper selection of cases is essential.

Recognition of the end point of treatment is difficult and comes only with appreciable clinical experience of the technique.

Adequately treated lesions heal completely with an absolute minimum of scarring.

The apparent absence of deep scarring and endarteritis permits the safe use of superficial irradiation at a later date should there be a residue or recurrence within the treated area.

Superficial recurrences within previously irradiated areas can be treated successfully without the risk of inducing radionecrosis or additional scarring.

Prolonged application to large areas or tumours does not produce any systemic disturbance or detectable changes in the peripheral blood picture.

Treatment is virtually painless, and in my experience can be on a domiciliary basis with weekly supervision.

It may well be that topical chemotherapy has a distinct therapeutic advantage over low voltage irradiation for the treatment of spreading superficial lesions involving irregular surfaces, especially around the pinna and external ear.

It would be a great pity if at this stage the impression is gained that topical chemotherapy has nothing to offer in the treatment of any type of skin cancer. Rather should it be stated that this treatment may well have an important role in its own right as the primary treatment of certain specific types of skin tumours.—I am, etc.,

Sheffield National Centre
for Radiotherapy,
Sheffield 10.

G. M. KING.

Two Types of Breast Cancer?

SIR,—For the past two decades it has been debated[1] whether the change which occurs at middle age in the rate of breast cancer mortality is evidence for two types of breast cancer. The presence of the rate change is confirmed by recent mortality data[2] (Fig. 1) for which random fluctuations were minimized by calculating mean annual mortality values for a period of years (1958–63) and for large populations (England and Wales, Denmark, Finland, and Japan). On the assumption that two distributions (I and II) of breast cancer were present, the incidence of II was estimated by extrapolating linearly, on a log-log plot, the mortality rates for older ages, which were assumed to refer essentially to II. The conjectured incidence of I was then obtained by subtraction (Fig. 2).

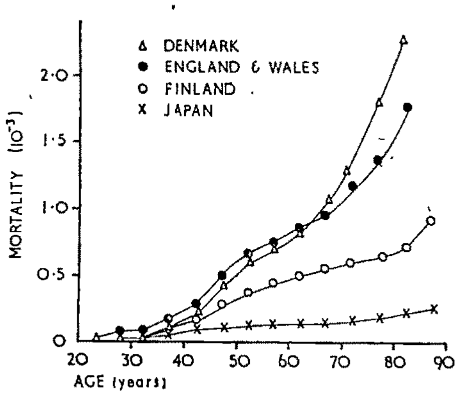


FIG. 1

From the areas under each curve (Fig. 2) I would account for approximately half of the total breast cancer mortality in England and Wales, Denmark, and Japan (data not shown). For England and Wales, the relative frequency of I and II is approximately five, in the age group 30–55 years, and unity for 55–70 years. At ages greater than 70 years, II increases steeply and is 10 times more frequent than I at 75 years, and 100 times at 80 years.

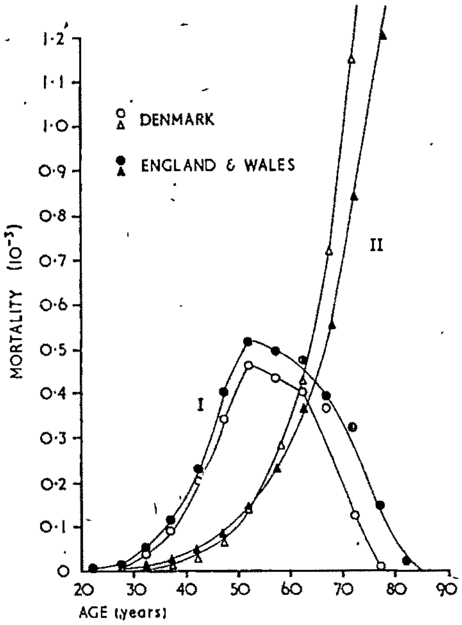


FIG. 2

It is reasonable to postulate that I would be oestrogen-dependent, while II would thrive in the absence of oestrogen. Thus, comparison of success rates of endocrine therapy for breast cancer, in the three age groups quoted above, might provide evidence in support of, or against, the existence of two biochemically distinct types of breast cancer, for which the above epidemiological evidence is highly indicative but not, by itself, conclusive.—I am, etc.,

GORDON HEMS.

Department of Public
Health and Social Medicine,
Aberdeen.

REFERENCES

[1] Clemmesen, J., *Statistical Studies in the Aetiology of Malignant Neoplasms*, 1965, 1, pp. 254–60. Copenhagen.

[2] Segi, M., and Kurihara, M., *Cancer Mortality for Selected Sites in 24 Countries*, 1964, Nos. 3 and 4. Tohoku University, Japan.

Digital Ischaemia and Malignant Disease

SIR,—I was interested in the association of digital ischaemia and malignant disease (22 July, p. 208), but disappointed with the authors' speculations on the mechanism, and particularly the reluctance to attribute the phenomenon to intravascular coagulation.

Increased blood viscosity in the small digital arterioles, which are subject to surface cooling, must be the final mechanism and be the result of red cell and platelet aggregation together with hypercoagulability of the plasma. Crenated red cells,[1] increased platelet numbers and stickiness, raised levels of fibrinogen and of factor VIII with accelerated generation of thromboplastin,[2] are all recognized in malignancy. As evidence of intravascular coagulation raised levels of cryofibrinogen may be found,[3] and fibrin breakdown products detected. Certainly in some cases the trigger is the release of tissue thromboplastin from disseminating carcinoma cells, and tumour emboli can be shown to be associated with fibrin thrombi.[4 5] Particularly is this so with the mucinous adenocarcinomata[6]; fibrin or fibrinoid may be found in the renal glomeruli.

Intravascular coagulation is a common pathogenetic mechanism in diverse pathologies,[7 8] and our understanding of these states will only be advanced when the clinician recognizes by the high index of suspicion the type of case that requires subtle investigations.—I am, etc.,

Royal Victoria Infirmary,
Newcastle upon Tyne.

E. N. WARDLE.

REFERENCES

[1] Brain, M. C., Dacie, J. V., and Hourihane, D. O'B., *Brit. J. Haemat.*, 1962, 8, 358.

[2] Amundsen, M. A., Spittell, J. A., Thompson, J. H., and Owen, C. A., *Ann. intern. Med.*, 1963, 58, 608.

[3] Kalbfleisch, J. M., and Bird, R. M., *New Engl. J. Med.*, 1960, 263, 881.

[4] Stefanini, M., Giammalvo, J. T., and Karaca, M., *Amer. J. Med. Sci.*, 1963, 246, 58.

[5] Sträuli, P., *Thrombos. Diathes. haemorrh. (Stuttg.)*, 1966, Suppl. No. 20, p. 147.

[6] Bagnoud, F., ibid., 1966, 15, 143.

[7] McKay, D. G., *Disseminated Intravascular Coagulation; An Intermediary Mechanism of Disease*, 1965. New York.

[8] Hardaway, R. M., *Syndromes of Disseminated Intravascular Coagulation with Special Reference to Shock and Haemorrhage*, 1966, Springfield, Ill.

SIR,—I enjoyed reading the paper by Dr. P. R. Hawley and colleagues (22 July, p. 208). However, I should like to point out that a definition of primary Raynaud's disease was formulated by Allen and Brown in 1932,[1] on the basis of their extensive experience of this condition. They stated that a diagnosis of Raynaud's disease should be made only when the following criteria were fulfilled: attacks of pallor and numbness of the extremities, proceeding to cyanosis and redness; *absent or minimal gangrene*, onset early in life and *duration of symptoms exceeding two years*; and no obvious demonstrable cause (my italics).

This definition would appear to be still valid in the light of more recent experience of this condition.—I am, etc.,

D. N. GOLDING.

Princess Alexandra Hospital,
Harlow, Essex.

REFERENCE

[1] Allen, E. V., and Brown, G. E., *Amer. J. med. Sci.*, 1932, 183, 187.

Undesirable Effects of Marijuana

SIR,—I have not seen the effects of marijuana as used in this country, but three cases of acute intoxication from smoking Indian hemp seen when a medical missionary in India come vividly to mind.

Some hospital outbuildings were under construction, leaving a series of unroofed gables. On the nine-inch wide (23-cm.) pinnacle of one of these stood a man, stark naked, shouting and singing and beating his chest by the light of the setting sun. I had to bring him down, fortunately without damage to either of us.

Two other cases might be described as "fighting drunk." A policeman at the local gaol ran amok, armed with a carbine. I was the medical officer, and was relieved to find his colleagues had overpowered and disarmed him by the time I arrived. On another occasion there was an uproar on the hospital veranda. Running out from my house to see what was the matter I was in time to see a male charge nurse felled with a blow from a powerful man. Grateful for the mosquito screening which separated us I kept the patient humoured in conversation until reinforcements arrived.

In other words, the effects of smoking Indian hemp can range from elation to manic violence.—I am, etc.,

E. GORDON WILKINS.

St. Mary's Hospital,
York.

Dopa and Parkinsonism

SIR,—My colleagues and I are thankful for the generosity displayed in your leading article (24 June, p. 783) about DL-dopa and Parkinsonism.[1] Your recognition of the necessity for continuing investigations is a service to those afflicted with this disease.

Our current studies with L-dopa strengthen the therapeutic effects listed in your article. Yet the following might be noteworthy: (1) Our initial failure to observe therapeutic effects in early, unilateral cases might well be a consequence of our reluctance to risk drug toxicity in mild cases. (2) To date, toxic manifestations have been sporadic, unpredictable, and reversible. They have included nausea, vomiting or faintness, depression of the circulating granulocytes, transitory eosinophilia, statistically significant elevation of the blood pressure, statistically significant elevation of the blood urea nitrogen, and involuntary movements, which usually affected the face, the jaw, the tongue, or the anterior neck, but occasionally the trunk or the extremities.

Parkinsonians represent as a rule the older segment of the population, and sometimes they suffer from complicating diseases as well. These patients have been often subjected to extensive drug exposure prior to receiving dopa. Inevitably, additional toxic manifestations will emerge while the action of dopa on Parkinsonism continues to be studied. Hence, we still consider our own studies as purely experimental. We are conducting them on informed patients, confined in a fully equipped metabolic ward, under systematic medical, nursing, and laboratory supervision of their health.—I am, etc.,

GEORGE C. COTZIAS.

Brookhaven National Laboratory,
Associated Universities, Inc.,
Upton, Long Island,
New York, U.S.A.

REFERENCE

[1] Cotzias, G. C., Van Woert, M. H., and Schiffer, L. M., *New Engl. J. Med.*, 1967, 276, 374.

Guillain-Barré Syndrome with Leukaemia

SIR,—I read with interest the report by Drs. R. L. Powles and J. S. Malpas of two cases of this syndrome in patients with chronic lymphatic leukaemia (29 July, p. 286) and note that one of them (Case 2) had also suffered herpes zoster 10 months previously.

In 1963 I admitted a known chronic lymphatic leukaemia patient to Bristol Royal Infirmary with a clinical diagnosis of acute polyneuritis occurring five days after an attack of zoster. After investigation this was confirmed and the case was subsequently reported by Drs. Etuk and Bridges.[1] These writers referred to three cases of polyneuritis complicating herpes zoster reported by Knox *et al.*[2]—the latter also reviewing 10 further cases from the literature. Whereas in my patient the latent period between the zoster and the polyneuritis had been only five days, Knox reported a range in the 13 cases of a few days to two months.

While "activation" of the varicella-zoster virus is a well-recognized hazard in patients with reticuloses (indeed sometimes characteristically to the extent of a generalized zoster) the added complication of polyneuritis even in these circumstances appears to be rare. None of Knox's 13 cases had any evidence, at the time, of reticulosis.

Although the 10 months which Drs. Powles and Malpas give as the latent period in their Case 2 would appear to be well outside Knox's range, is it not worth considering the possibility that the polyneuritis in this case may have been related more to the preceding zoster than to the pre-existing leukaemia?—I am, etc.,

Bristol D. S. RACTLIFFE.

REFERENCES

[1] Etuk, E. S., and Bridges, D., *Bristol med.-chir. J.*, 1964, 79, 91.
[2] Knox, J. D. E., Levy, R., and Simpson, J. A., *J. Neurol. Neurosurg. Psychiat.*, 1961, 24, 167.

Changed Character of Osteomyelitis

SIR,—Your leading article on the "Changed Character of Osteomyelitis" (29 July, p. 255) comments on many interesting aspects of this disease. But in children and adolescents, is not the usual site of disease the metaphysis and not the epiphysis?

I would also question the statement that the blood culture is usually negative even in subacute cases of the disease and the presence of a sequestrum is surely a common cause of a persistent sinus.

The importance of instituting antibiotic therapy as soon as the diagnosis is made is rightly stressed. Broad spectrum antibiotics are recommended but not named. Tetracycline and chloramphenicol are not ideal, as they are not bactericidal drugs, and ampicillin does not act against the penicillin-resistant *Staphylococcus aureus* which is now so commonly found in cases of osteomyelitis. As penicillin-sensitive and penicillin-resistant staphylococci cause the great majority of bone infections, the initial antibiotic therapy should be planned accordingly. Cloxacillin may be given alone[1] or combined with penicillin, fusidic acid, cephaloridine. lincomycin, or ampicillin. If pus forms under the periosteum, as it often does, it can be effectively removed by aspiration with less risk of secondary infection than if an incision is made.[2] If incision is favoured, suturing the wound lightly rather than accurately is likely to increase the risk of secondary infection and subsequent sinus formation.—I am, etc.,

J. H. BULMER.

The Royal Hospital,
Wolverhampton.

REFERENCES

[1] Green, J. H., *Brit. med. J.*, 1967, 2, 414.
[2] Neligan, G. A., and Elderkin, F. M., ibid., 1965, 1, 1349.

SIR,—While I agreed with much of your leading article on "Changed Character of Osteomyelitis" (29 July, p. 255) it contains in my view too many inaccuracies to pass unchallenged.

Surely the epiphysis is very rarely affected, even secondarily? The usual site is the metaphysis.

If the lesion needs surgical exploration, drilling the underlying bone is always wise; pus is quite often found under tension within the bone, even when a subperiosteal abscess is present. No harm results even if intraosseous pus be not found. Primary osteomyelitis in the adult, although admittedly uncommon, is by no means "extremely rare" in my experience.—I am, etc.,

Cambridge. T. J. FAIRBANK.

SIR,—Your leading article on the changed character of osteomyelitis (29 July, p. 255) suggests that the disease has lost its sting all over the world. This is certainly not the case in West Africa, where chronic osteomyelitis is one of the major orthopaedic problems. Both massive sequestration and diffuse infection leading to an enlarged sclerotic bone riddled with abscess cavities are commonplace.

In Nigeria the causative organism is usually, except in sicklers, a penicillin-sensitive strain of *Staphylococcus pyogenes*.

The majority of patients get no proper treatment in the acute stage. This may be due to lack of medical facilities, but often follows mistaken diagnosis. The child is brought to hospital with a painful swollen limb following a fall. If the doctor does not think of osteomyelitis he may examine the limb to exclude a fracture and discharge the patient, thereby losing the chance of curing the condition by the early administration of antibiotics.—I am, etc.,

D. R. RICHARD.

Department of Surgery,
University of Ibadan,
Nigeria.

Recognition of Heart Failure

SIR,—The article "Recognition of Heart Failure" (22 July, p. 219) is lucid and valuable, but there are two statements which I think are misleading.

Dr. C. S. McKendrick claims that "it is rarely necessary to differentiate which sort of triple rhythm is present." But an atrial sound is not in itself evidence of heart failure, though it does imply resistance to filling of a ventricle, and therefore abnormality. An atrial sound may be present intermittently, and for a long time, before left ventricular failure develops in patients with ischaemic heart disease, aortic stenosis, or hypertension. A third sound, on the other hand, is evidence of failure and of raised left atrial pressure in patients over 40 and without mitral regurgitation. These sounds, therefore, have very different implications and it is worth while trying to separate them. I agree that when tachycardia is present this may be impossible.

Secondly, it is claimed that the central venous pressure does not rise after myocardial infarction, but this is certainly not true. A raised jugular venous pressure is frequent following myocardial infarction when left ventricular failure is present. It is presumably due to consequent pulmonary arterial hypertension and right ventricular failure, and this may occur rapidly and therefore be seen when the patient still has pain. Elevation of the jugular venous pressure is therefore not a distinguishing point between pulmonary embolism and myocardial infarction, unless left ventricular failure can be confidently excluded.—I am, etc.,

PETER CARSON.

Cleveland Metropolitan
General Hospital,
Cleveland, Ohio,
U.S.A.

Cardiac Arrest in Asthma

SIR,—A great deal of interest has been shown recently in sudden death during status asthmaticus (25 March, p. 756, and 22 April, p. 244), and so we feel that the following case with two episodes of cardiac arrest following withdrawal of steroids may be worthy of description.

The patient, an asthmatic aged 47 years, who had been maintained on betamethasone 0.25–0.5 mg. daily for three years, was admitted on 2 December 1966 with a five-day history of melaena. Aspirin had been ingested, and he had a haematemesis on the day of admission. When seen in hospital he was pale and sweating, with a regular pulse (104/min.) and blood pressure of 150/85 mm. Hg. Hb 47% (6.9 g./100 ml.). Bronchospasm was minimal. 5 pints (2.8 l.) of blood was given. Barium meal examination showed a duodenal ulcer and steroids were withdrawn. In spite of tetracycline and long-acting isoprenaline he developed purulent sputum and increasing bronchospasm, failing eventually to respond to intravenous aminophylline. During a period of 17 days there were no signs of adrenal insufficiency.

On 19 December 1966 he was in severe bronchospasm and using his isoprenaline inhaler to excess, with less than a minute between five successive inhalations. At 10 a.m. cardiac arrest occurred in asystole. External cardiac compression was begun immediately with return of sinus rhythm within five minutes. Several ribs were broken during compression. Intubation was performed for assisted respiration with 100% oxygen. After 10 minutes spontaneous breathing started. Arterial blood gases showed metabolic and respiratory acidosis. The former was corrected by intravenous 8.4% sodium bicarbonate. Hydrocortisone was administered intravenously, and thereafter oral prednisolone. By 11 a.m. he was fully conscious. The E.C.G., continuously monitored, showed the development of right bundle branch block.

At 3 p.m. on the same day further cardiac arrest occurred in asystole. Further successful resuscitation followed, and on this occasion sinus rhythm returned spontaneously without bundle branch block. Flailing of the left chest was noted, and intermittent positive pressure ventilation was started in the intensive care unit. Severe bronchospasm persisted despite hydrocortisone and intravenous aminophylline, and indeed the Barnet ventilator was failing to inflate the chest despite a pressure of 45 cm. of water. A prophylactic left intercostal drain was inserted and bronchopleural leak became apparent. Tubocurarine 15 mg. and promazine 50 mg. were given at regular intervals, with 100 mg. ampicillin four-hourly, all by transvenous infusion. Repeated doses of dilute adrenaline were given intravenously to lessen the bronchospasm. Tracheostomy was performed the following day. Blood pressure remained satisfactory.

Assisted respiration was continued until 23 December 1966, when blood gas figures were satisfactory and adrenaline was no longer required. Uninterrupted clinical progress followed, and the prednisolone was reduced to a maintenance dose of 5 mg. b.d. At follow-up four months later bronchospasm was minimal.

In this case an isoprenaline inhaler was used over-enthusiastically during a severe asthmatic paroxysm, with resultant excessive sympathomimetic effect. This has been noted recently to be a likely mechanism of cardiac arrest in such patients.[1 2] The combination of status asthmaticus with flail chest is a desperate situation even with modern methods of respiratory assistance.[3] Our patient had bronchospasm of sufficient severity to resist artificial ventilation. The use of adrenaline intravenously is not without risk in itself, and continuous E.C.G. monitoring in such a situation would seem all important.—We are, etc.,

MARY MILLAR.
T. SEMPLE.

Victoria Infirmary,
Glasgow S.2.

REFERENCES

[1] Committee on Safety of Drugs (1967): *Aerosols in Asthma*, Adverse reactions series, No. 5.
[2] Graham, O. A., and Shields, W. O'N., *Med. J. Aust.*, 1965, 1, 524.
[3] Marchand, P., and van Hasselt, H., *Lancet*, 1966, 1, 227.

Pressurized Aerosols in Asthma

SIR,—I would like to add to the observations recently published in the *B.M.J.* concerning pressurized aerosols in asthma (13 May, p. 441, and 10 June, p. 699). It may not be generally appreciated that a drug administered into the tracheobronchial tree is absorbed very rapidly. In fact Redding *et al.*[1] have shown that dilute solutions of adrenaline in water administered by this route are as rapidly effective as intravenous or intracardiac injections.

This fact should be borne in mind when tracheobronchial aerosol administration of any drug is contemplated, and particularly so with powerful agents such as adrenaline and isoprenaline.—I am, etc.,

E. C. BLOCH.

Respiratory Unit,
Provincial Hospital,
Port Elizabeth, South Africa.

REFERENCE

[1] Redding, J. S., Asuncion, J. S., and Pearson, J. W., *Anesth. Analg. Curr. Res.*, 1967, 46, 253.

Stress Incontinence Treated by Electrical Stimulation

SIR,—Mr. Thomas Moore and Mr. P. F. Schofield (15 July, p. 150) point out that maximum perineal electrical stimulation can have a curative effect on stress incontinence. I have made the same chance observation on patients with stress and urge incontinence when stimulating their pelvic floor muscles during investigations of the electrical potentials of the levator ani under light anaesthesia. Although several hundred patients have had endoscopy and other manipulations under anaesthetic spectacular improvement in the condition has been confined to certain of those patients whose pelvic floor muscles were strongly stimulated, either during the procedure or later by electrodes temporarily inserted in the pelvic floor muscles during the anaesthetic, as a means of assessing the possible value of implanted electronic devices at a later date.

It has not been possible to predict the effect of strong stimulation in any given patient, but the results, in the main, accord with those of Moore and Schofield in that they are mainly confined to stress incontinence and "urge-frequency." However, one male adult patient with an incomplete cauda equina lesion due to spinal injury three years earlier has shown a remarkable improvement in that his constant dribbling has been replaced by pure stress incontinence and a number of children of both sexes with enuresis and diurnal urge-frequency have been relieved of their diurnal symptoms following strong stimulation during light anaesthesia.

My methods are rather similar to those of the authors in that, using a square wave of 1–2 milliseconds' duration and pulse frequency of 30 per second, I increase the voltage until the anus is seen to contract and then to be pulled forward and upward, indicating that there is a strong contraction of all the pelvic floor muscles.

This observation tends to confirm the view I have expressed[1 2] that the basic cause of many cases of stress and urge incontinence is "weak pelvic floor syndrome," but it is not as yet by any means fully explained.—I am, etc.,

S. A. VINCENT.

Anatomy Department,
Queen's University, Belfast.

REFERENCE

[1] Vincent, S. A., *Develop. Med. Child Neurol.*, 1964, 6, 23.
[2] —— *Lancet*, 1966, 2, 631.

Enuresis and Psychiatry

SIR,—I am rather surprised by some of the statements that have been made in the correspondence (15 July, p. 176, and 29 July, p. 308) on the above subject. In particular, I know of no evidence that treatment of enuresis with the buzzer may give rise to impotence later in life. Moreover, there is now quite an extensive literature supporting the effectiveness of conditioning treatment using the "pad and buzzer," the value of which has been pointed out in your columns, for example, by Gairdner.[1]

In this department we make regular use of the buzzer and hold a stock of about a dozen machines which are lent out to patients. There are, however, certain points which may be worth making about the treatment.

(1) We see a small minority of patients in whom the enuresis is part of a more general emotional disorder. In such cases it is usual to find that the child has become dry at night as a toddler and that with the subsequent development of anxiety symptoms of various sorts enuresis has also appeared. It is not our practice initially to treat such children with the buzzer but to apply whatever means of psychiatric treatment appear appropriate to the problem as a whole. Often the enuresis subsides when these measures are successful, but, if not, conditioning can then be employed.

(2) About 90% of the enuretics we see do not fall into the above category and in the majority of these (about four out of five) there is a prompt and satisfactory response to conditioning therapy. However, the relapse rate is quite high, in the vicinity of 50%, though relapse almost invariably responds promptly to a further short course of treatment; occasionally two or three further courses of treatment are required, but the later ones usually need to be only very brief.

(3) Most of these children suitable for treatment with the buzzer have had lifelong enuresis and there may be emotional symptoms secondary to the enuresis. These are consequent upon the disapproval which it has brought from members of the family and others, and the child may feel guilty, anxious, or even depressed. In these cases there is often a marked improvement in the child's emotional state following successful treatment of the enuresis.

(4) In using the buzzer it is important to gain the active and willing co-operation of both child and parents before treatment is commenced. Some children, particularly younger ones, are initially frightened of the apparatus, and the treatment has to be carefully explained and discussed with them, sometimes over the course of two or three interviews. Provided this is done it is often possible to treat successfully children as young as age 6 or even a little younger. I have also found it useful to arrange to see the patients quite frequently while they are undergoing treatment in order to ensure that the apparatus is being used properly and to give support and encouragement in its continued use.

I agree with Dr. I. G. Wickes (15 July, p. 176) that substitution symptoms rarely occur ; in fact the disappearance of other symptoms is more common. Occasionally, however, a persisting psychiatric problem is found to exist when the enuresis has ceased, and, if so, this has to be treated on its own merits. In my view it is wrong to regard enuresis as necessarily and invariably a symptom of a more deep-seated emotional disorder ; while it is sometimes this, I think it is much more often a " developmental " phenomenon, as described by Barbour and his colleagues.[2] Nevertheless, it must be admitted that there is a minority of children (about 20%) who, though apparently suitable for conditioning therapy, do not respond. They are usually in their teens, and one wonders if they would have done better treated younger. They present a very difficult treatment problem and are perhaps those which end up in Dr. R. A. B. Rorie's lap (29 July, p. 308).—I am, etc.,

PHILIP BARKER.

Department of Child
Psychiatry,
Royal Infirmary,
Dundee.

REFERENCES

[1] Gairdner, D., *Brit. med. J.*, 1965, **2**, 91.
[2] Barbour, R. F., Borland, E. M., Boyd, M., Miller, A., Oppé, T. E., *Brit. med. J.*, 1963, **2**, 787.

Coroners' Jurisdiction

SIR,—I have read with interest and not a little surprise the letter from Mr. H. A. Kidd (5 August, p. 372) and the two previous letters to which he refers. While not wishing to enter into discussion on the content of any of the Association's evidence submitted to the Brodrick Committee, I feel it is important to put the record straight on the *modus operandi* of submitting the evidence.

As is usual in specialized matters of this kind, Council refers the matter in the first place to one or more of the appropriate committees—in this instance the Private Practice Committee. This committee in turn referred it to its Forensic Medicine Subcommittee, which consists of specialists in this field, including consultant pathologists and police surgeons.

Dr. Ivor Jones (24 June, p. 845) makes it perfectly clear that the Private Practice Committee followed the normal procedure not only with the original report but also with the questionary received from the Brodrick Committee, and that ample opportunity was given to all interested parties to make their views known before Council's final approval. In my opinion, neither the Forensic Medicine Subcommittee nor its parent Private Practice Committee is in any way open to the charge of acting in an autocratic way in this matter.—I am, etc.,

JACK E. MILLER,
Deputy Chairman,
Private Practice Committee.

Glasgow W.2.

Asbestosis

SIR,—The leading article on " Asbestosis " (8 July, p. 62) is opportune. I would draw your attention, however, to a probable, hitherto unpublicized asbestos hazard. For some years past the filter pads of certain respirators have been made of wool-asbestos fibre. It is possible that inhalation of asbestos fibre takes place if such masks are in continuous use. It is also likely that many such filters are still being used.

Masks of this type were tested in 1962 for penetration.[1]—I am, etc.,

L. B. BOURNE.

London W.1.

REFERENCE

[1] Dorman, R. G., *Design and Use of Respirators*, ed. C N. Davies, 1962, p. 19. Oxford.

Psychological Factors and Ulcerative Colitis

SIR,—In your leading article (1 July, p. 1) there is an implied challenge to controversy in relation to the paper of Dr. F. Feldman and his colleagues (1 July, p. 14). These workers find little or no evidence that ulcerative colitis is a psychosomatic disorder and they give no credit to the accumulated evidence over the 37 years since Murray's paper.[1] You comment that this evidence is largely subjective and anecdotal. Every full personal history, though pejoratively labelled an anecdote, is an account of the substance of a man's life. I submit that this belittling of the life story is an impertinence to the patient and to those workers who are not afraid of involvement in psychological or even philosophical problems.

A person is a psychosomatic construct, hence medicine must be psychosomatic, and this means that the sick man needs to be studied both by physical methods and by the use of subjective methods dependent on observation and communication. It is erroneous to ask how the psyche produces somatic disease, because psyche and soma are the names of two aspects of man viewed in two different frames of reference which cannot be brought into such naive causal relationship. But history-taking has another subjective value, personal to the doctor who listens quietly while the patient finds his way through his own resistance up to the expression of his conviction of the relevance of his struggles, hopes, and fears to his somatic manifestations.

There is a great deal of evidence in previous studies of the role of the psyche in ulcerative colitis, of the relation of increasing stress to its onset and relapses, of the moulding of the subject through childhood and adolescence into a personality immature for age, over-dependent and of poor level in social communication, and also of the favourable effects of psychotherapy. Because this evidence is subjective and hence unpalatable to some workers is no reason for ignoring it—this is not a scientific attitude. Professor Groen[2] frankly avowed that he thought Murray's thesis would be easy to disprove, but his patients taught him otherwise. The reluctance to contemplate the role of the psyche is understandable. Medicine preserves the stability of Newtonian physics. Its basic sciences are chemistry, classical physics, and a biology based on these. We therefore prefer mechanical explanations or models which we can comprehend and hypotheses understandable in the light of our training and tradition. The modern physicist is not so bound. He deals with relativity, quantum theory, and uncertainty relations. Because of the latter he accepts that his observations cannot be exact, because there is a subjective element in observing. He does not demand that the phenomena of nature must be explicable within the limits of the present human mind. Cause is no longer a matter of contiguity and sequence of events ; physics is no longer the paradigm of exact science.

It is impossible to analyse the paper of Feldman *et al.* because of paucity of data ; the methods used are barely described though existing in a 200-page work-book. But it can be compared with the paper of O'Connor *et al.*[3] with its use of inventories, interviews, and scoring techniques, *but with entirely opposite conclusions.* Surely this must throw doubt on the validity of these techniques which workers have been compelled to use in order to be " scientific " and " with it." The concept of personality is subtle, but the word itself is useful, like mind or psyche. Can it be measured in these ways ? It would be accepted as impossible to measure the artistic value of a picture by counting categories of brush strokes, lines of tension, or distribution of masses. Similarly a man's life is too rich for methods of analysis which essentially summate factors from a hotchpotch of categories.

The psychosomatic hypothesis of ulcerative colitis is simply stated: the disease is largely determined by stress acting on an immature personality, this latter being the result of social and psychological forces acting during the period of personality development—the " strain " is most evident as the somatic disorder. This, like all hypotheses, cannot be proved but it can be supported or falsified. Its important corollary is the implication of appropriate treatment. It would be naive to consider that maturation of personality can be restored wholly at a time beyond the correct stages for this process. It would be equally naive to expect any psychotherapy to cope with the irremediable reality situations sometimes encountered.—I am, etc.,

HUGH GAINSBOROUGH.

London N.W.8.

REFERENCES

[1] Murray, C. D., *Amer. J. med. Sci.*, 1930, **180**, 239.
[2] Groen, J., and Van Der Valk, J. M., *Gastroenterologia (Basel)*, 1956, **86**, 591.
[3] O'Connor, J. F., Daniels, G., Flood, C., Karush, A., Moses, L. and Stern, L. O., *Ann. intern. Med.*, 1964, **60**, 587.

Pericarditis in the Tropics

SIR,—Dr. R. H. Llerandi (1 July, p. 48) and other colleagues have kindly brought to my notice a misleading statement which appeared in my discussion on the treatment of amoebic pericarditis (13 May, p. 423).

The treatment which I have recommended in the article is sound. However, the sentence " Chloroquine is necessary because emetine usually has no effect on hepatic amoebiasis " was an unsuccessful attempt to say something rather different from what appeared in the paper. As it stands, the statement is not true and should be deleted. I regret having given the impression that emetine is of little value in the treatment of hepatic amoebiasis. It is in fact of great value, as shown by Dr. L. Rogers.[1]—I am, etc.,

K. SOMERS.

Mulago Hospital Medical School,
Kampala, Uganda.

REFERENCE

[1] Rogers, L., *Brit. med. J.*, 1912, 1, 1424.

Sugar Consumption and Acne

SIR,—I was interested in the study by Dr. D. G. G. Bett and others (15 July, p. 153) in which they found raised sugar consumption in patients with seborrhoeic dermatitis but not in those with acne.

In a study of 2,720 soldiers it was established that there is no correlation between the incidence or severity of acne and dandruff.[1] There was also no correlation between acne and obesity in men under 20 years old—the age group studied by Bett *et al.* However, in older men (age 20–40) there was a significant correlation between acne and obesity. It appears, therefore, that perhaps Bett *et al.* should extend their study to see if there is raised sugar intake in this older group before it can be settled that sugar intake in acne is not raised.—I am, etc.,

London W.1. STANFORD BOURNE.

REFERENCE

[1] Bourne, S., and Jacobs, A., *Brit. med. J.*, 1956, 1, 1268.

Sliding Board for Severely Disabled Patients

SIR,—It is good to read in your issue (22 July, p. 244), Miss M. J. Seiffert's appreciation of the use of a sliding board for severely disabled patients in Britain. It has been popular in Australia for a considerable length of time. Perhaps some constructive comments from one who has seen this method in use by a near relative for many years will be acceptable.

In the first place, a board which is ¾ in. (2 cm.) thick is difficult to introduce under a patient's buttocks, by a second party in particular. A thinner board in 5-ply will support a 12-stone (76-kg.) man. A board which is only 2 ft. 6 in. (75 cm.) long is too short for use in a London taxi. A longer, lighter board can be carried around without any great inconvenience.

A short board, say 2 ft. (60 cm.) long or so, is particularly useful for getting on and off lavatory seats because it is not so liable to catch the edges of the plastic or wooden top.—I am, etc.,

R. E. JOWETT.

The Royal Infirmary,
Sunderland.

Is Anaesthetist Dentist's Agent?

SIR,—I was very interested to read Dr. A. M. Danziger's letter (29 July, p. 310). It raises a very pertinent point. Why should a patient not contract with an anaesthetist privately to give an anaesthetic to himself, and at the same time contract with a dentist to have treatment under the National Health Service?

There are a number of people (children and adults) who cannot, for various reasons, accept conservative dental treatment without going to sleep; but it is unrealistic to expect a specialist to spend hours giving endotracheal anaesthesia without adequate financial reward, as is the case at present.

In view of the recent recommendations that dental anaesthetics should be given by specialists[1] then it is only reasonable that realistic anaesthetic fees should be paid, not only for extractions, etc., but for conservative work as well.—I am, etc.,

Barrow-in-Furness. R. IAN DIXON.

REFERENCE

[1] *Dental Anaesthesia*, Report of a Joint Subcommittee of the Standing Medical and Dental Advisory Committees on Dental Anaesthesia, Ministry of Health, 1967. H.M.S.O.

Opportunities in British Medicine

SIR,—I am surprised that the advertisement sponsored by the Ministry of Health (15 July) on the above subject has provoked little comment. Directed toward the emigrant doctor, an interview board is to tour Canada and the U.S.A. in an attempt to attract doctors back to Great Britain.

"Payment of fares to selected applicants is authorized." Surely once a doctor has lifted his roots and faced life in a new country he is going to expect a guaranteed career structure as well, not only a free journey. Even the Ministry cannot expect to secure labour without being able to offer such a guarantee.

How can people abroad be offered posts in Britain and a progressive career? Are we going to apply for advertised vacancies to find appointments being made "in absentia"? There is enough time wasted by applicants travelling to interviews for posts which practically do not exist, as either a local man has been promised the vacancy or errors were made in the advertisement, which is not uncommon. Now it looks as though the additional factor of absent successful candidates has to be faced.

What career opportunities are available for those who remain? In a few weeks' time I personally may have to face a period in another specialty or general practice, in order not to be unemployed, until a post required for examination purposes becomes available. This is hardly "opportunity." While an effort must be made to attract doctors back to this country, it must not be made to the detriment of those who have remained, carrying the extra work load caused by colleagues leaving.

Last year I wrote in these columns (20 August, p. 470) about the future of junior staff, and asked could anyone see a future for us. No one has said "Yes" to this question. It looks as though the answer is to emigrate first, then the Ministry will offer a free passage home and career opportunities, which must carry some degree of guarantee.

I cannot help feeling that the activities of this interview board will need careful watching by our Junior Hospital Staffs Group. Any advantages offered to emigrants over staff who have remained in Britain must be opposed. It need hardly be stated that if conditions were good there would be no need to tempt anyone back.—I am, etc.,

Queens Park Hospital,
Blackburn. D. C. PRIOR.

Seniority Allowance

SIR,—I qualified from Madras Medical College, India, in 1949 and have been in general practice (N.H.S.) since 1954. Unfortunately I failed to register in this country until 1954, although my qualification is recognized by the G.M.C.

My recent application for seniority allowance was turned down by the Ministry on the grounds that "registration with overseas bodies does not count for the purpose of determining eligibility for seniority payments."

I consider this a gross injustice, especially as doctors who qualified in the Republic of Ireland are now eligible for this payment. —I am, etc.,

Coseley. A. M. POORNAN.

Seniority from 1913?

SIR,—May I draw attention to the often parlous plight of many retired "panel" general practitioners who have worked for many years in the admittedly underpaid service, often, as in my own case, from the inception of the N.H.I.—that is, 15 January 1913.

Could not some of the monies which were to have been paid for seniority awards be given to the elder pensioners so that each receives a minimum of £10 a week? I have never seen it stressed that the year 1988 will come before any general practitioner retires on "half-pay"—the "half-pay" one reads about in novels that the retired Army and Navy officers retire on. Did they have to wait 40 years?—I am, etc.,

Minehead,
Somerset. EGERTON C. WHITE.

Points from Letters

Self-expulsion of a Nasal Polyp

Dr. J. M. CRAWFORD (Chertsey, Surrey) writes: I do not know if it is a common occurrence to expel a nasal polypus from one's nose as Dr. B. Green's patient did (5 August, p. 372).

If it is of any interest to him, or others, I managed to do this myself at the age of 6. I was in bed with a cold at the time and I can tell that I was more than a little upset. I thought that I had literally blown my brains out.

Errors Caused by Language Barriers

Dr. E. V. BEVAN (Cambridge) writes: I read recently (daily press, 25 May) of the tragic mistake in a hospital where the wrong leg was amputated from a patient. The surprising thing is not that this should happen at all but that it does not happen every day. In very many hospitals a situation may arise where the nurses are Italian or Spanish, the registrar is a Nigerian, the houseman a West Indian or a Malaysian, and the patient a Glasgow Scot. How on earth any communication between this cross-section of the United Nations can take place at all is very difficult to understand.

Obituary Notices

THOMAS JOHN HENNELLY
M.D., D.P.M.

Dr. T. J. Hennelly, former physician superintendent of Whitchurch Hospital, Cardiff, and lecturer in psychological medicine at the Welsh National School of Medicine, died on 21 July. He was 63.

Thomas John Hennelly was born in Western Ireland on 7 June 1904, and received his medical education at Galway and Dublin, graduating M.B., B.Ch. B.A.O. with first-class honours in 1928. After a short time in general hospitals and in general practice he entered the field of psychological medicine in June 1929, holding appointments at Gloucester County Mental Hospital, Powick Hospital, Worcester, Brookwood Hospital, Surrey, and the West End Hospital for Nervous Diseases, London. He took the D.P.M. in 1931 and proceeded M.D. the following year. In May 1933 he was appointed senior assistant medical officer at Whitchurch Hospital, Cardiff, and became the deputy physician superintendent in 1934. In 1937 he was appointed at the early age of 32 to the position of physician superintendent, and remained at Whitchurch in this capacity until his retirement from the National Health Service in December 1959. He then emigrated to Canada, and was appointed director of the Center Lawn Hospital, Essondale, British Columbia, until his final retirement in July 1966. He returned to Britain and went to stay with an old friend and colleague at Woodbridge, Suffolk.

He took a keen interest in the Royal Medico-Psychological Association, and had been chairman of the South-western Division and secretary of the research and clinical section. He was president of the section of psychiatry at the Annual Meeting of the British Medical Association in 1953.

Tommy Hennelly was a great character with dynamic personality, keen sense of humour, of philosophical outlook, a first-class clinician, a profound reader, and he loved nothing better than a good argument. He retained his Irish brogue, and was known by his students as "tic and tin." The hospital nursing staff knew him affectionately as "father." Outside his work he read avidly books of an autobiographical and historical nature. A man of firm opinion who never curried flattery or sought any favours, he was highly esteemed by all those who worked with and under him.

His wife, Dr. Margot Hennelly, predeceased him by three years. There remain their five children, Michael, Mary, John Angela, and Dermot, to whom we extend our deepest sympathy.—A. C.

P. W. HAMPTON, M.D.

Dr. P. W. Hampton, formerly consultant surgeon to Noble's Isle of Man Hospital, died at his home in Governor's Road, Onchan, Isle of Man, on 1 July, at the age of 91.

Percy William Hampton was born on 22 March 1876, and received his medical education at the University of Edinburgh, graduating M.B., Ch.B. in 1899. He served as civil surgeon to the South African Field Forces in 1901–2. Returning from South Africa, in 1905 he proceeded M.D. with high commendation. He engaged in general and consulting practice in the Isle of Man, and in 1913 joined the staff of Noble's Isle of Man Hospital as honorary assistant surgeon. During the first world war he served in the R.A.M.C., with the rank of major, as surgical specialist at the Military Hospital at Ripon, Yorkshire. After demobilization he returned to the Isle of Man, but in 1927 ill-health obliged him to relinquish general practice, though he continued his work as honorary surgeon at Noble's Isle of Man Hospital. In 1944 he became honorary consulting surgeon to the hospital, a position he held until the introduction of the Manx National Health Service in 1948. In 1944–5 he was a representative at the Annual Meeting of the British Medical Association. He was appointed vice-president of Noble's Isle of Man Hospital in 1944, an office he held until October 1964, when the hospital was transferred to the Isle of Man Health Services Board.

A colleague writes: Both in his general practice and in his hospital work Dr. Hampton rendered outstanding service to the island of his birth. A capable all-round diagnostician, and an excellent surgeon and obstetrician, he also acted as surgical referee to the Isle of Man National Health Insurance Board, and was one of the outstanding medical personalities of the island.

He is survived by his widow, who nursed him devotedly for several years, and by two daughters, both doctors, and both married to members of the profession.

J. BROADFOOT, M.D., D.P.H.

Dr. J. Broadfoot, formerly a general practitioner in Ross-shire, died suddenly in hospital in Inverness on 13 July after a short illness. He was 80.

John Broadfoot was born in Hamilton, Lanarkshire, on 13 April 1887, and was educated at Glasgow High School and University, where he graduated M.B., Ch.B. in 1910. He held resident posts of house-physician and house-surgeon in the Western Infirmary, Glasgow, and acted for a time as a demonstrator in anatomy at the University. In 1913 he took over the practice in Dingwall of the late Dr. John Adam, and remained there for 27 years. He was medical officer to the Ross Memorial Hospital, Dingwall. For ten years he was a member of Ross County Council and of the Education Authority. In 1921 he proceeded M.D., and in the same year took the D.P.H. In 1930, seeking a change from the incessant strain of a busy practice, he was appointed assistant medical officer of health in Inverness. In 1935 he became a family physician again, and took up practice in Kilmacolm, Renfrewshire. He remained there until after the second world war. He retired in 1945 and went to live in Conon Bridge, Ross-shire, where he took a keen interest in the life of the village and in a wide variety of local causes. After his retirement from general practice he made several voyages as a ship's surgeon, and visited India, China, Australia, and South Africa.

The major part of Dr. Broadfoot's professional life was spent in Ross-shire, where he was a most popular and much respected doctor. A Ross-shire paper recalls that "weather never deterred him on his errands of mercy; when his car would go no further, he waded waist deep through snow-drifts to reach a sick-bed." He was always a brisk and energetic man. His somewhat abrupt and gruff manner was discounted by the twinkle in his eye, and could not conceal his underlying kindness. His main recreations were golf and bridge.

He is survived by his wife, a son, and two daughters. The son is in practice in Port Glasgow, and one daughter practises in Hampshire with her husband.—A. J. C. H.

H. SIMMONS, M.R.C.S., L.R.C.P.

Dr. H. Simmons, a general practitioner in Langley, Bucks, died in St. George's Hospital, London, on 22 July, aged 60.

Harry Simmons was born in London on 6 January 1907, and received his medical education at St. Bartholomew's Hospital, London. He qualified with the Conjoint diploma in 1931, and held hospital posts at the Royal Hospital, Richmond. After a period in general practice he joined the R.A.M.C. at the outbreak of the second world war, and served throughout. On demobilization he found that his practice no longer existed, and he settled in practice at Langley, at first in partnership and then alone. His country practice, however, changed in character as the district developed, and Harry Simmons, helped by his devoted wife, rose to the challenge and built a general practice service for a thickly populated area, with modern surgeries, taking on partners, and above all still caring for individual patients with the same regard and devotion to their welfare as he had done in his small country practice.

He had more than his share of ill-health, but he never gave in to it, and showed at all times boundless energy and interest in his work, refusing to give anything less than his best. He never lost an opportunity of helping a patient or a colleague, and did so quietly and with charm.

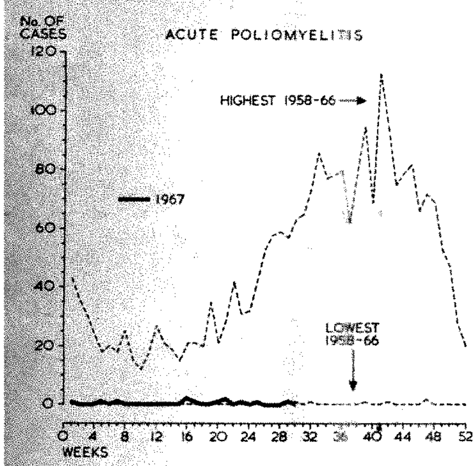
He leaves a widow, a daughter and her family, and a son, also a doctor, to whom our deepest sympathies are extended.—J. R. and N. G.

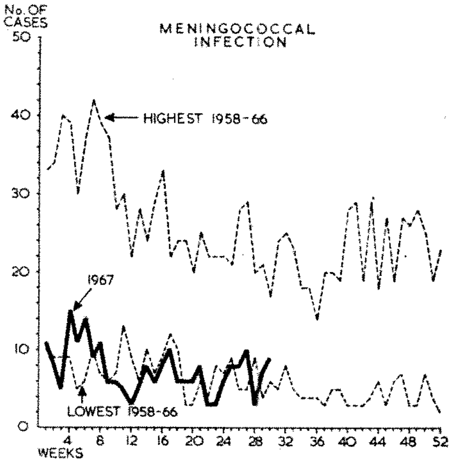
News and Notes

EPIDEMIOLOGY

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of acute poliomyelitis and meningococcal infection in England and Wales. Figures for 1967 are compared with the highest and lowest figures for each week in the previous years shown.





Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available.

	Week Ending 28 July	4 Aug.
Dysentery		
Greater London	77	**44**
Lancashire	33	**54**
Warwickshire	25	**26**
Yorkshire West Riding ...	35	**41**
Leeds C.B.	12	**27**
Edinburgh	38	**16**
Glasgow	27	**21**
Food-poisoning		
Greater London	26	**48**
Southwark	0	**10**
Hertfordshire	2	**14**
Rickmansworth U.D. ...	0	**12**
Lancashire	13	**38**
Denton U.D.	0	**14**
Surrey	7	**20**
Frimley & Camberley U.D.	0	**18**

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **29 July** (No. 30) and corresponding week 1966.

Figures of *cases* are for the countries shown and for Greater London. Figures of *deaths* and *births* are for the whole of England and Wales (London included), Greater London, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0		0	0	1	0	
Dysentery ..	292	77	87	3	7	356	89	58	6	3
Encephalitis, acute ..	6			0		0	0		0	
Enteric fever: Typhoid ..	2	0	0	0		6	2	1	0	
Paratyphoid	1	1	0	0		5	2	0	0	
Food-poisoning	170	26	7	2		128	34	15	6	
Infective enteritis or diarrhoea under 2 years				21	42				8	64
Measles* ..	4,453	198	24	94	155	8,300	855	93	61	106
Meningococcal infection ..	9	3	3	0		10	2	3	0	
Ophthalmia neonatorum	10	3	0	0		15	0	0	0	
Pneumonia† ..	79	6	51	5		52	7	64	0	
Poliomyelitis, acute: Paralytic ..	0	0	0	0		1	1	0	0	
Non-paralytic	0	0	0			1	0	0	0	
Puerperal fever§	105	55	0	0		62	23	11	0	
Scarlet fever ..	209	38	8	7	11	312	47	8	4	5
Tuberculosis: Respiratory ..	225	42	27	4		238	66	42	3	
Non-respiratory ..	63	16	7	0		36	8	13	4	
Whooping-cough	738	128	116	6	51	357	53	17	5	7

DEATHS	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0		0	0	0	0		0	0	0
Dysentery ..	5	0		0		0	0		0	
Encephalitis, acute ..					0					0
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	3	0	2	0	1	3	0	1	0	4
Influenza ..	1	0	0	0	0	5	1	0	0	0
Measles ..	0		0	0	0	0		0	0	0
Meningococcal infection ..			0					0		
Pneumonia ..	492	73	10	9	6	455	72	15	10	7
Poliomyelitis, acute ..	0	0		0	0	0	0		0	0
Scarlet fever ..	0		0	0	0	0		0	0	0
Tuberculosis: Respiratory ..	39	9	3	0	2	31	4	3	0	1
Non-respiratory ..				0	1				0	0
Whooping-cough	0	0	0	0	0	0	0	0	0	0
Deaths 0–1 year	265	50	26	7	10	265	43	13	6	17
Deaths (excluding stillbirths)	8,785	1389	536	119	172	8,979	1472	488	96	123
LIVE BIRTHS	16,149	2654	923	304	326	16,885	2927	953	298	511
STILLBIRTHS	223	31	26			259	45	9		

* Measles not notifiable in Scotland, whence returns are approximate. † Includes primary and influenzal pneumonia. § Includes puerperal pyrexia.

MOTORING

Synchromesh, and How to Use It

[FROM OUR MOTORING CORRESPONDENT]

Progress in motor-car design can sometimes take the form of a sudden advance resulting from an invention, but is more often painfully achieved by a great deal of intelligent experimental work. The history of synchromesh illustrates both these processes, and is also interesting because of the continued importance of synchronizing mechanisms in gearbox development.

The primitive kind of gearbox first used by Panhard and Levassor was adequately described by the inventors in the immortal phrase "It's brutal, but it works." Changes of ratio were made by sliding one gear into mesh with another and, as the speeds were different, a special trick called "double declutching" was needed in order to avoid destructive clashes between the gear teeth. By varying the speed of the engine and briefly re-engaging the clutch with the gearbox in neutral, the driver was able to match the peripheral speeds of the gears, after which they could be brought into mesh without shock or noise.

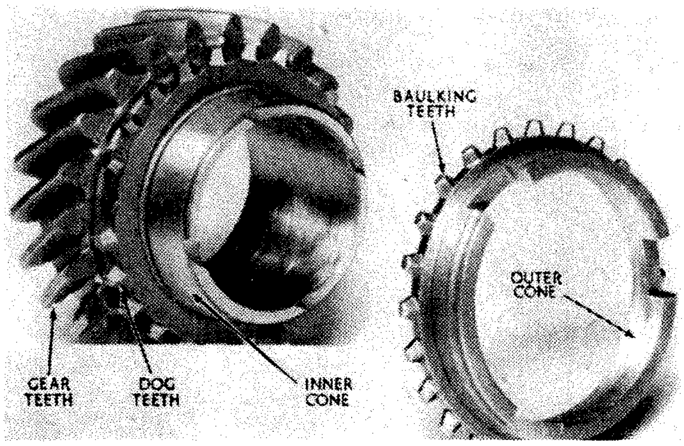


FIG. 1.—A gear wheel with dog teeth and synchromesh cone (left); the mating cone and baulking teeth are seen on the right.

Expert drivers found pleasure in exercising their skill in changing gear, but to the inexpert it remained a difficult and irritating process. There was also an element of risk when trying to change down on a steep ascent because the driver who failed to engage the gears could find himself in neutral with the car commencing to run backwards.

In the late 1920s a basic change occurred in gearbox design which paved the way for the subsequent introduction of synchromesh. Instead of sliding one gear into mesh with another, each pair of gears ran constantly in engagement but one of them was freely mounted on its shaft. A sliding member, called a dog clutch, enabled the "free" gear to be rotationally coupled to the shaft at the will of the driver. In this way the wear and tear caused by inexpert gear changing was transferred from the gear teeth to the more robust teeth of the dog clutches, but damage and noise could still result if the driver was unable to pre-adjust the rotational speeds by the double declutching process.

Several inventors then applied their minds to finding ways in which the rotational speeds could be synchronized automatically, and eventually this was done by bringing together the inner and outer cones of a small friction clutch before meshing the dogs themselves. Running in oil, the cones could slip without harm until their speeds were synchronized, after which the dogs could be engaged without difficulty. Of course the processes of frictional and positive engagement had to occur smoothly and consecutively as the driver moved the gear lever from one position to another, and this was easier to define than to achieve.

Much experimental work was necessary in order to arrive at the most favourable cone angles, surface finishes, and materials required for smooth (yet rapid) synchronization and a reasonable "life." The first production gearbox embodying synchromesh was offered by General Motors in a Cadillac in 1930, shortly followed by Vauxhall in England. A current Vauxhall design is shown in Fig. 1.

In spite of the universal use of synchromesh in manual gearboxes today, many drivers regard it as something of a mystery. Although simple in principle, the mechanism is difficult to describe or illustrate. But by explaining how it works rather than how it is designed I hope to be able to clear up some misunderstandings and causes of misuse.

Reduced to the simplest terms, the diagram (Fig. 2) shows the principal parts of a car transmission system. Note that although shafts A and B are in line, they are separate components which are disconnected within the box when the gear lever is in neutral. Another means of disconnecting the drive is by depressing the clutch pedal, which frees the friction grip normally applied to the clutch disc. Note, also, that shaft B is permanently connected to the back axle by the propeller shaft (not shown).

Now suppose that a car is travelling at 35 m.p.h. in top gear with the engine (and shaft A) turning at about 2,000 revs. per minute. Top gear is "direct," so that the speed of shaft B will also be 2,000 revs. per minute.

Changing Gear

The driver now decides to change down into third gear, to enable the engine to run faster in relation to the speed of the car and so to provide more power for climbing a gradient or for overtaking. It can be assumed that the change is made so quickly that the car loses very little speed during the process—in other words, that shaft B continues to turn at 2,000 revs. per minute or thereabouts. The sequence of events is as follows:

(1) Clutch pedal is depressed, disconnecting engine from clutch shaft A.

(2) Gear lever is moved into neutral, disconnecting shaft A from shaft B within the gearbox.

(3) Gear lever is moved towards the third gear position, bringing two synchromesh cones into contact.

(4) The mating cones enable shaft B to accelerate shaft A to a rotational speed determined by the third speed gears (say 2,800 revs. per minute), the clutch being still disengaged.

(5) Gear lever movement is completed, engaging dog teeth and so providing a positive drive (through the gears) between shafts A and B.

(6) Clutch pedal is released and engine speed is raised to 2,800 revs. per minute. Note that practised drivers will already have increased the speed of the engine appropriately (by using the accelerator) during the gear-changing process.

The clue to an understanding of this train of events is that it is the momentum of the moving car, acting through the wheels, back axle, propeller shaft, and shaft B, which drives the cones and gears while they are disconnected from the engine by the clutch. This applies equally to an upward gear-change, in the course of which the cones *slow down* shaft A in relation to shaft B before the engagement of the dog teeth.

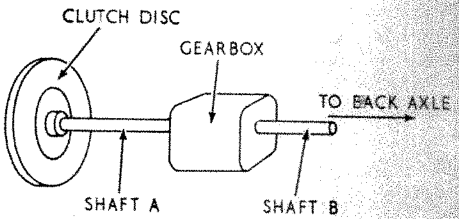


FIG. 2.—Car transmission system; the speed ratio between shafts A and B depends on the gears selected within the box.

The work done by the cones is therefore confined to altering the speed of relatively light gearing and shafting plus the clutch disc, which (though also light in weight) has considerable inertia because of its diameter. However, this is what the cones are designed to do, and they should survive thousands of engagements without appreciable wear. If they deteriorate early in life it is usually due to clutch drag; in other words, the disc is not completely free during the gear-changing process and consequently the cones have to overcome an unpredictable amount of frictional resistance.

There are various causes for clutch drag. Some drivers form the bad habit of not depressing the clutch pedal fully, so that the spring load on the disc is not completely relieved. In other cases the hydraulic device often used to connect the clutch pedal to the clutch fork may be at fault (owing to fluid leakage or ingress of air), so that the movement of the fork is inadequate even though the pedal is fully depressed. A disc that has become distorted by undue slipping in traffic (and consequent high temperature) may not be able to run completely free, even if the full withdrawal movement is being attained.

A more subtle cause of cone wear is sometimes traceable to the misguided attempts of a driver to "help" the synchromesh mechanism by inexpert double declutching. For example, if he grossly over-speeds the engine in neutral during a downward change, with the clutch temporarily engaged to accelerate the disc and shaft A, the cones may find more work to do in correcting his mistake than in their normal unassisted duty.

My advice is to let the synchromesh mechanism do the job for which it was designed while ensuring that the clutch is completely free during the process. As soon as the gear-change has been completed a smooth re-engagement of the clutch will be assisted if the engine has been accelerated during a downward change (but not too much) or allowed to lose speed during an upward change.

All modern synchromesh mechanisms embody a baulking device, intended to prevent premature dog engagement, but for the best and most consistent results it is advisable to apply a steady but not excessive pressure to the gear lever and to complete the change at one hit without hesitating part-way. This ensures that the cones do their job before the dog teeth slide into mesh.

MEDICO-LEGAL

Immigrants' Rights of Appeal

[FROM OUR LEGAL CORRESPONDENT]

The Divisional Court of the Queen's Bench Division refused[1] to intervene after an immigration officer had refused to allow an Indian into the country on medical grounds, despite a refusal by the Secretary of State to allow him an opportunity to rebut the medical evidence.

Avtar Singh arrived in England on 4 July to marry his fiancée, who was already in this country. On arrival he was examined by a medical inspector and refused admission. On 11 July the Home Office stated that after an examination by two medical inspectors the immigration officer formed the view that Singh was suffering from mental disorder. The mental disorder referred to was "subnormal mentality."

The Court held that as Singh had no right of entry into the country the immigration officer had an unfettered discretion to refuse admission without giving reasons. If he chose to give reasons, that did not give the would-be immigrant any right to rebut those reasons. The position might be different where the would-be immigrant had a right of entry subject to the possible grounds of objection referred to in Sections 2 (2) and 2 (3) of the Commonwealth Immigrants Act, 1962.

Subsequently, the Court of Appeal agreed to an expedited hearing of an appeal from the Divisional Court's decision, but the appeal was abandoned before the day fixed for hearing (31 July) and Singh returned to India.

---

[1] *The Times*, 26 July 1967.

MEDICAL NEWS

New Medical School for Southampton

A joint statement by the Department of Education and Science and the Ministry of Health says that the Government has decided to authorize the construction of a new medical school at Southampton University in conjunction with the Southampton General Hospital. Planning of the rebuilding of the hospital has started, and work on the medical school buildings should begin early in 1969. The school is at present being planned for an entry of 130 medical students a year.

The Royal Commission on Medical Education and the University Grants Committee have been consulted about this development and approved of its beginning before the Royal Commission's report, which is expected by the early part of 1968.

Committee on L.S.D. and Cannabis

The members of the subcommittee of the advisory committee on drug dependence set up by the Home Office and the Ministry of Health to consider L.S.D. and cannabis are: LADY WOOTTON OF ABINGER (chairman), Mr. K. J. P. BARRACLOUGH (chairman, Poisons Board), Dr. T. H. BEWLEY, Mr. P. E. BRODIE (Assistant Commissioner, Metropolitan Police), Dr. P. H. CONNELL, Dr. J. D. P. GRAHAM, Dr. N. B. MALLESON, Mr. H. W. PALMER (general manager, Glaxo Group), Mr. TIMOTHY RAISON (editor, *New Society*), and Mr. MICHAEL SCHOFIELD (research worker in sociology, Nuffield Foundation).

New M.R.C. Research Unit

The Medical Research Council is to set up an immunochemistry research unit at Oxford University under the honorary direction of Professor R. R. PORTER, F.R.S., who will take up his appointment as Whitley Professor of Biochemistry in the University on 1 October. The new unit will expand the work of the Council's research group in immunochemistry at St. Mary's Hospital Medical School, London. Its work will be concerned with elucidation of the structure of antibodies and the relationship of their structure to their function.

Anglo-French Exchange Bursaries

Applications are invited for the bursaries which will be awarded in 1968 to young British doctors under the exchange scheme arranged by the French Embassy in London between the Institut National de la Santé et de la Recherche Médicale in Paris and the Ciba Foundation in London. The value of the French grants is 1,400 F. a month tax free, and they will be awarded for periods of two to four months to medical men who wish to obtain clinical experience or carry out research in France. Details from Dr. WOLSTENHOLME, Director, Ciba Foundation, 41 Portland Place, London W.1. The closing date for applications is 15 October.

N.H.S. Research Projects

A grant of £4,772 for two years for studies of hospital cross-infection has been made to Dr. P. N. EDMUNDS, Fife District Laboratory, Windygates, Fife, and Dr. R. RANKIN, Group Laboratory, Royal Infirmary, Stirling. This is one of six grants for medical research approved by Mr. WILLIAM ROSS, Secretary of State for Scotland, on the recommendation of the Advisory Committee on Medical Research in Scotland. Others to receive support for projects are: Professor W. D. McHUGH, Department of Dental Health, University of Dundee, continuation of epidemiological studies of the long-term effects of dental education, £1,800 for two years; Dr. J. A. MILNE, Department of Dermatology, Glasgow University, continuation of a study of pigmented skin lesions, £1,500 for two years; Dr. H. F. V. RIDDLE, Ardclinis, Dysart, Fife, one-year study of fungal respiratory disease, £800; Dr. L. DUNCAN, Diabetic and Dietetic Department, Royal Infirmary, Edinburgh, serum fucose response in diabetics, £1,100 for two years; and Dr. T. ANDERSON, Department of Biochemistry, Glasgow University, cancer research, £2,000 for one year.

Pregnancy Tests

In a letter to hospital authorities the Ministry of Health states that two reagents (Pregnosticon and Prepuerin) used in immunological tests for pregnancy are now available to hospital pathology departments on central supply. These tests are considered to be as reliable as the Hogben toad test. The Ministry recommends that pathology laboratories should accept requests for pregnancy tests on referral from general practitioners. (See leading article, p. 448.)

Inquiry on Elderly Patients

Allegations of ill-treatment of elderly patients made in the book *Sans Everything* will be investigated in private by independent committees, the Ministry of Health said in a statement last week (see *B.M.J.*, 22 July, p. 250). Queen's Counsel will act as chairmen, other members being a doctor, a nurse, and at least one lay man or woman. No member of a committee will have connexion with any hospital authority in the region in which the hospital concerned is situated. The statement contains an assurance that patients and staff will be able to give evidence "in complete confidence." Persons named will hear the allegations and have the opportunity of defending themselves. The Minister proposes to publish the findings and recommendations of the committees, also the names of the hospitals, when the investigations have been completed. (See review of *Sans Everything* at p. 484.)

"British Medical Index"

The medical department of the British Council announces that the *British Medical Index* succeeds the *Indice Medico*, which was prepared and issued by the British Council office in Italy for the past 20 years. The quarterly *Index*, as before, will be arranged alphabetically by periodical title, as abbreviated in *World Medical Periodicals*, the contents of the issues of a periodical included in a particular *Index* being arranged in a continuous sequence in page order. Some selection will be made. Brief congress reports and news items will be omitted, as will correspondence, except letters published in the *British Medical Journal* and the *Lancet* referring to new work or giving important supplementary information about articles already published in these journals.

Meeting in South Africa

The 46th South African Medical Congress, held at the University of Natal, Durban, from 17 to 22 July, was attended by a number of overseas visitors, including Mr. ROBERT V. COOKE, President of the British Medical Association and a vice-president of the congress. Speaking at the end of the meeting, Dr. N. R. POOLER, President of the Medical Association of South Africa, said that many delegates had described the congress as an outstanding one. He was sure, he said, that the South African medical profession had benefited greatly by the visit of their overseas colleagues.

Formation of Audiology Group

An audiology group, open to members of the Society of Medical Officers of Health, is to be set up, with Dr. MARY SHERIDAN as honorary president. It will form a subgroup of the school health services group of the Society. Inquiries should be sent to Dr. L. SOLOMON, Castle Road Clinic, 15 Castle Road, Torquay, Devon.

Report on War Pensioners

At the end of 1966 the Ministry of Social Security was paying 595,000 war pensions at a cost of about £117m. a year. The total was made up of 435,400 disablement pensions, 119,300 widows' pensions, and 40,800 pensions for parents, orphans, and other dependants. In England and Wales some 2,830 pensioners were being treated as in-patients in National Health Service hospitals. The report gives details of limbs and appliances supplied by the Ministry of Health. These included about 3,500 legs and arms, 600 artificial eyes, and more than 9,000 surgical boots. The number of invalid chairs and tricycles in use was 4,300. During the year 579 pensioners received a motor car for the first time. The report refers to the planning of new artificial limb and appliance centres that are to be built in hospital grounds to ensure close association with orthopaedic and rehabilitation services. (H.M.S.O., 8s. net.)

Social Education of Young People

In May this year the Ditchley Foundation arranged a conference, chaired by the DUKE OF EDINBURGH, on the training and use of young people for rescue, first aid, and other forms of service. Participants included members of the medical profession. A summary of the proceedings has now been published in the form of a preliminary report. Copies can be obtained from the Medical Commission on Accident Prevention, 50 Old Brompton Road, London S.W.7, price 5s. plus 6d. postage.

Dr. N. R. Pooler (left) and Mr. Robert Cooke at the civic welcome during the recent South African Medical Congress in Durban.

British Pharmacopoeia Commission

From 29 August the address of the offices and laboratory of the British Pharmacopoeia Commission will be 8 Bulstrode Street, London W.1 (telephone 01-935 7604).

People in the News

▶ Dr. ERASMUS BARLOW has been appointed chairman of the London branch of the Mental Health Research Fund.

News in Brief

A new division of virology has been established at Leeds University within the department of bacteriology under the headship of Dr. JAROSLAW CZEKALOWSKI, senior lecturer in the department.

The Medical Research Council's unit for experimental investigation of behaviour, in the department of psychology, University College, London, has been renamed Unit for Research on Neural Mechanisms of Behaviour. Professor G. C. DREW is honorary director of the unit and Dr. I. S. RUSSELL has been appointed deputy director.

From 1 November the sale of celluloid toys is prohibited under regulations made by the Home Secretary, also the sale of toys coated with paint that contains more than 1.1% of lead.

"Help the Disabled Week" will be held this year from 2 to 8 October. The purpose is not to raise money but to encourage acts of consideration.

The Association for Spina Bifida and Hydrocephalus has opened its first full-time office at Benjamin Franklin House, 36 Craven Street, London W.C.2.

Grants and Awards

Dr. D. J. WEATHERALL, of the Nuffield Unit of Medical Genetics, Liverpool University, has been awarded a grant of $1,000 a year for two years by the World Health Organization in aid of a study of haemoglobin synthesis in thalassaemia. It will be a joint study by the Nuffield Unit of Medical Genetics and the Haematology Research Group at the Siriraj Hospital, Bangkok.

A grant of £2,500 a year for a minimum period of five years has been made by the trustees of the Astor Foundation to the College of Pathologists to finance a research fellowship in experimental pathology. The fellowship is to be designated "The Astor Research Fellowship."

The National Fund for Research into Crippling Diseases has made grants totalling £20,000 to the University of East Africa, Makerere, Uganda, to support research to help the disabled.

Coming Events

Hackney Hospital, London.—Course for general practitioners, September to December. Details from Mr. M. F. PILCHER, F.R.C.S., Clinical Tutor.

Royal Medical Benevolent Fund.—Annual general meeting, 5 September, 5 p.m. Medical Society of London, 11 Chandos Street, London W.1.

Leukaemia Research Fund.—Annual guest lecture by Professor H. S. KAPLAN (Stanford University, California), "On the Natural History of the Murine Leukaemia," 19 September, 5.30 p.m., Institute of Child Health. Admission by ticket, obtainable from Secretary, Medical Advisory Panel, Leukaemia Research Fund, Institute of Child Health, Great Ormond Street, London W.C.1.

King Edward's Hospital Fund for London.—Conference, "Design of Hospital Bedsteads," 28 September. Details from Mr. IRFON ROBERTS, Hospital Centre, 24 Nutford Place, London W.1.

London Nursing Exhibition and Conference.—16–20 October, Seymour Hall, London. Details from Mr. DEREK PAGE, Dorset House, Stamford Street, London S.E.1.

Cambridge University Medical School.—Symposium, "Old Age and Anaesthesia," 28 October, Addenbrooke's Hospital. Fee £1 1s. Applications to Secretary, the Medical School, Tennis Court Road, Cambridge.

Societies and Lectures

For attending lectures marked ● a fee is charged or a ticket is required. Applications should be made first to the institution concerned.

Wednesday, 23 August

STOKE MANDEVILLE HOSPITAL.—(1) 12.15 p.m., Dr. A. O. Robson: Some Aspects of Bronchial Asthma. (2) 6 p.m., Dr. M. Ikram: Malabsorption Syndrome.

Friday, 25 August

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. H. Nicholson: clinical demonstration.

Appointments

MANCHESTER REGIONAL HOSPITAL BOARD.—J. C. J. L. Bath, M.B., M.R.C.P.Ed. (whole-time or maximum part-time consultant physician, Bolton and District group of hospitals); A. Ashworth, M.B., F.R.C.S. (consultant urologist, South Manchester group of hospitals—nine half-days weekly); E. A. Shaw, M.B., F.F.A. R.C.S., D.Obst. R.C.O.G. (whole-time consultant anaesthetist, Salford group of hospitals); F. R. Glover, M.B., D.P.H. (whole-time or maximum part-time consultant physician in geriatrics, Bury and Rossendale group of hospitals); Kathleen M. Watson, M.B., F.F.A. R.C.S. (whole-time consultant anaesthetist, Oldham and District group of hospitals); W. R. Grundy, M.B., D.M.R.D. (whole-time or maximum part-time consultant radiologist, South Cheshire group); W. G. Brown, M.B., M.C.Path. (whole-time or maximum part-time consultant pathologist, North Manchester group of hospitals).

NORTH-WEST METROPOLITAN REGIONAL HOSPITAL BOARD.—H. Westbury, M.B., M.R.C.P., F.F.R., D.M.R.D. (consultant radiologist, Harefield and Mount Vernon Hospitals); F. S. Busaidy, M.B., D.O. (assistant ophthalmologist (medical assistant grade) Royal Northern Hospital and School Eye Clinics); R. P. M. Urquhart, M.B., D.P.M. (consultant child psychiatrist, Uxbridge Child Guidance Clinic, Hayes Child Guidance Clinic, and Hillingdon Hospitals); J. L. McClure, M.B., M.R.C.P., D.P.M. (consultant psychiatrist, St. Bernard's Hospital and Ashford Hospital); L. Kreel, M.B., M.R.C.P., F.F.R., D.M.R.D. (consultant radiologist, District Hospital and Clinical Research Centre, Northwick Park).

UNITED BIRMINGHAM HOSPITALS.—P. W. Dykes, M.D., M.R.C.P., M.R.A.C.P. (consultant physician to the United Birmingham Hospitals); G. Hall Davies, M.B., F.F.A. R.C.S., and J. S. Mather, M.B., F.F.A. R.C.S. (joint appointments of consultant anaesthetists to the United Birmingham Hospitals and the Birmingham Regional Hospital Board).

Universities and Colleges

CAMBRIDGE

M.D.—A. M. Fisher, M. H. Davies, J. E. Stark, R. Schram.

M.CHIR.—*T. J. S. Patterson.

M.B., B.CHIR.—*G. A. H. Buttle.

M.B.—*K. G. E. Brown, *R. J. G. Irons, *T. A. Trevelyan, *J. R. Shelley, *C. W. G. Redman, *J. R. Sibert, *J. S. Yudkin, P. H. Gentle, *C. A. Ellison, R. Lendrum, *A. J. W. Hilson, N. J. Ireland, J. B. Endacott, C. S. Kolb, *Patricia M. Martin, *Margaret S. Povey, *(Mrs.) Gillian D. Yudkin, *Harriet M. Hargreaves.

*By proxy.

LONDON

Mr. Ian McColl, lecturer at Guy's Hospital Medical School, has been appointed to the readership in surgery tenable at St. Bartholomew's Hospital Medical College.

M.D.—S. E. H. Brooks.

MANCHESTER

Appointments.—Dr. Elizabeth B. Butler (senior lecturer in cytology (cellular pathology), Department of Pathology); Dr. N. P. Mallick (lecturer in medicine); Dr. L. Forrest and Dr. K. W. R. Tuson (assistant lecturers in physiology).

BIRMINGHAM

In Congregation on 7 July the following degrees were conferred:

M.D.—[1]K. Horsfield, W. I. H. Shedden, [9]N. Segel.

PH.D.—*In the Faculty of Medicine:* Susan Johnson, [9]B. N. Sharma.

M.B.—[1 2 4]J. R. Jackson, [3]C. P. Abson, [3]I. Appleyard, [3]D. G. Arkell, [3]J. E. Bent, [3]M. Berry, [3]W. P. Beynon, [3]E. M. Botheroyd, [3]B. J. Boughton, [3]P. J. Bradwell, [3]A. C. D. Brown, [3]Rosemary A. Brown, [3]Gwynneth I. Buchan, [3 5]Jennifer N. Bulman, [3]R. Burford, [3 6]D. J. Campbell, [3]D. F. Child, [3]N. M. Chitimba, [3]Mary R. Churchill, [3]P. R. Cleland, [3]A. G. Cohen, [3]M. R. Cooper, [3]Christine P. Cowell, [3]L. S. Culank, [3]M. J. R. Donovan, [3 4 6]Jennifer Faid, [3]M. J. Y. Fisher, [3]J. F. Forrest, [3]D. I. M. Forster, [3]T. A. French, [3]Carole A. Frost, [3]J. G. Geater, [3]R. H. George, [3]M. R. Glass, [3]T. P. Goh, [3]H. D. Graham, [3]R. C. Hall, [3]Diana G. Hawkes, [3]R. E. D. Henebury, [3]M. A. Hughes, [3]T. B. J. Hughes, [3]A. P. F. Jackson, [3]C. M. Jones, [3]D. W. Kett, [3]Gillian A. Kings, [3]Margaret E. Kirkwood, [3]Arabelle M. Larkinson, [3]G. T. Lealman, [3]S. I. Lewis, [3]I. W. McCall, [3]D. L. MacDonald, [3]Kathleen M. Mackrodt, [3]J. J. McMillan, [3]D. T. Milledge, [3]Rosemary Moore, [3]Ann O'Donovan, [3]Gillian R. Osborn, [3]M. J. Ostrowski, [3]Ruth Ostrowski, [3]E. P. Owens, [3]M. Pabari, [3 7]N. A. J. Pereira, [3]A. P. Riley, [3]Gabrielle Round, [3]S. R. Sales, [3]Pauline Sambrook, [3]M. Sharratt, [3]E. Simchen, [3]C. J. Smart, [3 4 8]K. G. Smedstad, [3]D. N. Smith, [3]R. C. Stockdale, [3]R. L. Symonds, [3]T. F. T. T. K. Cheong, [3]Gertrude I. Terry, [3 8]R. W. P. Terry, [3]C. G. D. Thompson, [3]Elizabeth A. Treadwell, [3]D. P. Veerasamy, [3]E. Walker, [3]P. B. Welsh, [3]P. Y. Yeoh, [3]Anne B. Zachary.

Appointments.—Dr. M. G. Fitzgerald (part-time lecturer in medicine for dental students); Drs. F. Humphries and A. S. Ward (temporary lecturers, Department of Anatomy); Dr. T. Hollingworth (temporary lecturer, Department of Pathology).

[1] With honours. [2] Degree of Ch.B. with honours conferred *in absentia* by special warrant on 20 June 1967. [3] Degree of Ch.B. conferred *in absentia* by special warrant on 20 June 1967. [4] Distinction in medicine. [5] Distinction in obstetrics and gynaecology. [6] Distinction in pharmacology and therapeutics. [7] Distinction in surgery. [8] Distinction in pathology and bacteriology. [9] *In absentia.*

LIVERPOOL

Appointment.—Janine M. Miller, M.B., M.R.C.O.G. (lecturer in obstetrics and gynaecology).

ROYAL COLLEGE OF PHYSICIANS OF LONDON

At a meeting of the College held on 27 July licences to practise were conferred upon the following candidates who had passed the final examination in medicine, surgery, and midwifery of the Conjoint Board and had complied with the By-laws of the College:

C. K. Adrian, F. Afshar, P. J. Aggett, H. M. Agrama, J. K. Anderson, J. T. H. Anderson, D. Arrowsmith, C. C. Bailey, Q. R. Bailey, E. J. Barrington-Ward, A. M. Bateman, G. A. Battersby, M. J. Bendall, P. D. Black, J. C. Bolton, E. M. Bradbury, M. J. Britton, G. W. Brown, G. D. Budhlall, B. J. Burke, J. R. K. Butchey, E. W. M. Carrette, Susan Caton, M. G. T. Chapman, Elizabeth A. Charlesworth, N. M. Chitimba, W. R. L. Clemmey, D. F. Cochrane, R. G. Cockbain, Gillian M. Cockersole, P. J. Cole, A. J. Collyer, E. H. Compton, Catherine J. Crofton, C. W. Davies, E. P. Davis, M. H. Dober, G. O. Dunn, P. T. Edington, Judith M. Egerton, C. A. Ellison, B. T. Evans, C. W. Evans, M. Faruhar, R. H. Felix, D. P. Forster, A. P. Freeland, M. O. Freeth, R. S. Gale, R. H. L. Galliver, W. H. Goss, A. J. Hamilton, R. P. D. Hancock, P. Harker, R. Hart, A. R. Hayward, J. A. Hensel, Gillian I. Hodgkinson, Elizabeth A. Horder, G. L. Horner, Jane R. Howard, R. A. Hurlow, N. Irish, R. J. G. Irons, J. A. Isserlin, J. R. Jackson, J. D. James, I. M. Jaye, Sally A. Jobling, B. R. Jones, T. E. Jordan, R. K. Kolhatkar, Maureen E. Lawrence, T. R. Lee, P. J. Leopard, T. C. Leung, C. E. Lewis, M. J. Leyland, A. B. Loach, M. J. Lockwood, R. N. Lucas, A. H. Lynn, D. E. Macfarlane, G. P. C. McLaren, J. N. MacLean, Jennifer M. McMillan, W. D. McNicoll, Hilary J. Marcham, B. E. Mason, R. F. J. Matthews, R. S. Maurice-Williams, T. K. Meikleham, H. B. Meire, Margaret M. Miles, Susan C. Mitchell, R. J. C. Morris, H. M. T. Murphy, Rhinedd M. Peregrine-Jones, D. J. Peters, Susan A. Pettit, H. S. Phillips, Elizabeth R. Phipps, J. G. Pickering, Rita B. Rahman, A. D. Revel, J. C. Richardson, T. Rigby-Jones, R. C. G. Rowe, R. D. Rubens, T. J. Rudman, D. J. Seager, J. A. Seaman, M. E. Setchell, Lynn Sherlaw, R. B. Simonis, A. G. Simpson, Diana L. Smith, J. R. M. Smith, P. D. Snashall, B. Steer, M. J. Stevens, B. A. Stoner, D. Stratton, W. St. C. Symmers, D. R. Tant, R. E. Taor, J. F. Towers, C. Tranmer, C. F. Tredgold, Angela M. Trueman, I. M. Vickery, R. Warner, R. T. Watson, Caroline R. Weinberg, W. H. Weston-Davies, C. J. H. Williams, J. L. Williams, R. H. Williams, Janis A. Winter, Jean M. Worms, J. W. Wright, R. A. L. Young, Katherine H. Aplin

ROYAL COLLEGE OF PHYSICIANS OF EDINBURGH

At a quarterly meeting of the College held on 25 July, with the president, Dr. C. W. Clayson, in the chair, the following were elected Fellows of the College:

R. B. Mehta, J. G. Parekh, D. W. Burton, J. A. Morton, R. B. Baird, A. D. Muir, Sheila S. Paul (née Martin), Leila Ramakumar (née Nair), P. C. MacGillivray, S. G. F. Wilson, J. Hampson, B. Ll. C. Phillips, G. F. M. Russell, M. B. Azami, R. D. Montgomery, E. H. Mirando, R. Sougin-Mibashan, G. Arjundas, G. D. Forwell, Kee Jin Lim, Cheng Siang Seah, C. G. B. Downie, A. E. Hugh, A. D. Macdonald, R. G. Paley, L. G. Topham, R. D. Catterall, K. K. Gupta, Evelyn Hanam, Hau Cheong Kwaan, D. A. Seaton, I. W. Delamore, J. Syme, M. A. Z. M. Din, A. R. May, B. S. L. Kidd, M. A. A. Khan, S. O'Reilly, H. C. Jeffrey, F. S. Fiddes, F. M. Parsons, W. M. McCrae, W. L. MacD. Perry, T. N. Fraser, F. J. Gillingham.

The following were elected Members of the College:

A. S. Duncan, J. H. Tyrer, A. E. H. Emery, P. M. Ward, E. H. Wyatt, A. Razzaq, A. P. Brahman, A. Hamid, N. P. Misra, W. I. Lamont, H. G. Egdell, A. V. Barford, P. K. D. Gupta, P. F. Binnion, C. M. Tiwary, Joyce E. Richardson, L. M. Marinovich, P. J. C. Ashurst, A. R. Al Yusuf, W. E. Kirkpatrick, D. A. Rajapakse, M. M. Singh, A. Khaliq, V. P. Sachar, D. P. B. Goldberg, A. B. Kaplan, Isla M. Williams, N. N. Desai, M. A. Siddiqui, Urmila Bassi, S. K. Mondol, J. L. Waddell, A. T. Sinniah, A. D. Ginsburg, D. H. Kenward, M. M. Jaffe, N. B. S. Sarkari, B. Sharma, Sheila L. Waller, M. Black, A. R. M. Musa, G. K. Ahuja, M. Amare, A. I. Muir, N. Gitlin, B. Himpoo, S. M. Shrestha, E. J. W. Stephens, S. K. Kajubi, M. L. Oduori, B. Mason, A. G. Mowat, H. C. Mulholland, Jean S. Thomson, Mo-Wah Chan, Moinuddin, Lai Chan See, Rosemary H. Marshall, C. C. Smith, G. O. Cowan, R. H. Macdonald, J. E. Ogwo, A. H. de C. Freed, Yat Tung Wong, A. G. Knight, R. B. L. Ewart, N. D. C. Finlayson, M. R. Higgins, I. M. Murray-Lyon, T. J. Peters.

A Hill Pattison-Struthers bursary has been awarded to Dr. Ijaz Haider.

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

At a meeting of the College held on 7 July the following were admitted *in absentia* to the Fellowship:

S. Lourdenadin, E. D. U. Powell.

G. H. Cussen was admitted to the Licence and Membership of the College.

Deaths

Stanford.—On 14 July 1967, at King Edward VII Hospital, Midhurst, Sussex, Russell Aubrey John Stanford, M.B., B.Ch., B.A.O., of Scunthorpe, Lincs, aged 58.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON W.C.1. TELEPHONE: 01-387 4499. TELEGRAMS: *Aitiology, London W.C.1.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs.

ADVERTISEMENT AND SUBSCRIPTION ORDERS should be addressed to The Manager at B.M.A. House, London, or at 415 Bourke Street, Melbourne, Victoria, Australia.

MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the British Medical Association, B.M.A. House, London, or to the Scottish Secretary, B.M.A. Scottish Office, Drumsheugh Gardens, Edinburgh.

BRITISH MEDICAL JOURNAL

LONDON SATURDAY 26 AUGUST 1967

Pointers

Acute Tubular Necrosis: Follow-up studies by Dr. J. D. Briggs and colleagues revealed that 75% of patients had reduced glomerular filtration rate, but were clinically well up to three years after acute renal failure (p. 513).

Bradford Maternity Experiment: The discharge of mothers from hospital 72 hours after delivery resulted in no greater mortality or morbidity of their babies compared with those born at home, according to Drs. M. W. Arthurton and F. N. Bamford (p. 517). Mr. G. A. Craig and Dr. J. M. B. Muirhead consider the early discharge scheme has not increased maternal morbidity but enabled the maximum number of patients to have the benefit of hospital care (p. 520). Leader at p. 508.

Prognosis in Breast Cancer: Mr. B. S. Thomas and his colleagues confirm the usefulness of a simple ratio of total urinary 11-deoxy-17-oxosteroids to the 17-OHCS in predicting response to endocrine ablation (p. 523).

Mental Function in the Aged: Dr. J. A. C. Ball and Mr. A. R. Taylor found that cyclandelate appeared to improve mental function, probably owing to redistribution rather than increase of blood flow (p. 525).

Tic Douloureux: Review of 10 patients with glossopharyngeal and vagal neuralgia satisfactorily treated by intracranial nerve root section by Mr. Jagdish C. Chawla and Mr. Murray A. Falconer (p. 529).

Foetal Haemoglobin Variant: Dr. L. S. Sacker and colleagues found this in two unrelated families in Hull (p. 531)

Complication of Thyroid Cancer: Nine cases of paraplegia due to spinal metastases described by Dr. K. E. Halnan and Mr. P. H. Roberts (p. 534).

Case Reports: Babies with hypernatraemic dehydration from improper feeding (p. 536). Anaemia in scleroderma (p. 537).

Should the Patient Fly?: Dr. K. G. Bergin outlines contraindications, restrictions, precautions, and facilities available (p. 539).

Hypertension, Anuria, and Uraemia: Clinicopathological Conference at Royal Postgraduate Medical School (p. 544).

Speech in Respiratory Failure: Dr. R. M. L. Whitlock describes attachment to cuffed tracheostomy tube (p. 547).

Medicine in Burma: Professor A. W. Woodruff describes remarkable progress in the absence of extensive foreign aid (p. 551).

Banned Doctor: Letter about Dr. Raymond Hoffenberg (p. 556). Leader at p. 512.

Public Health Service Dispute: "Useful discussion" (*Supplement*, p. 124).

Rise in Industrial Accidents

The latest pair of annual reports from the Chief Inspector of Factories[1,2] show once again that serious accidents are far too common and that much more needs to be done to protect the health and safety of people at work. The number of reported accidents in Great Britain (entailing at least three days' absence from work) again rose in 1966 over the previous year's total. The actual number of 296,610 cannot provide any certain measure of whether the accident rate as such went up or down, partly because the numbers of people exposed to risk are not precisely known, and partly because the extent to which reportable accidents are in fact being reported may be improving. But what is specially worrying is the considerable rise in the number of fatal accidents—from 627 in 1965 to 701 in 1966. An increase of 12% in one year needs serious attention, especially since the general trend since 1948 had for some years been downwards.

Part of the present trouble is due to a continual increase in the exposure of men and women to the risk of accidental injury. New industrial processes are being introduced every year. With them come machines with unsuspected dangers as well as substances with scarcely known toxic hazards. The new technology of which all this forms a part is undoubtedly something with which man must come to terms. But it seems to be too often forgotten that the inventive talents engaged on increasing production should also be used to increase the safety of the new processes. The Factory Acts and the inspectorate can provide no more than the framework within which safe practices must ever be taught, encouraged, and insisted upon at every industrial site. The Chief Inspector emphasizes, as he has before, that top management in a firm must "plan for safety just as they plan for production." And to the planning must be added an impetus from the top to see that the procedures are safely carried out: "The first prerequisite of accident prevention is a safety consciousness on the part of all people working in the factory—from the Managing Director down to the lowest operative." These principles are apt to be neglected more in the small firms than the large. Almost invariably, it is reported, no particular person is made responsible for safety in such careless firms until a serious accident occurs.

That young people in industry are bound to present a special problem should need no emphasis, yet the Chief Inspector has to draw attention once again to the high accident rate among them. Partially trained, inexperienced, and with the natural impetuosity or even recklessness of their years, young people need more supervision than they are receiving among the hazards of working machinery. To deny it to them shows, in the words of the report, "a wanton disregard of moral responsibility," and it lays blame for most of the accidents to the young on the managers, supervisors, or foremen. These experienced people in authority too often fail to give sound guidance or set a good example. Probably the majority of the young people starting life on the factory floor are below the national average in intelligence owing to the opportunities for the cleverer ones to

© *British Medical Journal*, 1967. All reproduction rights reserved.

find work elsewhere, so that a particular obligation to care for their safety must be acknowledged. Nor is the transition from school to industry a smooth passage for some people,[3] coming for many at a time of rapid physiological and psychological development.

When he comes to report on industrial health[2] the Chief Inspector has a story with a happier ending—"With the exception of the lung dust diseases, the grosser forms of industrial poisoning have been virtually eliminated." Cheap to make, expensive to suppress, a multitude of dusts pervade the industrial environment, and a special section of the report by Mr. B. H. Harvey and Dr. W. D. Buchanan is devoted to them. Though initially they present a problem for each individual industry to solve, their effects closely concern the medical men who care for the workers in it, and for them some of the details in the present report will be of interest.

Despite improvement over the years in the industrial environment these reports show clearly that much remains to be done. Moreover, the quality of safety provisions varies enormously throughout the country—from the excellent to the deplorable. No comprehensive industrial health service has yet been set up, though often advocated by the British Medical Association.[4-8] From the latest reports it is evident that the need is still there. Indeed, the practice of many large firms with their own medical staff has abundantly demonstrated the benefits of thorough medical supervision in industry. There should be some way of bringing these benefits to the smaller firms, which, between them, employ the majority of workpeople.

---

[1] *Annual Report of H.M. Chief Inspector of Factories 1966*, Cmnd. 3358, 1967. H.M.S.O., London.

[2] *Annual Report of H.M. Chief Inspector of Factories on Industrial Health 1966*, Cmnd. 3359, 1967. H.M.S.O., London.

[3] Herford, M. E. M., *Brit. Hosp. soc. Serv. J.*, 21-28 August 1964.

[4] *Report of Commitee on Industrial Health in Factories*, 1941. British Medical Association.

[5] *Report on a Comprehensive Occupational Health Service*, 1949. British Medical Association.

[6] *Memorandum to Ministry of Labour and National Service on Future of Occupational Health Services*, 1953. British Medical Association.

[7] *Functions of an Occupational Hygiene Service*, 1959. British Medical Association.

[8] *The Future of Occupational Health Services*, 1961. British Medical Association.

Early Discharge of Maternity Patients

It is now some three years since the advantages and disadvantages of the early discharge of maternity patients were discussed in these columns,[1] and in view of the increasing support for the idea since then the two further reports in the *B.M.J.* this week are timely. Both of them are from Bradford—one by obstetricians and the other by paediatricians—and they present an impressive number of cases, for the regimen has now been in use there since 1956 and some 13,000 puerperal patients have been managed in this way. Mr. G. A. Craig and Mr. J. M. B. Muirhead report (page 520) that in their experience planned early discharge does not result in increased maternal morbidity nor does it add to the risks of birth. Discussing the effects on the babies, Drs. M. W. Arthurton and F. N. Bamford report (page 517) that the regimen has had no serious adverse effect and may have contributed to an improvement in child health. But they go on to say: "There is no evidence that early discharge offers any advantage for the individual baby as compared with staying in hospital for ten days, and in fact there are additional risks partly attributable to difficulties in neonatal diagnosis." That the general practitioners welcome and actively support the Bradford scheme can be seen by the report of a survey of 100 cases of early discharge carried out by members of the Bradford Group of the College of General Practitioners.[2]

The latest results are of great interest. Statistically there appears to be no difference between the number of patients readmitted after planned early discharge and those admitted as an emergency after domiciliary confinement. Likewise, the perinatal mortality is the same in the two groups.

The length of time a patient remains in hospital after delivery depends on many factors. While the present shortage of maternity beds undoubtedly plays a large part, to this must be added the rules of the Central Midwives Board—a subject on which Professor P. Rhodes has recently written forcefully.[3] Another factor affecting the situation is the view of the patient herself, and it is the experience of many practising obstetricians that puerperal mothers are asking to be allowed home at an increasingly early date after delivery. The doubts about the dangers to mother and baby from early discharge are largely dispelled by the Bradford reports. However, there is a considerable difference between a scheme of this nature working at a high level of efficiency, as at Bradford, and occasional early discharge of a patient without the complete arrangements that the existence of such a scheme implies.

The patients ideally suited for early discharge are those multiparae whose past history necessitates hospital delivery for fear of a possible recurrence of their previous complication. To this main group might be added those normal multiparae who are apprehensive about home confinements. The selection of these cases can be largely done in the antenatal period. And, though the final decision is not made in the Bradford scheme until after delivery, it would seem advisable that, whenever possible, the mother should be informed of this probability early in pregnancy so that she can make the necessary arrangements for additional help at home in good time.

The success and safety of early discharge depend on close liaison between hospital, district midwife, and general practitioner. It is essential for the hospital to notify both of them by telephone on the same day as the patient is discharged, giving such information as may be needed. The district midwife is an essential part of the scheme; indeed, without her active support it will not succeed. In future it may be found helpful for arrangements to be made to allow either the domiciliary midwife to come into hospital to deliver her patients or the hospital midwife to undertake the home visiting of them after discharge.

---

[1] *Brit. med. J.*, 1964, 2, 70.

[2] Bradford Group of the College of General Practitioners. *Lancet*, 1966, 1, 536.

[3] Rhodes, P., ibid., 1967, 1, 623.

[4] *Recommendations on the Principles and Organization of General Practitioner Maternity Units and their Relation to Specialist Maternity Units.* Royal College of Obstetricians and Gynaecologists. January, 1962.

[5] Pinker, G. D., and Fraser, A. C., *Brit. med. J.*, 1964, 2, 99.

[6] *The Planning of Early Discharge Schemes for Maternity Patients.* H.M.S.O. (65), 32.

From the Bradford reports it can be seen that the final decision to permit a mother and baby home after 48 hours must be made by someone at least of registrar status. It would also be of considerable value if the general practitioner and district midwife in charge of such a case could freely obtain an opinion by domiciliary consultation from either the hospital obstetric or paediatric department on any puerperal or neonatal complication before readmission of the woman after she has returned home.

When early discharge was discussed in these columns three years ago[1] the conclusion was drawn that, though it might be suitable in emergency conditions, it had little part in long-term planning. That reflected an opinion then prevalent and previously advanced by the Royal College of Obstetricians and Gynaecologists.[4] But it may well need revision. G. D. Pinker and A. C. Fraser[5] reported after a trial over three years at St. Mary's Hospital that the scheme was " safe and desirable " for both mother and baby and recommended that the voluntary early discharge of selected patients should be an accepted part of the maternity services. Advice on the planning of arrangements has been given by the Ministry of Health.[6] Now the two reports from Bradford indicate that it would be reasonable to explore the whole question further.

Activation Analysis

Radioactive isotopes have contributed to many advances in clinical science, especially during the last 20 years, when ample supplies have been available as by-products of the atomic energy programme. The complementary technique of activation analysis offers some distinctive advantages which deserve closer study.

The basis of this technique is that most elements are partially converted to radioactive isotopes on exposure to neutrons—for example, inside a nuclear reactor. The induced radioactivity is highly specific for the elements contributing to it. It is therefore possible to identify and estimate many of the elements present in a sample by studying the radioactivity induced by a short spell inside a nuclear reactor. This apparently roundabout procedure is, for many elements, the most sensitive method of analysis now available. Recently the use of this technique in the identification of human hair was discussed in these columns.[1]

The uses of activation analysis in clinical science are more often commended than practised, but useful progress was reviewed and discussed at the symposium on Nuclear Activation Techniques in the Life Sciences held in Amsterdam from 8 to 12 May under the auspices of the International Atomic Energy Agency. Several research projects are at present concerned with the elemental analysis of various body constituents in the hope of correlating pathological signs with abnormalities in the metabolism of minor elements not normally within the purview of the biochemist.

A typical inquiry entailed the estimation of seven trace elements in blood from normal persons and from patients with chronic uraemia. Levels of arsenic in the blood were on average three times higher in the uraemic patients. A suggestion that the apparent retention of arsenic may contribute to toxic manifestations of uraemia can hardly be supported, partly because the quantities are so small (about 5 μg. of arsenic per litre of blood) and also because no correlation has been found between arsenic level in the blood and degree of renal insufficiency as indicated by blood creatinine measurements. But speculative inquiries of this kind are worth while because they may sometimes provide the first clue to the solution of an intractable problem. Information of a more immediately useful kind can be expected from using activation analysis in problems where the underlying biochemical and physiological considerations are better understood.

Thyroid metabolism, much studied by radioactive isotopes, offers interesting problems for attack by activation analysis. Semi-automatic methods for the routine determination of protein-bound stable iodine have been elaborated, notably in France,[2] where the establishment of a laboratory to carry out such tests on a commercial basis is now being considered. The basis of the estimation is the partial conversion, under bombardment by thermal neutrons, of stable iodine-127 to the radioactive isotope iodine-128, which has a half-life of 25 minutes. Chemical manipulation is necessary to remove radioactive isotopes of sodium and other elements formed in abundance along with the iodine-128.

New prospects have resulted from the development (also in France) of techniques using iodine-129. This isotope has a very long half-life (1.6×10^7 years) and a number of other properties particularly useful for clinical applications. The gamma-radiation which it emits is of very low energy and gives a correspondingly small radiation dose to the patient, but can be detected in the thyroid gland by an external scintillation counter. It would be possible, by daily administration of small doses of iodine-129 to a patient, to attain isotopic equilibrium. When this state has been reached, the ratio of the concentration of iodine-129 to iodine-127 is the same throughout the body. Isotopic equilibrium cannot be reached with iodine-125 or iodine-131 because of the heavy dose of radiation which the patient would incur. With iodine-129 the total dose over a period of a year in isotopic equilibrium would be very much less than that incurred in a single tracer test with iodine-131, but the amount of information to be obtained by radioactive assay of blood, urine, and the thyroid itself would be substantially greater. The usefulness of this isotope is further enhanced by the fact that, on exposure to irradiation by thermal neutrons, it is partly converted to another radioactive isotope, iodine-130 (and its isomeric form, iodine-130m) allowing detection at excellent sensitivity by activation analysis.

The technique of activation analysis in vivo, first reported on by J. Anderson and others[3] in 1964, offers the possibility of direct measurement of the total stable iodine content of the thyroid. In principle, the stable iodine-127 in the thyroid can be activated by neutron bombardment to yield radioactive iodine-128, which can be measured by external counting. In practice this simple technique cannot give accurate results, mainly because of the impossibility of achieving uniform irradiation of the thyroid gland by neutrons. A technique entailing prior administration of iodine-129, followed by neutron irradiation of the thyroid and simultaneous estimation (by external scintillation counting) of iodine-128, 130, and 130m, provides an accurate estimate of thyroid iodine in the sheep and may soon be applicable to man.[4]

---

[1] *Brit. med. J.*, 1967, **1**, 584.

[2] Comar, D., and Le Poec, C., *Proceedings of the International Conference on Modern Trends in Activation Analysis*, p. 351. 1966. Texas Agricultural and Mechanical University, College Station, Texas.

[3] Anderson, J., *et al.*, *Lancet*, 1964, **2**, 1201.

[4] Lenihan, J. M. A., Comar, D., Riviere, R., and Kellershohn, C., *Nature (Lond.)*, 1967, **214**, 1221.

The remarkable sensitivity of activation analysis has been exploited in studies of the electrolyte equilibrium of the fluids of the inner ear. The dynamic equilibrium between perilymph (which is a fluid of the extracellular type, with sodium predominating over potassium) and endolymph (in which potassium ions greatly outnumber sodium ions) is linked with the functions of hearing and balance. Reliable estimates of the concentrations of sodium and potassium have been obtained by activation analysis of small samples of fluid (2–10 μl.) obtained from experimental animals, and there are grounds for hoping that this technique also may be extended before long to man.

Architectural Aids for Disabled

One of the shocks a patient commonly experiences on becoming severely disabled is to find how many activities that he formerly took for granted are now beyond his reach. Many disabled people adjust to restrictions on movement and activities by developing new skills, by using ingenuity to surmount obstacles, and so by sheer determination contrive to manage for themselves in an unsympathetic environment. Part of their adjustment lies in appreciating the things they cannot do. Rather than be frustrated in the attempt, they learn to leave them alone. Some retire into their disability and do less and less. Thus instead of trying to get up the imposing flight of steps that leads to the public library or cinema, up which normal folk skip so blithely, they prefer not to use the library or cinema at all.

In recent years architects have given more thought than formerly to the special physical characteristics of the people who will use the buildings they are designing. Schools were the first to be thought of in this way[1] and then to some extent hospitals. The Ministry of Housing published a design bulletin[2] in 1962 drawing attention to features and dimensions desirable to incorporate in flatlets built for old people so as to meet their physical limitations, the recommendations being based on investigations carried out by Ministry sociologists[3] and an anthropometric study.[4] But the special requirements of the disabled received little attention until the Royal Institute of British Architects' publication of 1963.[5] Now the British Standards Institution commendably publishes a new code of practice, C.P. 96: Part I. Access for the Disabled to Buildings. It details the architectural provisions which should be incorporated in new buildings to make them convenient for disabled and infirm people to use. It is the product of a committee in which many groups with special knowledge of the needs and capabilities of the disabled, such as the British Council for Rehabilitation of the Disabled, the Central Council for the Disabled, the Spastics Society, and the British Medical Association, shared that knowledge with representatives of the interested professional bodies, including the Royal Institute of British Architects, the Royal Institution of Chartered Surveyors, and various Government departments.

The new code covers ambulant-disabled people and the wheelchair-bound especially, but also incorporates a short section on the special requirements of the blind and the deaf. It is based both on empirical observation and on specific pieces of research—for example, into suitability of different designs of door handles,[6] into the manœuvring space of wheelchairs, and into the layout of sanitary and cloakroom accommodation. Many of these studies were sponsored by the bodies represented on the committee. The recommendations are such as can be carried out, for they are realistic rather than idealistic and economic considerations have been taken fully into account, as indeed they must be when any public building is planned. The new code of practice follows the lead of the American[7] and Canadian[8] standards, though it departs from the former in one significant feature in stressing the need for the signposting of special facilities for disabled people.

Nobody knows how many disabled there are in Britain. The American[7] and Canadian[8] recommendations take the figure of one in seven of the population as having a permanent physical disability or an infirmity associated with age. A survey carried out in Denmark[9] in 1961–2, based on one person in 140 of the total population, identified 6.5% of persons aged 15 to 61 as physically handicapped. Many of these are not so disabled as to need special facilities, but information from various sources, such as the number of wheelchairs issued by the Ministry of Health, suggests that even if a similar proportion is not applicable to the British population the total here runs into hundreds of thousands. The new code of practice, wherever implemented, will mean that these hundreds of thousands will have freer access to shops and stores and churches and libraries and cinemas and hotels than they have hitherto had and so will be able to take part more easily and more fully in everyday activities.

---

[1] Ministry of Education, Building Bulletins 1 to 9, 1951–65. London.
[2] Ministry of Housing and Local Government, *Some Aspects of Designing for Old People*, 1962. London.
[3] Ministry of Housing and Local Government, *Grouped Flatlets for Old People—A Sociological Study*, 1962. London.
[4] Roberts, D. F., *Ergonomics*, 1960, **3**, 321.
[5] Goldsmith, S., *Designing for the Disabled*, 1963, Technical Information Service, Royal Institute of British Architects, London.
[6] Nichols, P. J. R., *Ann. phys. Med.*, 1966, **8**, 180.
[7] American Standards Specifications for making buildings and facilities accessible to, and useable by, the physically handicapped, 1961. American Standards Association, New York.
[8] Building Standards for the Handicapped, 1965, Building Code, National Research Council, Ottawa.
[9] Social Research Institute, Copenhagen, "Fysisk Handicappede i Danmark," in press.

Allergic Gastroenteropathy

The combination of oedema of obscure origin, hypoalbuminaemia, and gastrointestinal disturbance suggests the possibility of exudative enteropathy or protein-losing gastroenteropathy. This syndrome may be associated with giant hypertrophy of the gastric rugae,[1] regional ileitis and ulcerative colitis,[2] sprue,[3] intestinal lipodystrophy,[4] gastric carcinoma,[5] intestinal lymphangiectasia,[6] constrictive pericarditis and congenital atrial septal defect,[7] neonatal steatorrhea with small-bowel dysfunction,[8] and hypogammaglobulinaemia.[9] To this growing list of causes of protein-losing gastroenteropathy may now be added a group of six young children with oedema, extreme hypoproteinaemia, anaemia, eosinophilia, and retardation of growth.[10] This new syndrome has been delineated on the basis of clinical features, gastrointestinal radiography, intestinal biopsies, and favourable response to corticosteroid therapy. The last distinguishes it in this age group particularly from intestinal lymphangiectasia, coeliac disease, and hypogammaglobulinaemia. T. A. Waldman and colleagues[10] propose the term allergic gastroenteropathy to delineate their series of cases because milk aggravated the protein-losing gastroenteropathy. Precipitating antibodies to milk were detected in the serum of three patients. The patients improved on a milk-free diet and relapsed when milk was reintroduced. The favourable response to the administration of corticosteroids, together with clinical signs of asthma, eczema, and rhinitis, all contributed to the concept of an allergic gastroenteropathy.

---

[1] Citrin, Y., Sterling, K., and Halsted, J. A., *New Engl. J. Med.*, 1957, **257**, 906.
[2] Steinfeld, J. L., Davidson, J. D., Gordon, R. S., jun., and Greene, F. E., *Amer. J. Med.*, 1960, **29**, 405.
[3] Parkins, R. A., *Lancet*, 1960, **2**, 1366.
[4] Laster, L., Waldmann, T. A., Fenster, L. F., and Singleton, J. W., *Gastroenterology*, 1962, **42**, 762.
[5] Jarnum, S., and Schwartz, M., ibid., 1960, **38**, 769.
[6] Waldmann, T. A., Steinfeld, J. L., Dutcher, T. F., Davidson, J. D., and Gordon, R. S., ibid., 1961, **41** 197.
[7] Davidson, J. D., Waldmann, T. A., Goodman, D. S., and Gordon, R. S., *Lancet*, 1961, **1**, 899.
[8] Cottom, D. G., London, D. R., and Wilson, B. D. R., *Lancet*, 1961, **2**, 1009.
[9] Waldmann, T. A., and Laster, L., *J. clin. Invest.*, 1964, **43**, 1025.
[10] —— Wochner, R. D., Laster, L., and Gordon, R. S., *New Engl. J. Med.*, 1967, **276**, 761.

This series of six children comprised four boys and two girls. The age at onset of oedema was under 3 years in all but one child. Oedema was most marked in the periorbital area. Gastrointestinal symptoms included diarrhoea and vomiting after milk; but lactose tolerance tests were normal. Gastrointestinal *x*-ray examinations showed mucosal oedema of the small bowel in four and puddling and segmentation of barium in one patient. The authors are confident that this distinctive syndrome is not attributable to any of the previously recognized conditions that give rise to excessive loss of protein into the gastrointestinal tract, and that a trial of treatment with a milk-free diet or with corticosteroids is worth while.

Hitherto the clinical patterns of disease associated with loss of protein have been classified according to whether the lesion is outside or inside the gastrointestinal tract: in the heart, liver, or pancreas, or in the stomach, small intestine, or the colon. We must now also keep in mind gastrointestinal allergens, whether food or drug, which may contribute in turn to this gastrointestinal upset, metabolic disorder, and systemic disease, for early recognition is the first step away from the label "idiopathic oedema" and towards a rational basis of treatment.

Correction of protein-losing gastroenteropathy has followed surgical treatment of constrictive pericarditis and other cardiac abnormalities.[7] Gastrectomy for giant hypertrophy of the gastric rugáe has effected a cure, and so has putting gluten-allergic patients on a gluten-free diet. Corticosteroid therapy has proved beneficial in ulcerative colitis, and now also for milk-allergy protein-losing gastroenteropathy.

Oxygen Therapy Equipment

Oxygen is usually given in low dosage (25% to 40%) for treatment of hypoxaemia due to uneven lung function. In particular it may be given for under-ventilation or over-perfusion of groups of alveoli. The patient is usually suffering from lung disease[1] or has a disturbance of the pulmonary circulation, as in some cases of myocardial infarction.[2] Oxygen is given in high dosage (70% to 100%) both to produce a high tension in the blood, as for treatment of carbon monoxide poisoning, and to increase the quantity of oxygen carried in solution in blood plasma. The latter procedure may contribute to the relief of tissue hypoxia due to ischaemia and of hypoxaemia due to blood by-passing ventilated regions of lung. Both these conditions arise in patients with severe myocardial infarction.[3]

A high dosage of oxygen in a patient whose breathing is not depressed may be secured with a half face mask which makes a good fit on to the face and is supplied with a generous flow of oxygen (6–10 l./min.). The effectiveness of the oxygen is enhanced by using a mask with a reservoir bag for conserving the gas which would otherwise flow to waste during expiration—for example, the Portogen mask. Use of a mask which falls from the face on interruption of the oxygen supply—for example, the Pneumask—has some advantage, but is not essential, because with adequate respiration the interruption is unlikely to give rise to asphyxia. If breathing may become depressed a more positive means of administration is desirable.

Oxygen in low dosage is easily provided and does not require a perfectly fitting mask. As only a low flow is required there is no need for conservation of oxygen during expiration except when portable equipment is used. The risk of asphyxia is small for patients who are hyperventilating—for example, those with a defect of gas transfer in the lungs or in a state of shock. But this type of therapy is usually needed for patients whose ventilation is low, perhaps owing to an acute chest illness superimposed on chronic lung disease or to depression of the respiratory centre. Here the oxygen should relieve the hypoxaemia sufficiently to prevent tissue damage, but preferably without eliminating the hypoxic drive to respiration. An arterial oxygen saturation of 90% is suitable for this purpose. The gas should be administered in controlled dosage and, when appropriate, with monitoring of the blood carbon-dioxide tension and *p*H. This is to prevent hypoventilation leading to carbon dioxide narcosis owing to reduction of the stimulus to breathing. For these patients the device should have minimal dead-space to avoid aggravation of the carbon dioxide retention. The dead-spaces of equipment in current use have recently been investigated.[4]

Plastic nasal catheters meet the requirement, are comfortable, and can be used during meals, but the oxygen then requires humidification, and for a few patients mouth breathing may lower the effective dose. The Ventimask is also satisfactory and has the advantage that the concentration of oxygen is nearly constant.[5] However, up to three face pieces may be needed per patient if a range of concentrations is required (24%–35%). Of the others which do not conserve oxygen during expiration, the M.C. mask was found to have a significant dead-space[6] and so to be inferior to the Edinburgh mask, in which there is free communication with the outside air.[7] The latter mask is probably the best single one for general use.

Masks which have a large dead-space include the Polymask, Pneumask, and those of the B.L.B. type. Because of the hazard of rebreathing these should never be used for patients who are liable to carbon dioxide narcosis. In addition, while the masks can provide high enrichment of oxygen for patients needing 100% oxygen, they are inferior in this respect to masks like the Portogen, mentioned above, in which rebreathing is prevented by use of valves.[8]

Modern oxygen therapy requires separate devices for administering oxygen in high and low doses. The physician is now in a position to select the most suitable one for each purpose from the equipment commercially available.

---

[1] Campbell, E. J. M., *Lancet*, 1960, 2, 10.

[2] Valentine, P. A., Fluck, D. C., Mounsey, J. P. D., Reid, D., Shillingford, J. P., and Steiner, R. E., ibid., 1966, 2, 837.

[3] MacKenzie, G. J., Taylor, S. H., Flenley, D. C., McDonald, A. H., Staunton, H. P., and Donald, K. W., ibid., 1964, 2, 825.

[4] Bethune, D. W., and Collis, J. M., *Thorax*, 1967, 22, 221.

[5] Campbell, E. J. M., and Gebbie, T., *Lancet*, 1966, 1, 468.

[6] Catterall, M., Kazantzis, G., and Hodges, M., ibid., 1967, 1, 415.

[7] Flenley, D. C., Hutchison, D. C. S., and Donald, K. W., *Brit. med. J.*, 1963, 2, 1081.

[8] Cotes, J. E., and Merrick, A. J., ibid., 1956, 1, 269.

Children in Care

Until about 1960 the annual numbers of illegitimate births and of marriages ending in divorce in England and Wales had not shown a distinct trend up or down since the peak years immediately after the second world war. Then in 1961 the rates for both rose sharply, and they have continued to do so. In 1965[1] the number of illegitimate babies born was 66,249, or 77 per 1,000 total live births, and the number of divorces was 37,785, or 3.1 per 1,000 married population. Since in many cases the welfare of young children is affected, it is no surprise to learn from the latest report of the Children's Department of the Home Office[2] that between 1959 and 1966 the total number of children in the care of local authorities and voluntary organizations in England and Wales rose from 78,648 to 79,995 But some comfort may be taken from the fact that the increase was not greater, for it actually represents a fall from 6.5 to 6 1 per 1,000 of the population aged under 18.

Illness of a parent and confinement of the mother together provide the main immediate cause of children coming into the care of local authorities; the second largest cause of being taken into care is desertion by the mother. The increase in the latter type of cases from 1963 to 1966 was 31%. More remarkable perhaps is the increase of 81% (from 1,319 to 2,283) in the same period of children taken into the care of local authorities owing to unsatisfactory home conditions. The continual improvement in housing for some years might have suggested that a diminution in this category would have been more probable than such a substantial increase.

Since it is now generally acknowledged that a child is better brought up in a family than in an institutional home, however kindly and carefully run, it is worth noting that children's departments are placing many more children with foster parents than formerly and that the numbers of legal adoptions continue to rise each year. Between 1959 and 1965 the number of children adopted annually rose by 50% from 14,000 to 21,000. Of the latter total 80% were illegitimate. In view of the important contribution that adoption is now making to the well-being of a considerable fraction of the population the special problems it poses deserve careful study. This is equally true of the individual case, in which a medical man may be called upon to give an opinion in a variety of circumstances. The pitfalls in trying to assess the future health of very young babies are well known, and they are more numerous than usual when one or both parents are inaccessible, as is a feature of many adoption cases. Some of the special problems have been discussed by J. A. Black and F. H. Stone.[3] But a doctor's role may extend far beyond an assessment of the child's health and thrust upon him legal as well as medical responsibilities. Of these Hilda Lewis[4] provided an instructive account.

As the report says, "Far too little is known about what makes for a successful adoption, or indeed about how one should measure 'success.'" It might perhaps have said the same of parenthood. However that may be, society must accept a special responsibility to ensure that the adoptive procedures it sanctions are as beneficial as possible. Consequently, the studies of its efficacy sponsored by the Home Office, and briefly mentioned in the report, are to be welcomed.

---

[1] *The Registrar General's Statistical Review of England and Wales for the Year 1965*, Pt. 2, Tables, Population, 1967. H.M.S.O.

[2] *Report on the Work of the Children's Department 1964–1966*, Home Office, 1967. H.M.S.O.

[3] Black, J. A., and Stone, F. H., *Lancet*, 1958, 2, 1272.

[4] Lewis, H. N., *Brit. med. J.*, 1965, 2, 577.

Sentence Without Trial

A letter in our correspondence columns (p. 556) draws attention to the case of Dr. Raymond Hoffenberg, senior lecturer in the Department of Medicine at Cape Town University, on whom the South African Department of Justice has recently served a banning order. Professor John F. Brock, head of the department in which Dr. Hoffenberg works and President of the College of Physicians, Surgeons, and Gynaecologists of South Africa, has already strongly condemned the action of the Department of Justice.[1]

Dr. Hoffenberg is a distinguished physician, medical scientist, and teacher at Groote Schuur Hospital, Cape Town, known and consulted internationally for his work on radioisotopes, thyroid function, and protein malnutrition. He was formerly acting chairman of the banned South African Defence and Aid Fund, a body which helped political prisoners.[2] Two years ago his passport was withdrawn. No charges were made against him, and inquiries by Professor Brock failed to elicit the reason for the withdrawal. Nor recently could he obtain permission for Dr. Hoffenberg to attend, on behalf of his hospital and university, an international atomic energy meeting in Vienna to which he had been invited. Now a five-year banning order has been imposed, again without any charges being made. The ban[3] restricts Dr. Hoffenberg to the Cape Town area, requires him to report weekly to the police, and prevents him from attending any gathering, social or otherwise, of more than one person. He is forbidden to publish, and this apparently includes scientific articles. He must give up his academic appointment at Groote Schuur Hospital at the end of this year. In the words of correspondents to *The Times*,[4] "He is removed from the world of medical science, to which he has made notable contributions; he is expunged from society"—all without trial.

Banning orders have been applied to other citizens of South Africa, but not before, it seems, to a medical man. Many South African doctors are shocked by what has occurred, and the College of Physicians, Surgeons, and Gynaecologists, the South African Medical and Dental Council, and the Medical Association of South Africa are to be asked to report on Dr. Hoffenberg's case.

By its actions the Department of Justice has effectively deprived the world of medicine, abroad as well as in South Africa, of the services of a distinguished doctor. No research worker can hope to maintain his impetus without freedom to associate with colleagues, to travel, and to publish his findings. It concerns the profession everywhere that any State, without charge or trial, should thus excommunicate a doctor from his professional life. South Africa will damage only its own reputation if it persists in penalizing Dr. Hoffenberg without a fair hearing.

---

[1] *Cape Times*, 2 August 1967.

[2] *The Times*, 4 August 1967.

[3] *Sunday Times*, 6 August 1967.

[4] *The Times*, 17 August 1967.

Papers and Originals

Renal Function after Acute Tubular Necrosis

J. D. BRIGGS,* M.B., M.R.C.P., M.R.C.P.ED., M.R.C.P.GLASG.; A. C. KENNEDY,† M.D., F.R.C.P.ED., F.R.C.P.GLASG.
L. N. YOUNG,‡ M.B., M.R.A.C.P.; R. G. LUKE,§ M.B., M.R.C.P., M.R.C.P.ED.
MARY GRAY,‖ B.SC.

Brit. med. J., 1967, 3, 513–516

As a result of a revision in the conservative methods of treatment (Bull *et al.*, 1949) and the availability of haemodialysis and peritoneal dialysis survival can now be expected in a substantial proportion of patients with acute tubular necrosis (Teschan *et al.*, 1960; Kennedy *et al.*, 1963). In the fatal cases death is usually due to the initiating illness, overwhelming infection, or a complication of uraemia such as uncontrolled hyperkalaemia or haemorrhage, and rarely to irreversibility of the renal lesion.

Recently the accuracy of the term "acute tubular necrosis" has been challenged (Sevitt, 1959; Finckh *et al.*, 1962) and alternatives such as acute reversible intrinsic renal failure have been suggested (Luke and Kennedy, 1967). However, in view of the common usage and widespread understanding of the meaning of the term acute tubular necrosis, it will be used in this paper.

Although it is widely accepted that the prognosis in general is good in patients who survive an episode of acute tubular necrosis, there remains some doubt about the exact degree to which glomerular and tubular function will ultimately recover. Lowe (1952), in a preliminary report, found in 14 patients followed for periods varying from 7 to 38 months that renal function tests tended to remain below normal limits, and these findings were largely confirmed by Finkenstaedt and Merrill (1956) in 16 patients followed for 3 to 76 months, though their patients had normal tubular function in spite of a diminished glomerular filtration rate. Edwards (1959), however, reported a return to normal of the rate in 14 out of 15 patients within three months.

The present paper describes the degree of recovery of various aspects of renal function after acute tubular necrosis in 50 patients studied on average at 35 months after the episode of renal failure.

Methods and Material

Fifty patients were studied, 22 male and 28 female, all of whom had a previous well-documented episode of acute tubular necrosis. A total of 138 patients with acute tubular necrosis were admitted to the artificial kidney unit of Glasgow Royal Infirmary during the period February 1960 to June 1965, and the 50 patients in the present study were selected from the 88 survivors. The only method of selection was on the grounds of availability and knowledge of their whereabouts: there is no reason to suspect that these do not form a representative sample of the patients recovering during this period. The ages of the patients at the time of development of the acute tubular necrosis ranged from 18 to 67 years, with a mean of 38 years. The diagnosis of acute tubular necrosis was made on the grounds of the clinical presentation, course of the illness (Loughbridge *et al.*, 1960), and biochemical investigations: the ratio of urine urea to blood urea fell at some stage in the illness to less than 4:1 in all patients.

The aetiology of the acute tubular necrosis is shown in Table I. The patients were subdivided in the conventional manner into medical, surgical, and obstetric groups. The commonest precipitating factors were abortion, antepartum haemorrhage, surgery, multiple injuries, and ingestion of nephrotoxins, these together accounting for 68% of the entire series.

TABLE I.—*Aetiology of the Acute Tubular Necrosis*

Medical (12)	Surgical (17)	Obstetric (21)
Nephrotoxins (4)	Postoperative (7)	Abortion (11)
Intravascular haemolysis (2)	Multiple injuries (5)	Antepartum haemorrhage (7)*
Pneumonia	Cholecystitis (2)	Postpartum haemorrhage (3)*
Anticoagulant bleeding	Burns + intravascular haemolysis	
Salmonella enteritis	Intestinal obstruction	
Carbon monoxide poisoning	Perforated duodenal ulcer	
Respiratory failure		
Staphylococcal septicaemia		

* Following pre-eclampsia in 9 out of 10 cases.
Number of patients in each group shown in parentheses.

All grades of severity of renal failure were encountered. This was assessed in two ways—by the duration of oliguria (urine volume of less than 600 ml. per 24 hours) and by the number of dialyses performed. Forty-four of the 50 patients were oliguric for periods ranging from 2 to 40 days, with a mean of 11 days; one patient was not oliguric at any stage of the illness; and in the remaining five patients the duration of oliguria was not known. Haemodialysis was required on at least one occasion in 43 patients. The greatest number of dialyses in any one patient was 15: this patient had a severe degree of renal failure after multiple injuries and was oliguric for 40 days. In the remaining seven patients conservative measures only were used.

Evidence of previous urinary tract disease was present in six patients. Three gave a history of recurrent urinary tract infection, two had symptoms suggestive of prostatic enlargement, and one was a mild maturity-onset diabetic, in whose urine a trace of protein had been noted on several occasions. In addition three patients had significant hypertension (diastolic blood pressure of 100 mm. Hg or higher) and nine had pre-eclampsia at the time of onset of the acute tubular necrosis.

---

* Medical Registrar.
† Reader in Medicine.
‡ Clinical Research Assistant.
§ Lecturer in Medicine.
‖ Biochemist.
University Department of Medicine, Royal Infirmary, Glasgow C.4.

The interval between the episode of acute tubular necrosis and the follow-up study varied from 4 to 75 months, with a mean and standard deviation of 35±19 months, but in only two patients was it less than one year. A less detailed interim follow-up study was also carried out in 14 of the 50 patients. The mean interval between the acute tubular necrosis and the interim study was nine months and between the interim and formal follow-up studies 37 months.

The formal follow-up study consisted of a clinical assessment plus the following investigations: quantitative urine microscopy and culture (McGeachie and Kennedy, 1963), estimation of proteinuria with the biuret method, blood urea and electrolytes, serum creatinine, and measurement of glomerular filtration rate, concentrating power of the kidney, and ability to excrete an acid load. The glomerular filtration rate was estimated by three methods—endogenous creatinine clearance (49 patients), inulin clearance (41 patients), and the clearance of ^{57}Co-labelled vitamin B$_{12}$ (Nelp *et al.*, 1964) (41 patients). Only the results of the inulin and endogenous creatinine clearances are presented here, as the ^{57}Co-labelled vitamin B$_{12}$ clearance was in fairly close agreement with the inulin clearance (Briggs, 1967). Concentrating power was assessed by measurement of urine specific gravity after 24 hours' dehydration and the ability of the kidney to excrete an acid load by the modified acid load test of Wrong and Davies (1959). In the interim follow-up the following studies were made: urine culture, estimation of proteinuria, blood urea, endogenous creatinine clearance, and pitressin test.

Results

At the time of follow-up all the patients were leading active lives and almost all had returned to their former occupation. Few symptoms which had a possible relation with the acute tubular necrosis were elicited. Three patients complained of excessive tiredness, in two of whom the glomerular filtration rate was moderately reduced. Nocturia was present in nine patients but was as common in those with a normal glomerular filtration rate as in those with a reduced rate. Four of the 17 married women under 40 years had one or more successful pregnancies after the acute tubular necrosis.

Blood pressure.—This was measured a few hours after the patient's admission to hospital while resting in bed. In 36 of the 50 patients the diastolic blood pressure was 90 mm. Hg or less. Eight patients had values between 91 and 100 mm. Hg, while in the remaining six the diastolic blood pressure was greater than 100 mm. Hg. Of this last group, two were known to have had hypertension before the acute tubular necrosis, while the remaining four had pre-eclampsia. Three of the eight patients with levels of 91–100 mm. Hg also had pre-eclampsia and one pre-existing hypertension.

Proteinuria and Urine Microscopy.—The urine was protein-free in 34 patients, and in a further 10 less than 1 g. of protein per 24 hours was recorded. The remaining six had 1 to 3 g. of protein per 24 hours: of these, three had pre-eclampsia before the acute tubular necrosis, one had recurrent pyelonephritis, and one had hypertension with impaired renal function. Urine microscopy revealed pyuria in seven patients, four of whom also had significant bacteriuria.

Urinary Infection.—Significant bacteriuria—that is, more than 100,000 organisms per ml. of urine—was present at the time of follow-up in six patients. This compared with the finding of bacteriuria at some stage of the acute tubular necrosis in 23 patients. Of the six patients with positive urine cultures at follow-up, two gave a history of recurrent urinary tract infection extending back beyond the acute tubular necrosis, one had radiological evidence of pyelonephritis with impaired renal function and was thought in retrospect to have long-standing, occult, chronic pyelonephritis, one had previous pre-eclampsia but no urinary tract symptoms, and in one the urinary infection followed a prostatectomy.

Blood Urea and Serum Creatinine.—The blood urea and serum creatinine values at the time of the follow-up study are plotted in Fig. 1. Taking 40 mg./100 ml. as the upper limit of normal for blood urea, 24 patients had elevated levels, the highest being 95 mg./100 ml.

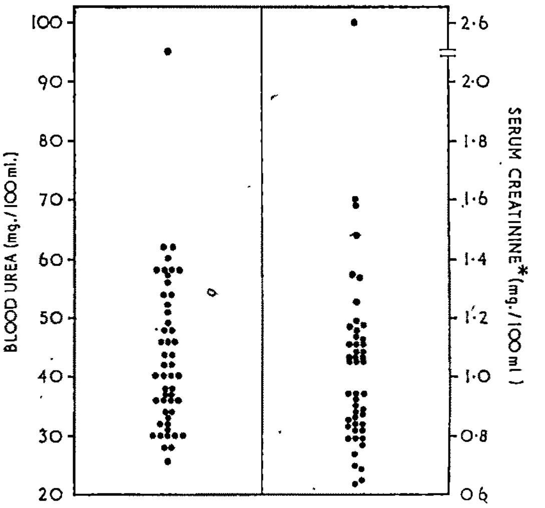


FIG. 1.—Blood urea and serum creatinine levels. *Measured in 48 patients.

Glomerular filtration rate.—The glomerular filtration rates measured by endogenous creatinine and inulin clearances are plotted in Fig. 2. Davies and Shock (1950) have recorded inulin clearances in a large series of normal males related to age, and the inulin clearances in the present study were regarded as normal if they fell within one standard deviation of the mean values of Davies and Shock for each decade. Although a series of comparable size to that of Davies and Shock is not available for females, the data of Homer Smith (1951) show the inulin clearance in females to be approximately 93% of that in males. Normal values for females were therefore arbitrarily taken as being 93% of those quoted for different decades in males by Davies and Shock. Again, the results in the present series were regarded as normal if they fell within one standard deviation of the mean. With the above criteria, 12 of the 41 patients (29%) in whom inulin clearances were performed had normal results.

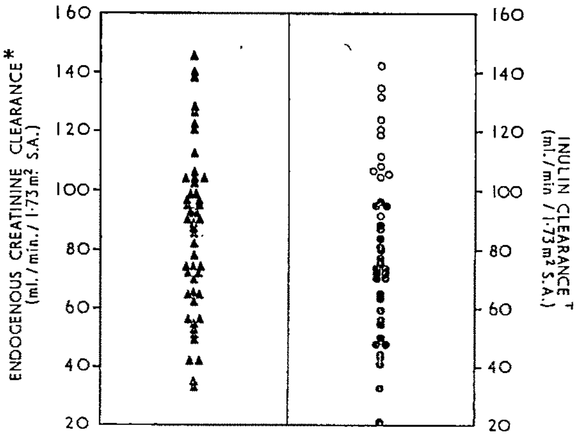


FIG. 2.—Glomerular filtration rate measured by endogenous creatinine and inulin clearance. *Measured in 49 patients. † Measured in 41 patients. ○ Within one standard deviation of. ● More than one standard deviation below, the mean inulin clearance values in normal subjects (Davies and Shock, 1950).

Concentration Test.—Of the 45 patients in whom the concentration test was carried out, 32 (69%) had a value above

1020 after 24 hours' dehydration. A specific gravity between 1016 and 1020 was obtained in six patients (13%), while in the remaining 8 (18%) the value was below 1016.

Modified Acid Load Test.—An inability of the kidney to reduce the urine *p*H to less than 5.4 was found in 14 (33%) of the 42 patients in whom this test was performed. Thirteen of these 14 patients had *p*H values of 5.4 to 5.8 and normal urine titratable acidity and ammonia production. In the remaining patient the urine *p*H was 6.1 with a very high urine ammonia level (101 μEq/min.). The serum electrolytes, however, were normal. The aetiology of this patient's acute tubular necrosis was mercuric chloride poisoning. The normal ranges of urine titratable acidity and ammonia production quoted by Wrong and Davies (1959) were 24 and 33 μEq/min. respectively. In 10 patients (24%) the titratable acidity was less than 24 μEq/min., in six of whom the ammonia production was below 33 μEq/min. Eight of these ten patients had other evidence of generalized renal damage such as lowered glomerular filtration rates, impaired concentration tests, and proteinuria.

Intravenous Pyelogram.—A pyelogram satisfactory for detailed analysis was obtained in 40 patients. The average length of the two kidneys was within normal limits—that is, within one standard deviation of the mean value in relation to body height[1]—in 35 patients (87%). In three patients the average kidney length was 1 to 2 cm. below the mean, while in the remaining two it was more than 2 cm. below the mean. There was a significant difference ($P<0.001$) between the mean glomerular filtration rates of the five patients with small kidneys (54 ml./min.) and that of the 35 patients with kidneys of normal size (91 ml./min.). Calcification of the renal cortex was not observed in any patient, while in one patient with a history of recurrent urinary tract infection before the acute tubular necrosis caliceal clubbing was present.

Interim Follow-up.—In the 14 patients who had both an interim and a formal follow-up study, the mean endogenous creatinine clearances were 87 and 94 ml./min. respectively, the difference not being statstically significant ($P>0.1$). Similarly, there was no significant difference between the mean blood urea values ($P>0.1$). In four of the 14 patients there was impairment of concentrating power at the interim follow-up with a return to normal concentrating power at the time of the formal follow-up, but this could be partly due to the more powerful stimulus of dehydration compared with that of pitressin. Table II summarizes the results of the investigations carried out during the formal follow-up study.

TABLE II.—*Summary of Follow-up Studies*

Type of Test	No. of Patients with Normal Results
Blood pressure	36 (72%)
Urine protein	34 (68%)
„ culture	43 (86%)
Blood urea	26 (52%)
Serum creatinine	32 (of 48) (67%)
G.F.R. (inulin clearance)	12 (of 41) (29%)
Intravenous pyelogram	35 (of 40) (87%)
Concentration test	31 (of 45) (69%)

Discussion

During this study we were impressed with the fact that normal well-being had been restored in almost all patients with a return to their former occupation. In contrast, analysis of the renal function studies showed that in only 13 of 50 patients were all results within strictly normal limits. It is of course likely that in a small number of patients renal function was impaired before the episode of acute tubular necrosis, in particular in the one diabetic patient, in the three patients with hypertension, and in the nine with pre-eclampsia. In the majority of patients, however, there were no features suggesting pre-existing renal damage, and the impairment of function noted during this study is therefore likely to be a consequence of the episode of acute tubular necrosis.

A reduction in glomerular filtration rate was the commonest abnormality, this being found in 71% of patients. This finding is in agreement with that of Lowe (1952) and of Finkenstaedt and Merrill (1956), who noted a reduction in glomerular filtration rate in the majority of their patients. However, in only seven patients (17%) in the present series was the glomerular filtration rate, measured by the inulin clearance, severely depressed—that is, below 50 ml./min.

Since the reduction in glomerular filtration rate was in most cases not associated with proteinuria, it is likely that it is due to some nephrons being totally non-functioning rather than urine being formed by some partially damaged nephrons. The pathophysiology of acute tubular necrosis is disputed: there is histological evidence that the primary change occurs in the tubules (Oliver *et al.*, 1951) and also evidence against this view (Finckh *et al.*, 1962). Support for the concept that the lesion is not limited to the tubules is provided by the study of De Luna *et al.* (1964), which showed that the pattern of acid excretion during the recovery phase of acute tubular necrosis—namely, a slightly raised urine *p*H with very low ammonia excretion—is similar to that seen in generalized renal disease (Wrong and Davies, 1959). The finding by Price and Palmer (1960) that the major histological changes in the kidneys after acute tubular necrosis are in the glomeruli lends support to the theory that the primary abnormality in acute tubular necrosis involves the glomeruli. Studies of animal models have supported the concept that the primary change is a marked drop in glomerular filtration rate (Oken *et al.*, 1966), though subsequent tubular obstruction is also an important factor (Jaenike and Schneeberger, 1966). Direct measurement of renal plasma flow has shown a reduction to about 50% of normal in the early stages of acute tubular necrosis (Reubi *et al.*, 1964 ; Shaldon *et al.*, 1964). Our findings cannot be taken to support either theory of the pathophysiology of acute tubular necrosis, since nephrons will cease functioning if either the glomerular or tubular damage is severe enough. They do, however, support the concept that there are structural changes at least in some nephrons in acute tubular necrosis, rather than simply a functional lesion (Sevitt, 1959 ; Finckh *et al.*, 1962).

Bull *et al.* (1950) suggested that after reaching a maximum value a few months after the episode of acute tubular necrosis there followed a steady fall in glomerular filtration rate. Also in animal experiments in mice, Fox (1967) has described progressive deterioration in renal function, accompanied by reduction in renal size and interstitial fibrosis, after recovery from ischaemic acute tubular necrosis. Our data, derived from comparison of the creatinine clearances at the interim and detailed follow-up, suggest, however, that following the slow improvement which takes place over the few months after the acute tubular necrosis renal function remains stable.

Although a prolonged oliguric phase is usually associated with a higher initial mortality, there was no relation in this study between the duration of oliguria and the degree of recovery of renal function in those patients who survived the acute phase. The results in the present series were also examined to see if there was any relation between the aetiology of the acute tubular necrosis and the degree of recovery. It was found that where pre-eclampsia had preceded the acute tubular necrosis there was a higher incidence of hypertension, proteinuria, and reduced kidney size than in the complete series, though the mean glomerular filtration rate in the patients with pre-eclampsia was not significantly lower than the mean of all 50 patients. A poorer prognosis in patients with pre-eclampsia during the course of the acute tubular necrosis has also been demonstrated by Smith *et al.* (1965). They found a higher mortality when acute tubular necrosis occurred in late pregnancy than in early pregnancy and a high incidence of pre-eclampsia in the former group.

---

[1] These results were calculated by means of the charts of radiographic kidney size prepared by the Department of X-ray Diagnosis, University College Hospital, London, and printed by Kodak Ltd., London.

Hypertension has been noted in a few patients after recovery from acute tubular necrosis (Lowe, 1952; Edwards, 1959; Price and Palmer, 1960). In the present series, of the six patients with diastolic blood pressures of over 100 mm. Hg at the time of follow-up, four had pre-eclampsia and two had pre-existing hypertension. There is therefore no evidence from this study that acute tubular necrosis leads to the development of hypertension.

A high incidence of urinary tract infection during the course of acute tubular necrosis has been recorded in a previous series (Swann and Merrill, 1953) and is confirmed in the present one, significant bacteriuria having been found in 46% of patients. In only six patients, however, was bacteriuria found at the time of follow-up, and in four of these six there was an adequate explanation for the finding (see Results). There is therefore no evidence that acute tubular necrosis per se predisposes to the development of persistent or recurrent urinary tract infection.

The finding that one-third of the patients had urine *p*H values in the range 5.4–5.8 during a modified acid load test is of dubious significance. The patients with low urine ammonia levels and reduced titratable acidity had in addition proteinuria, low glomerular filtration rates, and impaired concentration tests, and the abnormality of acid excretion therefore probably reflected generalized renal damage. The patient whose urine *p*H failed to fall below 6 is of special interest. The cause of his acute tubular necrosis was mercuric chloride ingestion. His serum electrolytes, glomerular filtration rate, and concentration test were normal and the urine ammonia high (101 μEq/min.). These findings are similar to those described by Wrong and Davies (1959) in their patients with incomplete renal tubular acidosis, and it may be that this patient has suffered specific damage to the hydrogen-ion excretion mechanism of his renal tubules.

In conclusion, this study shows that the long-term prognosis is good in patients who survive an episode of acute tubular necrosis. A normal state of health was almost always regained, though detailed investigation of renal function revealed some abnormality in most patients (74%), most commonly a lowered glomerular filtration rate (71%).

Summary

A detailed examination of renal function has been carried out in 50 patients with a previous well-documented episode of acute tubular necrosis. The time interval between the acute tubular necrosis and follow-up varied from 4 to 75 months, but was less than one year in only two cases. All patients at the time of follow-up had made a good clinical recovery and were leading active lives. However, investigation of renal function revealed some abnormality in 37 (74%) of the patients, the most common defect being a lowered glomerular filtration rate (71%). Tests of tubular function were found to be abnormal in a much smaller number of patients, the concentration test being impaired in only 31%. No correlation was found between renal function at the time of follow-up and either the severity of the renal failure or the precipitating cause, but patients in whom pre-eclampsia preceded the acute tubular necrosis did have a high incidence of residual renal damage. There was no evidence that the episode of acute tubular necrosis led to hypertension, any alteration in renal size or caliceal changes, or predisposed to urinary tract infection. Serial studies in 14 patients suggested that no subsequent deterioration in renal function followed the initial recovery.

REFERENCES

Briggs, J. D. (1967). Unpublished observations.

Bull, G. M., Joekes, A. M., and Lowe, K. G. (1949). *Lancet*, **2**, 229.

—— —— —— (1950). *Clin. Sci.*, **9**, 379.

Davies, D. F., and Shock, N. W. (1950). *J. clin. Invest.*, **29**, 496.

De Luna, M. B., Metcalfe-Gibson, A., and Wrong, O. (1964). *Nephron*, **1**, 3.

Edwards, K. D. G. (1959). *Aust. Ann. Med.*, **8**, 195.

Finckh, E. S., Jeremy, D., and Whyte, H. M. (1962). *Quart. J. Med.*, **31**, 429.

Finkenstaedt, J. T., and Merrill, J. P. (1956). *New Engl. J. Med.*, **254**, 1023.

Fox, M. (1967). *J. Urol. (Baltimore)*, **97**, 196.

Jaenike, J. R., and Schneeberger, E. E. (1966). *J. exp. Med.*, **123**, 537.

Kennedy, A. C., Luke, R. G., Linton, A. L, Eaton, J. C., and Gray, M. J. B. (1963). *Scot. med. J.*, **8**, 97.

Loughridge, L. W., Milne, M. D., Shackman, R., and Wootton, I. D. P. (1960). *Lancet*, **1**, 351.

Lowe, K. G. (1952). Ibid., **1**, 1086.

Luke, R. G., and Kennedy, A. C. (1967). *Postgrad. med. J.*, **43**, 280.

McGeachie, J., and Kennedy, A. C. (1963). *J. clin. Path.*, **16**, 32.

Nelp, W. B., Wagner, H. N., jun., and Reba, R. C. (1964). *J. Lab. clin. Med.*, **63**, 480.

Oken, D. E., Acre, M. L., and Wilson, D. R. (1966). *J. clin. Invest.*, **45**, 724.

Oliver, J., MacDowell, M., and Tracey, A. (1951). Ibid., **30**, 1307.

Price, J. D. E., and Palmer, R. A. (1960). *Arch. intern. Med.*, **105**, 114.

Reubi, F. C., Gossiveiler, N., Gurtler, R., and Huber, A. (1964). *Acute Renal Failure*, edited by S. Shaldon and G. C. Cook, p. 25. Oxford.

Sevitt, S. (1959). *Lancet*, **2**, 135.

Shaldon, S., Rae, A. I., Rosen, S. M., Silva, H., and Walker, J. G. (1964). *Acute Renal Failure*, edited by S. Shaldon and G. C. Cook, p. 35.

Smith, H. W. (1951). *The Kidney*, p. 545. New York.

Smith, K., Browne, J. C. McC., Shackman, R., and Wrong, O. M. (1965). *Lancet*, **2**, 351.

Swann, R. C., and Merrill, J. P. (1953). *Medicine (Baltimore)*, **32**, 215.

Teschan, P. E., Baxter, C. R., O'Brien, T. F., Freyhof, J. N., and Hall, W. H. (1960). *Ann. intern. Med.*, **53**, 992

Wrong, O., and Davies, H. E. F. (1959). *Quart. J. Med.*, **28**, 259.

Paediatric Aspects of the Early Discharge of Maternity Patients

M. W. ARTHURTON,* M.D., M.R.C.P., D.C.H. ; F. N. BAMFORD,† M.B., CH.B., D.C.H., D.P.H.

Brit. med. J., 1967, 3, 517–520

Planned early discharge of mothers and babies from St. Luke's Maternity Hospital, Bradford, has been taking place since 1958. The purpose of this paper is to describe the effect it has had on child health in the city, and, in particular, to consider its safety and acceptability from a paediatric point of view.

Theobald (1959, 1962) depicted the form and purpose of the "Bradford experiment," and Douglas *et al.* (1961) have published the results of the scheme from its inception until the end of 1960. The results of early discharge elsewhere have been described by Hellman *et al.* (1962) and Pinker and Fraser (1964).

Our review covers a period of seven years from January 1959 to December 1965, during which time 9,718 babies were discharged within 72 hours of birth. It is believed that up to the present this represents the greatest numerical experience of planned early discharge in Great Britain. The survey does not include babies taken home early against advice or those discharged to other units, nor to areas outside the city boundary. Full responsibility for neonatal care was accepted by the paediatric department in August 1962.

Results

The total number and the proportion of babies discharged within 72 hours to the city area during each of the seven years is shown in Table I.

TABLE I.—*Babies Discharged Within 72 Hours*

	1959	1960	1961	1962	1963	1964	1965	Total
No. of babies discharged early ..	922	1,176	1,358	1,350	1,669	1,562	1,681	9,718
Proportion of total hospital births discharged early (%)..	37·3	37·0	41·9	39·4	48·7	44·1	47·6	41·6

Mortality

Fig. 1 gives the perinatal mortality rate of Bradford in comparison with the national rate. Of the 9,718 babies who were discharged early 8 (0.82 per thousand) died before they reached the age of 11 days. Out of a total of 15,887 babies born on the district during the same period 20 died between the ages of 2 and 10 days inclusive, giving a comparable mortality rate of 1.26 per thousand. The difference between the two groups is not statistically significant (S.E. (difference), 0.40 ; P=0.24).

Details of the eight babies from the early discharge group who died are as follows:

Case 1.—Tentorial tear: spontaneous occipitoposterior delivery; fourth child; birth weight 9 lb. (4.080 g.). Discharged by obstetric registrar at age 34 hours; readmitted on third day and died next day.

Case 2.—Atrial septal defect with hypoplastic left ventricle and aorta: normal delivery; second child; birth weight 6 lb. 2 oz. (2.780 g.). Discharged by obstetric house-surgeon at age 39 hours; readmitted on eighth day in cardiac failure but with normal heart sounds; died on the following day.

Case 3.—Perforated caecum with peritonitis: normal delivery; third child; birth weight 7 lb. 4 oz. (3,290 g.). Discharged by obstetric house-surgeon at age 29 hours. Vomited blood on the second day; readmitted on the fifth day because of persistent vomiting. Immediate laparotomy with exteriorization of caecum and peritoneal drainage; died five hours later.

Case 4.—Ventricular septal defect: normal delivery; third child; birth weight 8 lb. 5 oz. (3,770 g.). Discharged by obstetric registrar at age 28 hours; readmitted in cardiac failure with a cardiac murmur on the sixth day of life; died on the following day.

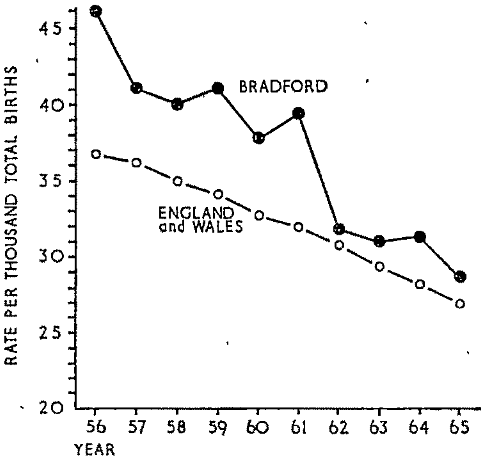


FIG. 1.—Perinatal mortality rates.

Case 5.—Bronchopneumonia: normal delivery; fourth child; birth weight 6 lb. (2,720 g.). Discharged by paediatric senior house-officer at age 32 hours. Midwife subsequently refused admission to house; died at home on the third day.

Case 6.—Fallot's tetralogy: shoulder presentation corrected to vertex; third child; birth weight 8 lb. 6 oz. (3,800 g.). Discharged by paediatric registrar at age 27 hours; readmitted on sixth day of life with peripheral cyanosis, rapid pulse, enlarged heart, but no cardiac murmur or signs of failure; died next day. Necropsy also revealed a small cerebral haemorrhage.

Case 7.—Bronchopneumonia: normal delivery; first child; birth weight 7 lb. (3,175 g.). Discharged by paediatric registrar at age 39 hours. Died at home on the ninth day of life.

Case 8.—Left adrenal haemorrhage: normal delivery; third child; birth weight 6 lb. 5 oz. (2,865 g.). Discharged by paediatric senior house-officer at age 36 hours. Readmitted on the same day; died of peripheral circulatory failure a few hours later.

In addition to the eight babies described above nine who were discharged early died between the twelfth and twenty-ninth days, inclusive. The causes of death were as follows:

Bronchopneumonia	6 babies aged 15 to 25 days
Transposition of great vessels ...	1 baby aged 13 days
Gastroenteritis	1 baby aged 21 days
Tentorial tear	1 baby aged 15 days

The cause of death was confirmed at necropsy in every case.

Morbidity

Of those babies who were discharged early 85 (8.74 per thousand) were readmitted to hospital within the first 10 days, compared with 145 (9.12 per thousand) babies of the same age born on the district and admitted to hospital between the ages of 2 and 10 days inclusive. This difference is not significant (S.E. (difference), 1.21; P=0.75).

---

* Consultant Paediatrician, Bradford.
† Principal Medical Officer in Child Health, Bradford.

The age at the time of readmission of early discharge babies is shown in Fig. 2.

Table II shows the cumulative percentage of early discharge babies readmitted between the ages of 1 and 10 days inclusive.

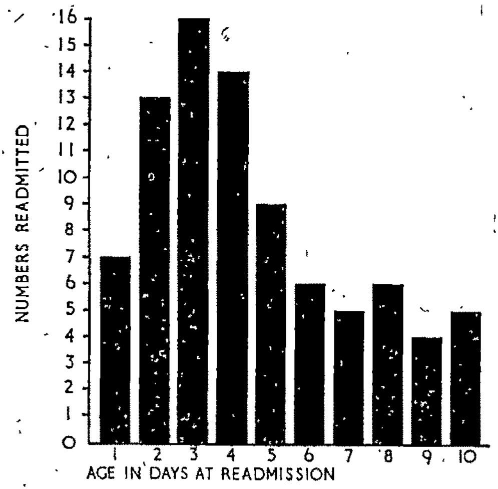


FIG. 2.—Early discharge readmissions (City of Bradford).

TABLE II

Age (days) ..	1	2	3	4	5	6	7	8	9	10
Cumulative % of admissions ..	8	24	42	59	68	76	82	89	94	100

The reasons for readmission of babies are shown in Table III and comparable figures are given for babies of the same age who were born at home and required admission to hospital.

TABLE III.—*Reasons for Readmission*

Diagnosis on Admission/Readmission	No. of Early Discharge Babies	No. of Domiciliary Babies
Infections	21 (24·7%)	41 (28·2%)
Physiological conditions	15 (17·6%)	10 (6·9%)
Feeding problems	9 (10·6%)	16 (11·0%)
Haemorrhagic disease of newborn	9 (10·6%)	9 (6·2%)
Congenital defects	8 (9·4%)	18 (12·4%)
Cerebral injury and irritation ..	5 (5·9%)	13 (9·0%)
Prematurity..		7 (4 8%)
Atelectasis		2 (1·4%)
Miscellaneous	18 (21·2%)	29 (20·1%)

Any early discharge baby readmitted before the age of 48 hours was included in Table III, whereas domiciliary delivered babies admitted before that age were excluded from consideration.

Babies discharged before the age of 24 hours required readmission significantly more often than those sent home on the second day. During the period covered by Craig and Muirhead (1967) 3.7% of mothers were discharged before 24 hours, but 17.6% of the babies readmitted to hospital in the same period had been discharged on the first day of life (S.E. (difference)=5.33%).

Table III gives no indication of the incidence of minor morbidity. An attempt was made to assess this by an analysis of midwives' medical aid request forms, but the differing practice of general practitioners in neonatal visiting and the variable experience of individual midwives made the results inexact. However, during the last two years of the survey 7.4% of the domiciliary group and 2.9% of the early discharge babies were the subject of medical aid calls between the second and tenth days of life.

Breast-feeding

A postal questionary was sent to all women delivered in Bradford in the first six months of 1964 with the exception of those cases where there was an obstetric, paediatric, or social abnormality which could interfere with the establishment or maintenance of breast-feeding. The number of "normal" confinements in the long-stay group was at first insufficient for statistical comparison, and this group was enlarged by the inclusion of similar women delivered during the following 18 months. A total of 743 patients returned the questionary; 515 of these were delivered on the district; 163 stayed in hospital for less than 72 hours and 65 for more than 72 hours (Table IV).

TABLE IV.—*Breast-feeding*

	Domiciliary	Hospital Short-stay	Hospital Long-stay
Percentage of women breast-feeding for one week or more	57 9	67·5	73·8
Percentage of women breast-feeding for six weeks or more	21·0	31·9	23·1

We tried to find out what caused women in each of the groups to discontinue breast-feeding. They were given a choice of six reasons, and were asked to select the one that applied to them (Table V).

TABLE V

	Reasons for Breast-Feeding Less Than One Week (% of Reasons Given)			Reasons for Stopping Breast-Feeding After the First Week (% of Reasons Given)		
	District	Hospital Short-stay	Hospital Long-stay	District	Hospital Short-stay	Hospital Long-stay
Preferred to bottle-feed	54·1	38·3	26·7	12·3	11·6	21·3
Returned to work ..	1·0	1·7	—	1·6	—	—
Illness	1·9	3·3	—	3·8	5·4	2·1
Not enough milk ..	19·3	20·0	26·7	49·3	45·5	61·7
Pain or difficulty ..	23·7	36 7	46·6	21·4	23·2	10·6
Baby old enough to stop	—	—	—	11·6	14·3	4·3

Discussion

Bradford is an industrial city which had a high incidence of toxaemia of pregnancy and a perinatal mortality rate considerably higher than the national average. The original purpose of planned early discharge was to release hospital beds for the treatment of toxaemia without reducing the number of hospital confinements. Since the inception of the scheme there has been an absolute improvement in perinatal mortality and also an improvement relative to the national rate (Fig. 1).

Better facilities for the treatment of toxaemia might have been expected to result in a reduction in the number of premature births, and it is disappointing that this has not occurred. There has, however, been a decrease in the proportion of premature babies of low birth weight—for example, those of 3 lb. 4 oz. (1.475 g.) or less—the total number of which has remained constant despite a rising birth rate.

Unfortunately it is difficult to be certain of the exact effect of early discharge because the figures have been confused by a changing population structure during the seven years of the study, but it is clear that the scheme has had no serious adverse effect and may have contributed to an improvement in child health.

Deaths among babies who were the subject of early discharge have been compared with the number who died between the ages of 2 and 10 days, inclusive, after domiciliary confinement. We believe that this comparison is valid, since domiciliary confinement has been the only practicable alternative for the majority of mothers in the city.

There is no evidence that early discharge offers any advantage for the individual baby as compared with staying in hospital for 10 days, and in fact there are additional risks partly attributable to difficulties in neonatal diagnosis. Some congenital defects and cerebral lesions do not show themselves within the first 48 hours, nor, in the case of one of our late deaths, within the normal 10-day lying-in period. Though it was undesirable, on general grounds, to have discharged the eight babies who subsequently died, it is unlikely that early discharge adversely affected the chances of survival of Cases 1 and 2. Early discharge was ill-advised in Cases 3 and 6. None of the nine deaths occurring after 10 days could be related to early discharge.

The longer a baby remains in hospital the less likely it is that pathological lesions will be undetected before discharge. It is preferable to avoid the need for readmission, and in our experience this would be reduced by 59% if mothers and babies left hospital on the fifth day (Fig. 2). Unfortunately, this would not be practicable without a fundamental reorganization of the maternity services. At present such an arrangement might lead to a false sense of security, because the interest taken by domiciliary midwives could be inversely proportional to the length of hospital stay of the baby. Furthermore, it would be sensible to discharge breast-fed babies as early as possible so that the early phases of feeding could be supervised by one adviser.

The incidence of feeding problems severe enough to warrant readmission was virtually the same in the two groups of babies, though a survey by members of the College of General Practitioners (1966) did show a higher incidence of minor feeding problems in their early discharge group. In our review of the early discharge babies readmitted five were underfed on the breast, two mothers lost their milk owing to emotional disturbance, and in one case faulty technique in artificial feeding was noted.

It was noticeable and understandable that in the early years of the survey a greater proportion of early discharge babies were readmitted with physiological conditions, including swallowed-blood syndrome, vaginal bleeding, urates in the urine, and physiological jaundice. There was a statistically significant difference ($P<0.05$) in admission rates for these conditions between the early discharge and domiciliary groups (see Table III).

As might have been anticipated, cases of haemorrhagic disease were readmitted early, two-thirds of them by the third day and all of them by the fifth day of life.

Babies with congenital defects who were readmitted consisted of five with congenital heart disease and three with hiatus hernia. In only one case of the former was a murmur heard on readmission. Careful perusal of admissions to the genito-urinary department during the period of the survey failed to reveal any missed cases of obstructive lesions of the genito-urinary tract, though such cases could easily be missed in the first two days of life.

Two cases of subarachnoid haemorrhage (one fatal), one case of subdural haemorrhage, and two babies with cerebral irritation were readmitted. The fatal case was an occipitoposterior delivery, and in one case of cerebral irritation delivery was by low forceps. Otherwise the confinements were normal. The number of cerebral complications did not differ significantly between the two groups of babies.

Unfortunately, owing to differences in methods of ascertainment by different observers and lack of strictly comparable groups, it was not possible to compare the incidence of infection in babies delivered at home, those discharged early, and those remaining in hospital for 10 days, many of the latter group being abnormal deliveries. The readmission rates for infection in the first two groups did not differ significantly. It is noteworthy that during the period of the survey four cases of gonococcal ophthalmia of late onset were observed in babies staying in hospital for 10 days.

Included in the miscellaneous group were convulsions (4), choking attacks (3), anal excoriation (2), haemolytic disease of the newborn due to rhesus incompatibility (2), and one case each of left adrenal haemorrhage (fatal), congenital spherocytic anaemia, hypothermia, meconium plug, perforated caecum (fatal), pyloric stenosis, and urticaria. No cause was found for the convulsions, and the deliveries of all these cases were normal. The two babies with haemolytic disease and one with meconium plug were erroneously discharged by junior hospital staff. Reference has already been made to the fatal cases.

Prior consultation between general practitioner and paediatrician would have made unnecessary the readmission of 18 (21%) cases in the early discharge group. A further eight babies who were readmitted had been erroneously discharged early because of faulty judgement. Thus there remained 59 babies in our series whose readmission would have been unavoidable, and it is therefore desirable to have special accommodation reserved so that mothers and babies can be readmitted together.

The Cranbrook Report (Ministry of Health, 1958) and the *British Medical Journal* (1964) suggest that early discharge adversely affects breast feeding, but this is contrary to our experience. In this city, of "normal" women delivered in hospital a greater proportion breast-fed for one week or longer than did women confined at home, and relatively more of them continued to feed for six weeks or longer. The differences between the short-stay and domiciliary groups are highly significant and pertain to all ages. It was shown that, though more of the younger mothers start to breast-feed—that is, feed for one week or more—a greater proportion of older mothers become established breast-feeders—that is, feed for six weeks or more. Social class was not significant in determining the number of women starting to breast-feed, but feeding was shown to become established more frequently in social groups I and II. The difference between the early discharge and long-stay hospital groups was not statistically significant.

A disturbing finding in the breast-feeding survey was that relatively more women delivered in hospital discontinued feeding after less than one week because of pain or difficulty (see Table V). Of those confined in hospital who fed for one week or longer the proportions in the early discharge and long-stay groups are about equal, which suggests that the disparity is due to an adverse influence in hospitals and that it is not assisted by the mother remaining for 10 days.

An early discharge scheme of the type that has been in operation in Bradford during the past seven years can be operated with advantage to the neonate, and he suffers no disadvantages as compared with the baby born on the district. We would emphasize, however, that the arrangements have to be planned in advance, and that close and continuing co-operation is necessary between all people concerned. Success depends on the competence and reliability of midwives, nurses, and junior medical staff, who carry out 10 or more routine neonatal examinations every day of the year. An efficient neonatal follow-up clinic is vital, as is the willingness of the paediatrician to deal promptly and personally with the medical and social consequences of neonatal abnormality. Provided that this degree of effort is made, the scheme can be safe and effective.

Summary

During 1959 to 1965, inclusive, a total of 9,718 babies were discharged from hospital within 72 hours of birth. An improvement in perinatal mortality has been described, and the mortality and morbidity experience of "early discharge" babies has been compared with those born at home during the same period. The difference between the two groups was not statistically significant. An inquiry into breast-feeding in the domiciliary,

early discharge, and long-stay hospital patients is recorded; it has shown that mothers confined in hospital begin to feed their babies and become established breast-feeders more often than do women delivered at home.

We wish to thank Dr. A. P. Roberts for permission to review cases in his care; Miss G. Clayton, Matron of St. Luke's Maternity Hospital, and Miss E. R. Entwhistle, Supervisor of Midwives, for their invaluable help on numerous occasions; and Dr. G. Hill for statistical advice. We wish to pay tribute to a very loyal junior staff.

REFERENCES

Brit. med. J., 1964, **2**, 70.

College of General Practitioners, Bradford Group (1966). *Lancet*, **1**, 536.

Craig, G. A., and Muirhead, J. M. B. (1967). *Brit. med. J.*, **3**, 520.

Douglas, J., Edgar, W., and Horne, K. (1961). *Med. Offr*, **106**, 333.

Hellman, L. M., Kohl, S. G., and Palmer, J. (1962). *Lancet*, **1**, 227.

Ministry of Health (1958). *Report of the Maternity Services Committee* (Cranbrook Report). H.M.S.O., London.

Pinker, G. D., and Fraser, A. C. (1964). *Brit. med. J.*, **2**, 99.

Theobald, G. W. (1959). Ibid., **2**, 1364.

—— (1962). *Lancet*, **1**, 735.

Obstetric Aspects of the Early Discharge of Maternity Patients

G. A. CRAIG,* M.B.E., F.R.C.S., F.R.C.O.G.; J. M. B. MUIRHEAD,* M.B., B.CH., M.R.C.O.G.

Brit. med. J., 1967, **3**, 520–522

It is now nine years since planned early discharge of the normal mother and normal baby on the second day of the puerperium was commenced in Bradford. The scheme has since been in continuous operation, and to date approximately 13,000 puerperal women have been managed in this way. Theobald (1959, 1962) and Douglas *et al.* (1961) described the reasons for and the initial planning of the scheme, and recorded its early results. In 1966 members of the College of General Practitioners (Bradford group) reported on a survey of 100 early discharge cases.

Five thousand consecutive case records have been analysed in order to show the types of patients that have participated in the scheme. Abnormalities that occurred but which were not thought sufficiently important to warrant retaining the patient in hospital for longer than 60 hours have been recorded. The purpose of the paper is to present these results, and it also includes a discussion of our experience.

Patients Discharged Early

Of the 5,000 patients whose records were analysed 70% were booked for hospital confinement and 30% were emergency admissions either during the antenatal period or during labour. The age distribution is recorded in Table I. The number of women in each parity group is shown in Table II. The length of stay in hospital of the 5,000 patients is given in Table III.

TABLE I.—*Age Distribution of Patients Discharged Early*

Age Group	Primigravidae	Multigravidae
Under 20 years	421 (8·4%)	89 (1·8%)
20–24 years	644 (12·9%)	695 (13·9%)
25–29 years	320 (6·4%)	1,028 (20·6%)
30–34 years	136 (2·7%)	848 (17·0%)
35 years and over	30 (0·6%)	789 (15·8%)

TABLE II.—*Parity Distribution of Patients Discharged Early*

Para ..	1	2	3	4	5+
No. (%)	1,551 (31)	1,300 (26)	818 (16·4)	498 (10)	833 (16·7)

TABLE III.—*Patients' Duration of Stay in Hospital*

Duration of Stay	Primiparae		Multiparae		Total	
	No.	%	No.	%	No.	%
Patients discharged in less than 24 hours ..	56	1·1	127	2·5	183	3·7
Patients discharged in 24–36 hours.. ..	1,094	21·9	2,450	49·0	3,544	70·9
Patients discharged in 36–60 hours.. ..	401	8·0	872	17·4	1,273	25·4

The original policy was to discharge on the second day those mothers and babies whose condition did not seem to justify further hospital care. A number of women who had had abnormalities during labour or at the time of delivery have participated in the scheme. The incidence of intrapartum complications in the 5,000 patients whose records were analysed is shown in Table IV. The complications that occurred at the time of delivery in patients discharged early are recorded in Table V.

TABLE IV.—*Intrapartum Complications in Patients Discharged Early*

Intrapartum Complication	Primigravidae	Multigravidae
Artificial rupture of membranes ..	512 (10·2%)	916 (18·3%)
Oxytocin drip	84 (1·7%)	197 (3·9%)
Pyrexia 99–99·8° F. (37·2–37·7° C.) on two or more occasions ..	17 (0·3%)	38 (0·8%)
Pyrexia 100° F. (37·8° C.) and over	3 (0·06%)	9 (0·2%)

TABLE V.—*Complications at Time of Delivery in Early Discharge Patients*

Complication	Primigravidae	Multigravidae
Ruptured perineum	520 (10·4%)	866 (17·3%)
Episiotomy	533 (10·7%)	324 (6·5%)
Forcepsdelivery	185 (3·7%)	79 (1·6%)
Breech delivery	27 (0·5%)	69 (1·4%)
Other vaginal delivery	16 (0·3%)	31 (0·6%)
Manual removal of placenta ..	9 (0·2%)	30 (0·6%)
Postpartum haemorrhage without transfusion	49 (1·0%)	85 (1·7%)
Postpartum haemorrhage with transfusion	2 (0 04%)	9 (0·2%)

Hospital Organization

The early discharge scheme has resulted in a considerable increase in the work done in the hospital. St. Luke's Maternity Hospital is the only maternity hospital in Bradford. It was designed to manage approximately 1,500 confinements a year. Before the introduction of the scheme in 1958 this figure had risen to 2,000 a year and since then it has continued to rise until in 1964 it almost reached 4,000. Such an increase imposes a very severe strain on all members of the hospital staff, particularly those engaged in the labour ward. In such circumstances it is difficult to maintain standards and the continuous

---

* Consultant Obstetrician and Gynaecologist, Bradford.

supervision that is necessary. It was therefore necessary to review the existing arrangements within the hospital and to effect any changes that would help a willing and competent nursing staff, whose numbers were inadequate, to meet the increased demands made upon them.

Ward clerks and ward and theatre orderlies have been appointed as liberally as our financial resources permit in order that the nursing staff may be relieved, so far as is possible, from all non-nursing duties. The labour ward of 12 beds is at the time of writing staffed with six sisters, six midwives, five pupil midwives, two ward clerks, four theatre orderlies, and five ward orderlies. Staff rotation between the various wards is practised. The theatre is now in charge of a sister who is not a midwife. This particular innovation has been a success. So far as is possible, all operative procedures and abnormal deliveries are performed in the operating-theatre.

Patients in labour are admitted direct to the labour suite, which is situated on the ground floor of the hospital. This suite has accommodation for 12 patients in labour, has two delivery rooms, an anaesthetic room, and an operating-theatre. Continuous with the labour suite is a recovery ward of 12 beds. Patients who are thought to be suitable for early discharge are accommodated in the recovery ward until the decision to discharge or not to discharge them is made.

If for any reason a patient and her baby are not discharged early they are immediately transferred to one of the lying-in wards. Those mothers who are to remain in hospital for 10 days are usually transferred from the labour ward to one of the lying-in wards shortly after their delivery has been completed. If, however, it is thought that their condition after delivery warrants continued close supervision then they are accommodated in the recovery ward until their condition has improved sufficiently to warrant their transfer to a lying-in ward. As a result of this reorganization the acute work of the hospital is accommodated on one floor and there has been a considerable reduction in the movement of patients within the hospital. It has also facilitated both medical and nursing arrangements.

We have been greatly impressed with the advantages that have resulted from a centralized labour ward, with adjacent delivery room, operating-theatre, and recovery room. We believe that single rooms should be provided for women in labour and that these should be large enough to allow normal deliveries to be conducted in them. Such an arrangement would reduce the movement of patients within the hospital and make it much easier for those who wish to have their husbands with them during labour.

It is undoubtedly better if patients who are expected to be discharged early are not accommodated alongside those who have to remain for 10 days.

Results

Mortality.—There have been no maternal deaths.

Readmission.—The incidence of readmission has been compared with the admissions to hospital of patients confined in their own homes (see Fig. 1). The most common indications for readmission were persistent bleeding from the uterus and delayed involution. A few patients were readmitted with pyrexia. Those who were readmitted were not dangerously ill and responded rapidly to appropriate treatment.

Eclampsia.—The number of cases of eclampsia that have occurred in patients booked for confinement in St. Luke's Maternity Hospital during the years 1948–65 inclusive is shown in Fig. 2. Since the inception of the early discharge scheme the number of patients booked for confinement in the hospital has risen by nearly 50%, and the admissions of patients with hypertension, proteinuria, and oedema have increased. The majority of the latter are counted as booked patients unless delivery occurred shortly after admission. Despite this, the incidence of eclampsia in booked patients has not gone up and has remained consistently below that of non-booked patients.

Table III shows that it has not been possible to discharge all patients on the morning of the second day; in nearly all cases the decision to discharge a patient in less than 24 hours was taken because beds were urgently required. Patients whose discharge was delayed until the morning of the third day included those whom it had not been possible to get home by midday on the second day and some about whom our information on their home conditions was incomplete or in need of verification.

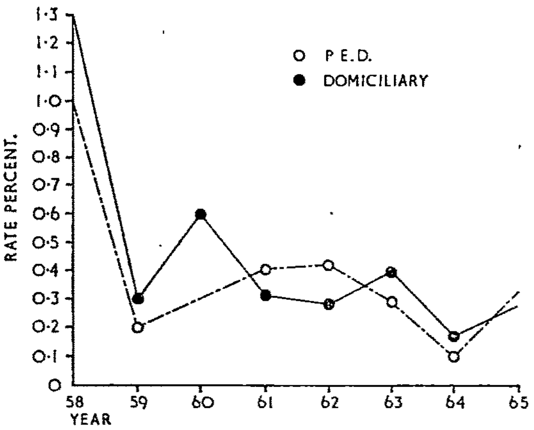


FIG. 1.—Readmission rates, domiciliary and planned early discharge patients.

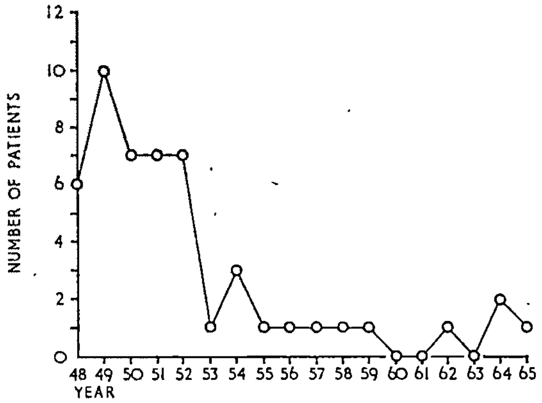


FIG. 2.—Eclampsia in booked patients, St. Luke's Maternity Hospital, 1948–65.

Discussion

The Bradford scheme has had a mixed reception from those engaged in obstetrics. Some are opposed to it (Claye, 1964; Corbett, 1964; Annual Report of the Health of Kingston-upon-Hull, 1964). Others have accepted it with reluctance, without conviction, and as an emergency measure whereby inadequate obstetric services could be enabled to meet the demands of the population explosion, until such times as adequate hospital, nursing, and medical facilities became available (Ministry of Health, 1958; Report of the Maternity Services Emergency Informal Committee 1963; *B.M.J.*, 1964). A third group appears to have accepted the scheme as being a safe and practical way of managing the normal mother and normal baby once the hazards of confinement are over (Douglas *et al.*, 1961; Hellman *et al.*, 1962; Rhodes, 1964; Pinker and Fraser, 1964).

The early discharge of patients who have had abnormalities is probably the most reasonable basis of criticism, but our results have shown that early discharge can take place without apparent detriment to the patient or her baby, even though certain abnormalities have occurred during the process of labour and delivery.

St. Luke's Maternity Hospital continues to make frequent use of artificial rupture of the membranes not only as a method of induction but also to help labour to become established. The oxytocin drip is used when necessary. It is not thought that the need to use either or both of these procedures precludes early discharge if the condition of the mother and baby is satisfactory after delivery.

Pyrexial patients were not discharged if the pyrexia persisted after delivery. The wisdom of discharging patients who have been pyrexial during labour may be questioned, but there has been no reason to regret the decision taken in the 67 patients included in this inquiry. Our policy has been to repair all ruptured perineums with catgut, in order to avoid the necessity for suture removal at home. This policy has worked well, and wound healing has been satisfactory. If the forceps or the ventouse has been used to deliver the head from the pelvic outlet early discharge takes place if the baby's condition is satisfactory. This is not considered wise if operative delivery has been effected from the mid-cavity of the pelvis. Many babies in the latter group do not show signs of abnormality on the second day. The great majority of these could be discharged early with safety, but a few could not, and the paediatrician obviously requires more time before he can feel confident that intracranial injury has not occurred. For the same reasons the early discharge of all babies delivered by the breech has now been discontinued.

The analysis showed that 36 of the 5,000 patients had some form of cardiac disability. They were all "stage I cardiacs," who had been well throughout their pregnancy and labour and on the first two days of the puerperium. Their discharge was necessary in order to release beds for incoming patients, and, though none of them is known to have suffered any ill effect as a result of early discharge, it is not recommended that cardiac patients should participate in the scheme.

Readmission rates are a good index of morbidity among patients discharged early. The provision of suitable accommodation for mothers with their babies when readmission is necessary is obviously desirable irrespective of whether early discharge is practised or not. It is unfortunate that St. Luke's Maternity Hospital has not yet got suitable accommodation to permit this to be done. An attempt to compare the medical state of a group of early discharge mothers with that of a group of mothers confined at home has not been pursued, as very soon it was apparent that valid conclusions could not be reached because of the many variable factors encountered.

It is desirable that the patient should be home by midday, as this allows ample time for the domiciliary midwife to assure herself that the mother and baby are satisfactorily settled. Patients are transferred as sitting patients, two per ambulance. They are accompanied by a part-time midwife employed by the local health authority. A few patients go home by private transport.

Doubts have been expressed that the Bradford scheme would interfere with the training and attitude of midwives. In our experience this has not been so. The local health authority has been able to maintain a full quota of domiciliary midwives, and on occasion has a waiting-list of women who wish to join the service. The hospital has never found it necessary to close beds because of staff shortages, and, while it is true that the staffing position is never fully satisfactory, difficulties were being experienced long before the introduction of planned early discharge. The existing administrative arrangements for the maternity services make it difficult to achieve the close and continuous co-operation between the three branches of the service that is necessary to ensure the continuity of medical and nursing care which is essential if planned early discharge is to be successful. If it is accepted that early discharge is a safe procedure then future policy should take into account the wishes of the patient regarding her place of confinement, provided that her medical and obstetric state is satisfactory.

An inquiry was made during 1964–5 of 225 women who had had normal confinements in hospital. Of these, 161 remained in hospital for less than 72 hours, and 64 of them for 10 days. They were asked to state where they would have preferred to have their baby: 50% of the 10-day group and 43.5% of the 2-day group were satisfied with their place of confinement (S.E. (Diff.) = 7.4%—that is, a difference that is not significant). No marked difference in preference was noted in the different age groups and there was no statistically significant difference expressed by women in different social classes. An earlier inquiry of the 161 women who had been confined in hospital and discharged in less than 72 hours showed that 44% of them were satisfied with the arrangements.

Early discharge has many attractions for the high-risk multigravidae, who are not infrequently reluctant to be admitted to hospital.

Our experience has shown that it is not necessary for 40–50% of puerperal patients to occupy a hospital bed for 10 days if their homes are suitable and adequate, and medical and nursing care can be provided for them. It has been alleged that early discharge of the puerperal patient from hospital means that she will return to her full range of domestic duties immediately. There is no reason why she should do so to any greater extent than those women who have been confined at home, and it may even be that the earlier ambulation and performance of light household duties are beneficial. There is no reason why the quality of postnatal care provided by the family doctor and the domiciliary care should be inferior to that provided in hospital.

Summary and Conclusions

The case records of 5,000 consecutive patients who were discharged from hospital within 60 hours of delivery have been analysed. Our experience has been that planned early discharge does not result in increased maternal morbidity nor does it add to the maternal risk. Modifications in the internal arrangements and staffing of the hospital have been described.

The scheme has proved to be an efficient and economic way of ensuring that the maximum number of mothers and babies receive the benefit of hospital care at the time of their greatest need for it.

An appreciable number of patients like and request early discharge. It is to be hoped that this will be recognized by the various authorities and that a more flexible approach to the management of the first 10 days of the puerperium will become the accepted rule.

We are indebted to the Leeds Regional Hospital Board for a grant to enable the analysis of the patients' records to be carried out. Thanks are due to our colleague, Mr. A. C. Muir, who kindly gave permission for the records of patients under his care to be included in the analysis. In addition, we have received valuable help from Mr. Haley, the Secretary, from Miss Clayton, Matron of St. Luke's Maternity Hospital and her staff, and from Mr. H. A. H. Melville. We also wish to express our appreciation for the help given by the Health Department of the City of Bradford.

References

Annual Report of the Health of Kingston-upon-Hull, 1964.
Brit. med. J., 1964, **2**, 70.
Claye, A. (1964). *Brit. med. J.*, **2**, 1007.
College of General Practitioners, Bradford Group (1966). *Lancet*, **1**, 536.
Corbett, H. V. (1964). *Brit. med. J.*, **2**, 1263.
Douglas, J., Edgar, W., and Horne, K. (1961). *Med. Offr*, **106**, 333.
Hellman, L. M., Kohl, S. G., and Palmer, J. (1962). *Lancet*, **1**, 227.
Ministry of Health (1958). *Maternity Services Committee* (Cranbrook Report). H.M.S.O., London.
Pinker, G. D., and Fraser, A. C. (1964). *Brit. med. J.*, **2**, 99.
Report of the Maternity Sevices Emergency Informal Committee 1963. London.
Rhodes, P. (1964). *Lancet*, **2**, 746.
Theobald, G. W. (1959). *Brit. med. J.*, **2**, 1364.
—— (1962). *Lancet*, **1**, 735

Urinary Steroid Assays and Response to Endocrine Ablation

B. S. THOMAS,* M.I.BIOL.; R. D. BULBROOK,* M.SC., PH.D.; J. L. HAYWARD,† M.B., B.S., F.R.C.S.

Brit. med. J., 1967, 3, 523–524

Bulbrook, Greenwood, and Hayward (1960) found a close relation between the subsequent clinical response of patients with advanced breast cancer to endocrine ablation and the amounts of androgen and corticosteroid metabolites in the urine before operation. They noted that in their small series of patients the best correlation between steroid assay results and clinical response was obtained if a discriminant function was used. This function was: 80-80 (17-OHCS mg./24 hours) + aetiocholanalone (μg./24 hours). The function is positive in patients excreting large amounts of aetiocholanolone relative to the amounts of 17-OHCS, and patients in this category generally responded well to endocrine ablation. Conversely, patients in whom the discriminant is negative (low aetiocholanolone excretion relative to that of the 17-OHCS) generally do not benefit from adrenalectomy or hypophysectomy (see Hayward and Bulbrook, 1965).

Miller, Durant, Jacobs, and Allison (1967) have described a high degree of correlation between the discriminant and a simple ratio of the total urinary 11-deoxy-17-oxosteroids and the 17-OHCS. It should follow, therefore, that their ratio would be as useful as the discriminant in the prediction of response to adrenalectomy or hypophysectomy.

We had available the assay results of the total 11-deoxy-17-oxosteroids, the 17-OHCS, and the discriminant in 210 patients with advanced breast cancer whose clinical response to endocrine ablation was already known. This paper is a report of a retrospective comparison of the predictive value of the discriminant and of the ratio described by Miller *et al.* (1967).

Methods

The 17-OHCS were determined by the method of Appleby, Gibson, Norymberski, and Stubbs (1955). It should be noted that Miller *et al.* (1967) used the method of Metcalf (1963) for the determination of the 17-OHCS. These methods are not strictly comparable: the latter method is based on a short-term hot oxidation of the 17-OHCS with sodium metaperiodate and the results are expressed in cortisol equivalents. The method of Appleby *et al.* (1955) is based on oxidation at room temperature with sodium bismuthate and results are expressed in terms of dehydroepiandrosterone. In practice, this means that the results of the 17-OHCS assays may differ by 1–2 mg./24 hours, but the difference between the methods should be approximately constant (see, for example, Thomas, 1965).

In the first 119 patients dehydroepiandrosterone, androsterone, and aetiocholanolone were determined by the method of Kellie and Wade (1957) and the value for the total 11-deoxy-17-oxosteroids was obtained by summing the amounts of these three steroids. In the remaining patients the total 11-deoxy-17-oxosteroids were measured as a group by the method of Thomas and Bulbrook (1964). The results of the two methods are very similar.

Either three or five consecutive 24-hour urine specimens were collected from 210 patients with metastatic breast cancer awaiting combined oophorectomy and adrenalectomy, or hypophysectomy. Clinical evaluation of response to treatment has been described in detail by Hayward and Bulbrook (1965) and the methods used have been discussed at length (see Hayward and Bulbrook, 1966).

Results

The usefulness of the discriminant function in differentiating between responsive and unresponsive patients at adrenalectomy or hypophysectomy can be judged from the data in the Table. In this series of 210 patients the remission rate is three times as great in patients with positive discriminants as in those with negative discriminants.

Relation Between the Response of Patients with Advanced Breast Cancer to Adrenalectomy or Hypophysectomy and the Discriminant Function

	Discriminant Positive		Discriminant Negative	
	No.	%	No.	%
Success	41	38·7	12	11·5
Intermediate	26	24·5	29	27·9
Failure	39	36·8	63	60·6
Total	106		104	

χ^2 for trend = 19·91. $P < 0{\cdot}001$.

The relation between the clinical response of patients to adrenalectomy or hypophysectomy and either the discriminant function or a ratio of the total 11-deoxy-17-oxosteroids to the 17-OHCS is shown in Fig. 1. It can be seen that the majority of successful responses to treatment occur in patients with positive discriminants and with high ratios. Conversely, the

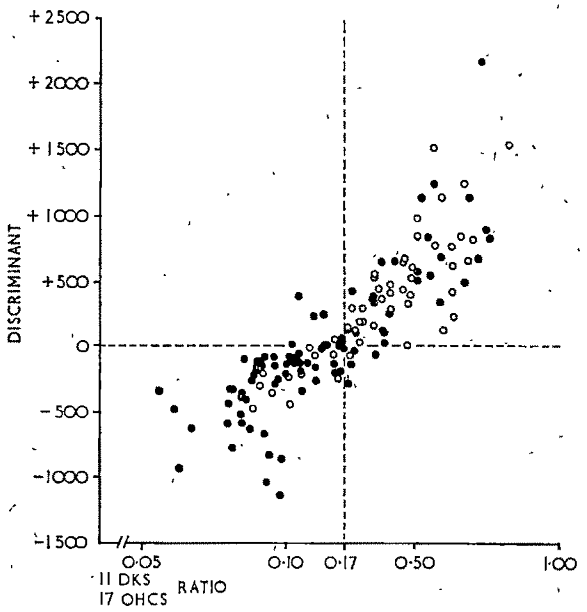


FIG. 1.—Relation between clinical response to adrenalectomy or hypophysectomy and the discriminant function or the 11-deoxy-17-oxosteroid/17-OHCS ratio. This Figure is based on results from 197 patients, of whom 52 responded to treatment and 92 failed to respond. ○ = Successful response. ● = Failure.

---

* Division of Chemistry and Biochemistry, Imperial Cancer Research Fund, London W.C.2.

† Department of Surgery, Guy's Hospital, London S.E.1.

majority of the failures occur in patients with negative discriminants and low ratios. If a ratio is used such that

$$\frac{\text{11-deoxy-17-oxosteroids (mg./24 hours)}}{\text{17-OHCS (mg./24 hours)}} = 0.17$$

then patients with ratios equal to or below this figure have a response rate that is identical to that found for patients with negative discriminants. Similarly, patients with a ratio above 0.17 also have a response rate that is virtually the same as that for patients with positive discriminants (see Fig. 2).

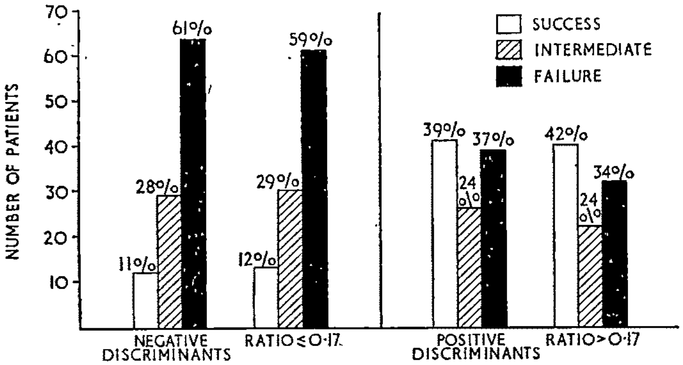


FIG. 2.—Clinical response to endocrine ablation in relation to discriminant or ratio of 11-deoxy-17-oxosteroids to the 17-OHCS.

Discussion

The results in this paper show that a simple ratio of the 11-deoxy-17-oxosteroids to the 17-OHCS can be chosen which in retrospect will give the same prediction of response to endocrine ablation as the discriminant function. This finding is to be expected from the results of Miller *et al.* (1967). It should be recalled that the discriminant function was calculated originally from the results of an investigation of a small series of 59 patients, of whom only 14 responded to treatment. The misclassification of only one or two of these successful cases would have had a pronounced effect, and a discriminant function gave the best separation of responsive and unresponsive cases at that time.

The easier analytical methods used by Miller *et al.* (1967) could be substituted, therefore, for the more cumbersome ones required for the calculation of the original discriminant for patients with advanced breast cancer.

There is a considerable degree of misclassification of response, whether the discriminant or the ratio is used. The results in the Table show that 37% of patients with positive discriminants fail to respond to treatment, whereas 12% of patients with negative discriminants enjoy an objective remission of the disease. To a very large extent the same patients are misclassified by the ratio or by the discriminant.

While there is now a considerable consensus of agreement that the response of patients to adrenalectomy or hypophysectomy is related to the amounts of androgen and corticosteroid metabolites found in the urine before treatment, the results of individual workers differ in detail and emphasis. Thus, Juret, Hayem, and Flaisler (1964) found that the sum of the androsterone and aetiocholanolone values was related to the response of their patients to destruction of the pituitary by yttrium-90.

Wilson, Crocker, Fairgrieve, Bartholomay, Emerson, and Moore (1967) have found a relation between clinical response to adrenalectomy and a discriminant function based on 17-oxosteroid and 17-OHCS response to A.C.T.H. stimulation, and they also make use of the predictive information provided by the free period (see below). Kumaoka, Abe, Sakauchi, Takatana, and Kusama (1966) have found significant differences in total 17-oxosteroid excretion between their responsive and unresponsive patients.

An additional complication is the recognition that factors other than the endocrine environment are of considerable importance in relation to response to treatment. The free period (the time between mastectomy and first recurrence of the disease) is longer in responsive patients than in unresponsive patients (see Taylor, 1966). When the length of the free period is taken into account in conjunction with the steroid assay results, there is a considerable increase in the accuracy of prediction of response. The menopausal status of the patient is also important (see Bulbrook, 1966). Whether the ratio described by Miller *et al.* (1967) will be as useful as the discriminant when employed in conjunction with such factors in patients with advanced breast cancer has yet to be determined.

The most probable development in the future is likely to be the development of even more complicated methods of discriminating between responsive and unresponsive patients as the importance of steroids other than the androgens and corticoids is recognized and as the effect of biological variables such as free period and menopausal status are appreciated.

Bulbrook, Hayward, and Thomas (1964) found that the discriminant function was related to recurrence and death rate after mastectomy. The use of a simple ratio instead of the discriminant in these patients is now being evaluated.

Summary

In women with breast cancer there is a high degree of correlation between the urinary discriminant function 80–80 (17-OHCS mg./24 hours) + aetiocholanolone (μg./24 hours) and a simple ratio of total 11-deoxy-17-oxosteroids to the 17-OHCS.

In a retrospective study on 210 women with advanced breast cancer subjected to either adrenalectomy or hypophysectomy the prognostic values of both the discriminant function and the simplified ratio were virtually identical.

Easier analytical methods are used for the calculation of the 11-deoxy-17-oxosteroid : 17-OHCS ratio than for the calculation of the discriminant function.

REFERENCES

Appleby, J. I., Gibson, G., Norymberski, J. K., and Stubbs, R. D. (1955). *Biochem. J.*, **60**, 453.
Bulbrook, R. D. (1966). In *Clinical Evaluation in Breast Cancer*, edited by J. L. Hayward and R. D. Bulbrook, p. 77. London.
—— Greenwood, F. C., and Hayward, J. L. (1960). *Lancet*, **1**, 1154.
—— Hayward, J. L., and Thomas, B. S. (1964). Ibid., **1**, 945.
Hayward, J. L., and Bulbrook, R. D. (1965). *Cancer Res.*, **25**, 1129.
—— —— (editors) (1966). *Clinical Evaluation in Breast Cancer.* London.
Juret, P., Hayem, M., and Flaisler, A. (1964). *J. Chir. (Paris)*, **87**, 409.
Kellie, A. E., and Wade, A. P. (1957). *Biochem. J.*, **66**, 196.
Kumaoka, S., Abe, A., Sakauchi, N., Takatani, O., and Kusama, M. (1966). *Abstracts 9th Int. Cancer Congress, Tokyo*, p. 653.
Metcalf, M. G. (1963). *J. Endocr.*, **26**, 415.
Miller, H., Durant, J. A., Jacobs, A. G., and Allison, J. F. (1967). *Brit. med. J.*, **1**, 147.
Taylor, S. G. (1966). In *Clinical Evaluation in Breast Cancer*, edited by J. L. Hayward and R. D. Bulbrook, p. 205. London.
Thomas, B. S. (1965). *J. clin. Endocr.*, **25**, 710.
—— and Bulbrook, R. D. (1964). *J. Chromat.*, **14**, 28.
Wilson, R. E., Crocker, D. W., Fairgrieve, J., Bartholomay, A. F., Emerson, K., and Moore, F. D. (1967). *J. Amer. med. Ass.*, **199**, 474.

Effect of Cyclandelate on Mental Function and Cerebral Blood Flow in Elderly Patients

J. A. C. BALL,* M.D., B.SC., M.R.C.P.ED. ; A. R. TAYLOR,† M.A., M.B., F.R.C.S.

Brit. med. J., 1967, 3, 525–528

There is no demonstrable impairment in the ability of the cerebral blood vessels of elderly subjects to dilate in response to physiological stimuli (Lassen, 1959), but there is general agreement that chemical agents are relatively ineffective in producing such dilatation. Recently, however, reports have appeared that dilatation of cerebral vessels has occurred in response to cyclandelate (Eichhorn, 1965 ; Kuhn, 1965), and there is some uncontrolled evidence that cyclandelate produces an improvement in mental function in elderly patients (Drift, 1961 ; Ravina, 1963 ; Ward, 1964).

As the production of a substantial improvement in mental function in elderly patients would be of inestimable value, a controlled trial of cyclandelate has been made so that its effect on mental function and cerebral circulation in elderly patients could be investigated.

Present Trial

Selection of Patients.—From a population of approximately 200 patients in the long-stay wards of Wakehurst House, the Geriatric Unit of the Belfast City Hospital, 32 were selected whose disabilities were static and who were not so deaf, blind, or demented as to make the mental function tests used unsuitable. There were nine men (average age 75.6 years, range 57–98) and 23 women (average age 76.9 years, range 50–89).

Method.—The 32 patients were divided into two groups of 16 by randomly allocating to each either cyclandelate or placebo. Before the trial began one of us (J. A. C. B.) made a full clinical examination and carried out mental function tests on all the patients. Within 24 hours of the mental function tests mean cerebral circulation time was measured by the other of us (A. R. T.). The patients in group A were then given a 200-mg. tablet of cyclandelate and those in group B an inert tablet identical in size, shape, and colour four times daily for four months. Until the trial was completed only the hospital pharmacist knew which tablets contained cyclandelate.

Mental function tests and radiocirculograms were repeated after two months and again after four months.

Mental Function Tests

The tests used were chosen to illustrate as many aspects of mental function as possible. As most of the patients in the trial had considerable mental impairment only simple tests could be used. Each test consisted of a series of simple questions and a set of simple tasks, and took about 30 minutes to complete.

The questions were similar to those used by Isaacs and Walkey (1964) and determined spatial, temporal, and personal orientation. Short-term memory was assessed by the method of paired associates (Isaacs and Walkey, 1964). Constructional skill and spatial orientation were estimated by means of building blocks and a pegboard (Isaacs and Walkey, 1964 ; Adams and Hurwitz, 1963). To provide a measure of reason, imagination, and verbal expressive ability, the patients were asked to differentiate between a pond and a stream and between a ladder and a staircase and to describe a series of picture absurdities (Terman and Merrill, 1955).

In the final part of the mental function test patients were asked the battery of questions described under the headings of clinical sensorium test (Part 1), clinical questionary, and memory questionary used in the Institute of Psychiatry at the Maudsley Hospital for assessment of mental function in elderly patients (Shapiro *et al.*, 1956). These questions examined separately general orientation, memory for past personal events, memory for recent personal events, memory for general events, and ward orientation.

With the questions and the paired associates, one mark was given for each correct answer. In the tests with the building blocks and the pegboard, additional marks were given when assembly was completed quickly, and marks were deducted when demonstration or assistance was necessary or when the task was not finished within a set time.

Answers to the questions about differences and the responses to the picture absurdities were given up to five marks each, according to how close they came to predetermined levels of accuracy and appropriateness.

The scores obtained in the tests were dependent on the patient's alertness, concentration, and co-operation, but not on special skill, educational background, or social status.

Cerebral Circulation Time

The criterion adopted and thought to be the best simple indicator of blood flow was the mean circulation time (M.C.T.). This was obtained by the method described by Oldendorf (1963). In this, 50 μCi of ^{131}I Hippuran (iodohippurate) is rapidly injected to an antecubital vein and a stream or bolus of radioactivity approaches the head through the carotid and vertebral vessels after passage through the heart and lungs and holds together for one circulation through the cerebral blood pool. Its passage is detected by a collimated crystal directed through the inion towards a point 1 in. (2.5 cm.) above the nasion. Impulses are amplified and passed via a ratemeter to a pen-recorder. A typical curve of counts per second with time is seen in the upper part of Fig. 1. The height P (peak activity) is an indication of the flow rate, as are the angles of rise and fall of the curve. When the first order derivative of the activity curve is drawn, however, as in the lower part of Fig. 1, more accurate measurements can be made. This second curve shows the rate of change of activity with time and has positive and negative peaks indicating maximum rates of change in a positive and negative direction. These two points correspond to the passage of the dense central part of the bolus to and from the scanned area. The interval between the two points is the mean carotid-to-jugular time (M.C.T.). This is the time taken by the average blood cell to cross the cerebral blood pool, and varies in inverse ratio to the cerebral blood flow.

That there are many such times was shown by Nylin *et al.* (1960), who injected ^{32}P-labelled red cells into the carotid

---

* Physician (Geriatrics), Belfast City Hospital, Belfast.
† Neurological Surgeon, Royal Victoria Hospital, Belfast.

artery and monitored the radioactive stream in both jugular veins by mechanical sampling once every second. The first cells arrived in 1–2 seconds, and the last in 12–15 seconds. The average M.C.T. found by Nylin *et al.* in a group of normal patients was 7.3 seconds (standard error 0.9 second). This closely corresponds to an average M.C.T. of 7.41 seconds (S.E. 0.1 second) found here in a group of normal patients whose mean age was 32 years (Taylor and Bell, 1966).

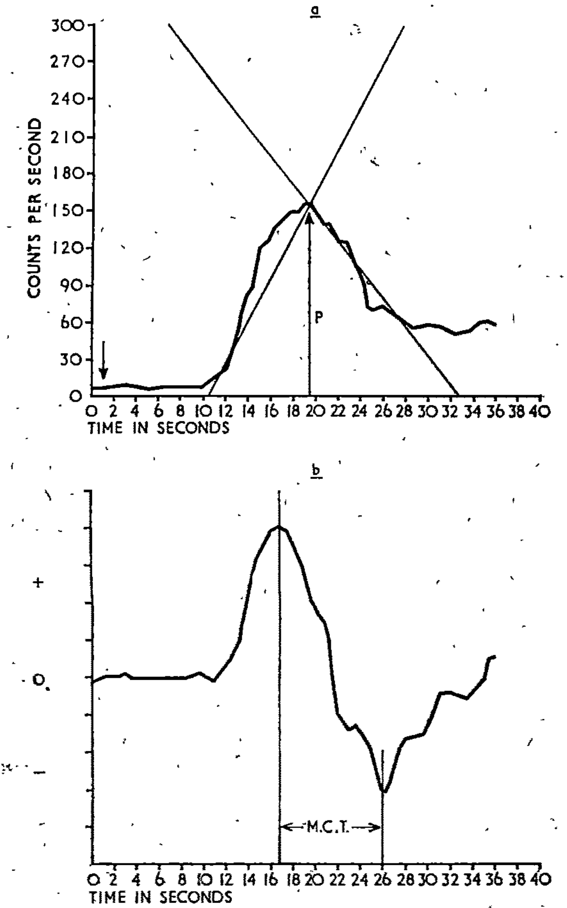


FIG. 1.—(a) Normal radiocirculogram. (b) Differentiated curve.

Course of the Trial

Three patients refused to take their tablets shortly after the trial began. Two of them were on cyclandelate and one on placebo. Four patients died during the course of the trial; one was on cyclandelate and three were on placebo. One patient on placebo was too ill at the end of the first trial period for mental function testing to be possible. Mental function tests were thus completed on three occasions on each of the remaining 24 patients, 13 of whom were on cyclandelate and 11 on placebo.

One patient who had completed four months' treatment with cyclandelate had a right cerebral thrombosis on the morning after her mental function test. The results of this test have been included in the analyses, but further cerebral circulation studies were not made. Another patient, also on cyclandelate, had a technically unsuccessful radiocirculogram, the results of which could not be analysed. Three successful radiocirculograms were thus performed on each of 22 patients, 11 of whom were on cyclandelate and 11 on placebo.

Results

In all the analyses a result is termed significant when the probability of its occurrence by chance is less than 0.05.

Comparison of the ages of the patients in each of the two groups by use of a *t* test showed that, on average, they were not significantly different. Calculation of exact probability showed that the distribution of males and females between the two groups of patients was random (P (double tail) = 0.67918). There was no significant difference between the average initial scores in the mental function tests or in average initial mean circulation times in the two groups.

The two groups of patients were therefore comparable initially.

Mental Function Tests

The analysis of the results of the mental function tests is set out in Table I. Analysis was made of the differences between the average initial scores and the average scores obtained after the first and the second treatment periods in each of the two groups, and the differences between the average scores on each occasion in the two groups. The scores obtained at the end of the first and the second periods were also compared with each other in order to show whether continuation of treatment for the second two months resulted in further significant change.

After the first two months group A patients obtained significantly higher average scores in the tests with the differences and picture absurdities (which were considered together), and with the pegboard. After four months significantly higher average scores were obtained in all the mental function tests except those with the paired associates and the building blocks.

TABLE I.—*Analysis of Results of Mental Function Tests*

	Group	Mean Test Score			Mean Test Score Differences			Standard Error of Mean Differences		
		I	II	III	I–II	II–III	I–III	I–II	II–III	I–III
Questions	A	6·54	7·15	8·85	+0·61	+1·70*	+2·31*	0·42	0·38	0·55
	B	6·91	7·00	6·27	+0·09	−0·73	−0·64	0·48	0·38	0·65
	A−B	−0·37	+0·15	+2·58	+0·52	+2·43*	+2·95*	0·63	0·54	0·85
Paired associates	A	10·00	11·92	11·62	+1·92	−0·30	+1·62	1·17	0·73	0·92
	B	9·55	10·82	10·82	+1·27	+0·00	+1·27	0·98	0·80	1·11
	A−B	+0·45	+1·10	+0·80	+0·65	−0·30	+0·35	1·53	1·08	1·44
Differences and pictures	A	14·62	17·85	19·38	+3·23*	+1·53	+4·76*	1·04	1·15	1·33
	B	14·27	15·54	16·18	+1·27	+0·64	+1·91	1·85	0·88	1·72
	A−B	+0·35	+2·31	+3·20	+1·96	+0·89	+2·85	2·12	1·45	2·17
Building blocks	A	4·15	4·54	4·00	+0·39	−0·54	−0·15	0·31	0·35	0·32
	B	3·18	3·55	3·91	+0·37	+0·36	+0·73	0·38	0·36	0·51
	A−B	+0·97	+0·99	+0·09	+0·02	−0·90	−0·88	0·50	0·51	0·60
Pegboard	A	5·85	6·92	7·15	+1·07*	+0·23	+1·30*	0·49	0·57	0·44
	B	5·82	7·00	6·82	+1·18	−0·18	+1·00	0·81	0·60	0·98
	A−B	+0·03	−0·08	+0·33	−0·11	+0·41	+0·30	0·94	0·82	1·08
Maudsley questions	A	24·31	24·38	30·46	+0·07	+6·08*	+6·15*	1·05	0·96	1·39
	B	23·55	23·55	23·00	+0·00	−0·55	−0·55	0·92	0·85	1·10
	A−B	+0·76	+0·83	+7·46	+0·07	+6·63*	+6·70*	1·40	1·28	1·77

I = Initial. II = After first treatment period. III = After second treatment period. * Significant result at $P < 0{\cdot}05$.

Group B patients showed no significant improvement in the average scores obtained in any of the mental function tests at the end of either treatment period.

Radiocirculograms

The positive and negative peaks of the rate of change of activity curve can be precisely defined in normal records. Where the circulation is greatly slowed, however, as it was in most of the patients studied, the rate of change of activity as the bolus leaves the cerebral circulation is small and the negative peak may be blurred or double (Fig. 2). To define this peak the curve has to be artificially smoothed, and this introduces a possible error of one to two seconds. The curves were read by us, by a third doctor (not associated with the trial), and by an architect without medical knowledge. The architect's method of smoothing the curves differed slightly from ours and his mean circulation times, in doubtful cases, were consistently a little longer, but the results in terms of improvement or worsening were the same in all cases.

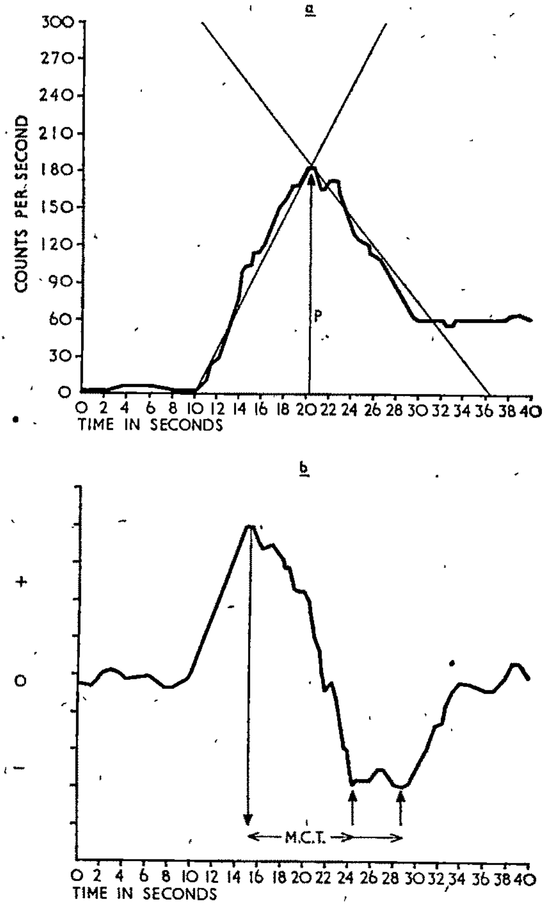


FIG. 2.—(*a*) Abnormal radiocirculogram. (*b*) Differentiated curve showing double negative peak.

The analysis of the results of the radiocirculograms is set out in Table II. Over the four-month period the average mean circulation time in group A patients decreased by 0.86 second (S.E. 0.39 second), and in group B patients there was an average increase of 0.55 second (S.E. 0.43 second). These average mean circulation-time changes are not significant. However, when the changes in group A are compared with those in group B, the average mean circulation-time difference 1.41 seconds (S.E. 0.58 second), is significant.

Correlation Between Mental Function Test Scores and Mean Circulation Times

Absolute values of cerebral blood flow can be derived from mean circulation times when the constants of proportion are known (Oldendorf, 1963). These constants depend on total blood volume and the ratio of brain blood volume to total blood volume, and therefore vary greatly from patient to patient.

If it is assumed that mental function test scores are related to cerebral blood flow, the constants of proportion would again be expected to vary greatly from patient to patient.

Two different kinds of constant, both of unknown value, are thus involved in the relation between mental function test scores and mean circulation times. In order to test for a relation by use of the figures obtained in the present trial, it was necessary to derive an expression in which the unknown constants did not appear.

The relation between mean circulation time in seconds (m) and cerebral blood flow in litres per minute (c) is

$$m = \frac{K}{c}$$

Where the constant K is dependent on total blood volume and the ratio of total blood volume to brain blood volume.

If mental function test score (x) is proportional to cerebral blood flow, then x=kc.

So that $$m = \frac{Kk}{x} \qquad \text{(I)}$$

As in any one patient Kk will be constant, m will vary inversely as x, and if m and x change then

$$m + dm = \frac{Kk}{x+dx} \qquad \text{(II)}$$

where dm represents the change in m and dx represents the change in x.

Subtracting (I) from (II)

$$dm = Kk\frac{-dx}{x(x+dx)}$$

and dividing by (I) to eliminate Kk

$$dm = \frac{-mdx}{x+dx}$$

A significant positive correlation between dm and the expression $-\frac{mdx}{x+dx}$ would support the hypothesis that mental function test scores vary with cerebral blood flow. Low correlation coefficients would suggest that the two are not related.

Correlation coefficients were calculated between changes in mean circulation time over the whole period of the trial and the changes in score in each separate section of the mental function tests as incorporated in the derived expression. In the calculations a few results had to be neglected because the numerator or the denominator of the expression became zero. None of the correlation coefficients so calculated was significant.

TABLE II.—*Analysis of Results of Radiocirculograms*

Group	Average Mean Circulation Times			Average Mean Circulation Time Differences			Standard Error of Mean Differences		
	I	II	III	I–II	II–III	I–III	I–II	II–III	I–III
A	12·64	11·96	11·77	−0·68	−0·18	−0·86	0·42	0·54	0·39
B	12·14	12·36	12·68	+0·23	+0·32	+0·55	0·39	0·51	0·43
A−B	+0·50	−0·40	−0·91	−0·91	−0·50	−1·41*	0·57	0·74	0·58

* Significant result at $P < 0{\cdot}05$.

Patients' and Ward Sisters' Opinions

Four of the patients on cyclandelate and three of those on placebo thought that the tablets had done them good.

The ward sisters were asked to say if the tablets had had any effect on the patient's general mental state. They thought that there had been no change in 18 of the patients, that 4 patients on placebo and 2 on cyclandelate had improved, and that none was made worse.

An examination made of all the patients who remained on treatment until the end of the trial showed that there had been no change in their general clinical condition.

Side-effects

Only one patient complained of any ill effect from the tablets, saying that they made her dizzy. She was persuaded to continue taking tablets, which later turned out to be placebo.

Discussion

The improvement which occurred in mental function in group A patients was not expected, and yet in the tests with the questions and in those described by Shapiro *et al.* (1956) the increase in the scores was highly significant ($P<0.001$).

The design of the trial ensured that bias on the part of the investigators, ward staff, or patients was removed; but the number of patients involved was small, and became smaller by the end of the four-month trial period. The assessment of improvement was made on the basis of an arbitrary scoring system, and the analysis of the score figures is made on the assumption that these are normally distributed. With such a small number of figures, however, it is not possible to validate or invalidate this assumption.

Nevertheless, as a significant improvement in mental function did occur in group A patients and not in group B patients, it must be concluded that the improvement was brought about by the action of cyclandelate.

The radiocirculogram results showed an average decrease in mean circulation time, indicating an average increase in cerebral blood flow only in group A patients. When the two groups were compared with each other the difference in the average mean circulation times over the four-month period was significant. It must be pointed out, however, that the change became significant only because group A showed a decrease in mean circulation time whereas group B showed an increase.

In patients with advanced arteriosclerosis, mean circulation times are prolonged and cerebral blood flow decreased (Nylin *et al.*, 1960). Parallelism has been found between decreased mental function and reduced cerebral blood flow (Schmidt, 1950).

A change in mean circulation time indicates a proportional change in cerebral blood flow, so that should changes in mental function test scores result from changes in cerebral blood flow correlation between mean circulation time differences and the expression relating them to mental function test score differences would be expected, but no such correlation was found.

Eichhorn (1962), in a study of patients with hypertensive encephalopathy, made the interesting observation, from detailed analysis of the rising slope of his blood-flow curves, that the improvement which occurred was in the precapillary (arteriolar) phase of the circulation. He concluded that improvement was caused by a more efficient distribution of the available blood rather than to an increase in total flow.

The improvement in mental function brought about by the action of cyclandelate may similarly result from a redistribution of, rather than a total increase in, cerebral blood flow.

It has been suggested that the decrease in cerebral blood flow encountered in elderly patients involves preponderantly those areas in which perfusion normally is relatively high (Sokoloff, 1960). Even minor increases in flow to such relatively ischaemic areas might well result in their improved function.

Summary

A controlled clinical trial is described in which the effect of prolonged administration of cyclandelate on mental function and cerebral flow in elderly patients was tested. Group A patients were given cyclandelate and group B patients were given a placebo, each for a period of four months.

A significant improvement in the results of mental function tests occurred only in group A patients.

An increase in the average cerebral blood flow occurred in group A patients and a decrease occurred in group B patients. Neither of these changes was itself significant, but when the two groups were compared with each other a significant difference occurred between them.

As there was no significant correlation between the changes in patients' scores in the mental function tests and changes in their mean circulation times, it is suggested that cyclandelate may bring about an improvement in mental function by producing a redistribution of blood flow within the cerebral circulation rather than an absolute increase in it.

We wish to thank Dr. J. D. Merrett for his help with the statistics; Mrs. E. T. Hutchinson and Mr. J. Coulter, who dispensed the tablets; Mr. Richard Wall, of Messrs. Brocades (Great Britain) Ltd., for supplies of cyclandelate and placebo and for much helpful criticism; and Miss M. Carey and Miss E. Johnston who prepared the manuscript.

Details of the mental function tests and of the scoring system used, together with individual test scores, mean circulation times, and their correlation coefficients, can be obtained on application to J. A. C. Ball.

REFERENCES

Adams, G. F., and Hurwitz, L. J. (1963). *Lancet*, **2**, 533.
Drift, J. H. A. van der (1961). *Angiology*, **12**, 401.
Eichorn, O. (1962). *Medicamundi*, **8**, 76.
—— (1965). *Vasc. Dis.*, **2**, 305.
Isaacs, B., and Walkey, F. A. (1964). *Geront. Clin. (Basel)*, **6**, 114.
Kuhn, R. A. (1965). "The Effects of Cyclandelate Upon Cerebral Blood Flow in Patients with 'Stroke.'" American College of Angiology, July 1965.
Lassen, N. A. (1959). *Physiol. Rev.*, **39**, 183.
Nylin, G., Silfverskiöld, B. P., Löfstedt, S., Regnström, O., and Hedlund, S. (1960). *Brain*, **83**, 293.
Oldendorf, W. H. (1963). *Nucleonics*, **21**, No. 4, p. 87.
Ravina, A. (1963). *Presse méd.*, **71**, 727.
Schmidt, C. F. (1950). *The Cerebral Circulation in Health and Disease*. Springfield, Illinois.
Shapiro, M. B., Post, F., Löfving, B., and Inglis, J. (1956). *J. ment. Sci.*, **102**, 233.
Sokoloff, L. (1960). In *Handbook of Physiology*, edited by J. Field, H. W. Magoun, and V. E. Hall, Sect. 1, vol. 3, p. 1843. Baltimore.
Taylor, A. R., and Bell, T. K. (1966). *Lancet*, **2**, 178.
Terman, L. M., and Merrill, M. A. (1955). Printed Card Material for Revised Stanford–Binet Tests, Form M, Picture Absurdities. London.
Ward, P. J. (1964). *Med. Dig. (Lond.)*, **9**, 525.

Glossopharyngeal and Vagal Neuralgia

JAGDISH C. CHAWLA,* F.R.C.S.; MURRAY A. FALCONER,† M.CH. F.R.C.S.

Brit. med. J., 1967, 3, 529–531

Tic douloureux involving the glossopharyngeal nerve is rare and when it does occur probably often involves the vagus nerve as well. Many cases are undoubtedly not recognized, and yet the condition responds favourably and permanently to intracranial section of the glossopharyngeal nerve and upper filaments of the vagus nerve. We therefore propose to review the literature, discuss our own experiences, and try to clarify the clinical syndromes that this condition presents and the surgical approach that is required.

Review of the Literature

The condition of glossopharyngeal neuralgia was first described by Weisenburg (1910), who recognized it in a patient with a tumour of the cerebellopontine angle. In most cases, however, there is no known pathological condition. Harris (1926) described it as the idiopathic glossopharyngeal neuralgia. The usual description is of paroxysms of pain of a stabbing or lancinating character located in the base of the tongue and faucial region on one side, and provoked by swallowing, talking, and coughing. When the pain is severe the patient may not even be able to swallow his own spittle. Bouts of recurrent pain may last a few minutes, hours, or even days at a time, each individual stab, however, being momentary. The majority of patients are elderly, and in our series of 10 cases the ages ranged from 32 to 77 (average 62.6 years). Males are more often affected than females (9 to 1 in our series). Similar observations were made by Dandy (1927), but Bohm and Strang (1962) reported an equal occurrence in the sexes. As time goes by, however, recurrent bouts of pain tend to become more frequent and the periods of remission shorter.

One of the largest series so far reported is that of Bohm and Strang (1962), who made the point that the pain could radiate in other directions, notably into the vagal territory. This has been our experience also. Quite often the stabs of pain are felt deep in the external meatus of the ear and beneath the angle of the jaw, and sometimes even deeply in front of or behind the external auditory meatus. In some cases it may reach the tragus of the ear (with a trigger area there), but the main site of the pain is deep. When this occurs differential diagnosis from atypical forms of third-division tic douloureux becomes difficult (see below).

The surgical treatment reflects these difficulties in diagnosis as well as the efficacy of the various surgical approaches. There are three approaches, which may be described as cervical, tonsillar, and intracranial. The first successful approach was that of Sicard and Robineau (1920), who carried out a dissection of the glossopharyngeal nerve and pharyngeal branch of the vagus nerve in the neck and avulsed them. Harris (1926) was uncertain of the involvement of the vagus nerve and wondered whether section of the pharyngeal branch of the vagus nerve was necessary. Dandy (1927) also at first suggested that the vagus nerve is not implicated, and later advocated the intracranial approach with section of the upper filaments of the vagus nerve in addition to the glossopharyngeal nerve (Dandy, 1945). Adson, in 1925, was the first to use this approach, but his intervention was first reported by Love (1944). Dandy (1945) did record two cases in which, after intracranial section of the glossopharyngeal nerve alone, pain persisted, but it disappeared after a second operation in which the upper vagal rootlets were cut, an experience which Bohm and Strang (1962) also shared. Wilson and McAlpine (1946) reported a single case in which the glossopharyngeal nerve had been dissected in its tonsillar bed and avulsed with relief. Our experience, however, suggests that recurrence can arise after this procedure, and has led us to recommend intracranial section of the glossopharyngeal nerve plus section of the upper two vagal rootlets.

Present Series

This study is based on a review of 10 patients admitted to this unit for treatment of glossopharyngeal neuralgia, with reference to type of pain, its aggravating factors, surgical treatment, and other relevant observations (see Table).

Duration and Type of Pain

The length of history varied from 15 months to 15 years. The pain was paroxysmal, and was described as lancinating or lightning-like jabs. The paroxysms occurred in characteristic bouts lasting from a few seconds to two minutes. Dandy (1927) wrote that the pain rarely lasted over a minute. In one of our cases, however, some bouts lasted up to five minutes, and paroxysms of pain continued to occur at frequent intervals throughout the day over a period of a few days to a few weeks before a spontaneous period of remission ensued. The pain is very severe, and in Case 3 the paroxysms occurred so often that section of the glossopharyngeal nerve was performed as an emergency to enable the patient to swallow. The period of remission before operation was also variable in this series: the longest was four years (Cases 1 and 4). Adson (1924) reported a remission of three years and nine months. One observation which stands out in this series is that the periods of remission become shorter with ensuing attacks, but an identical pain always returns in the same area of distribution.

The location and distribution of pain in this series was always unilateral, and was as follows (see Table): back of tongue (Cases 9 and 10), fauces (Cases 3 and 10), tonsillar region (Case 7), deep in the ear (Cases 1, 2, 5, and 6), in front of or behind the ear (Cases 2 and 5), deep to the angle of the jaw (Cases 3, 5, 6, and 8), deep in the upper side of the neck (Cases 1, 4, and 8), and deep in the throat (Cases 1 and 2). Only one patient (Case 9) had pain confined to the back of the tongue with no radiation.

Aggravating Factors

The commonest method of precipitating attacks of the pain was swallowing, but attacks were also induced in other ways, such as coughing, sneezing, talking, touching the tragus of the ear, turning the head towards the side of pain, and rolling towards the site of pain.

In only one patient (Case 4) was there a trigger zone. His pain was brought about by touching the tragus on the painful side, but in three other patients the tragus was also sensitive.

---

* Registrar, Guy's-Maudsley Neurosurgical Unit, London S.E.5.
† Director, Guy's-Maudsley Neurosurgical Unit, London S.E.5.

Other Observations

There was no seasonal influence on the symptomatology, except in one patient (Case 1) who had pain only in winter. One patient (Case 2) had vertigo without tinnitus or deafness. Bohm and Strang (1962) reported two similar cases. None of our patients had any sensory impairment in the area of the distribution of pain. All were symptom-free in between attacks of pain, apart from one patient (Case 1) who complained of a hot, flushed feeling in the affected area between the bouts of pain. Our follow-up periods (excluding one patient (Case 7) who died postoperatively) have ranged from four and a half weeks to six years, and all patients appear to have been relieved during that time.

Treatment

Seven out of the ten patients were treated by section of the glossopharyngeal nerve and the upper rootlets of the vagus nerve, and two by section of the glossopharyngeal nerve alone. One patient (Case 10) was pain-free on admission, but was admitted later to another neurosurgical unit with recurrent pain. He was operated on and remained free from pain until he committeed suicide because of depression. The postoperative death, on the 11th day, on a 77-year-old patient, was due to intestinal obstruction (Case 7). Seven out of the remaining eight patients with an adequate follow-up have remained pain-free. The eighth patient (Case 9) originally had pain in the back of the tongue on one side, and after operation was free of pain for four months. Pain then occurred in the lower jaw. He was treated by alcohol injection of the trigeminal ganglion and has since remained pain-free. It is possible that he had both glossopharyngeal and trigeminal neuralgia. Bohm and Strang (1962) described a similar case in which second division trigeminal neuralgia occurred five years after a glossopharyngeal section.

Postoperative Course

Only one patient (Case 4) had transient difficulty in swallowing. Six patients showed detectable sensory depression in the oropharynx, the faucial region, the posterior third of the tongue, and the adjacent half of the soft palate. Two patients had sensory depression in the concha, one of them having had no sensory depression in the oropharynx. In one case no mention of any sensory loss was recorded. Another patient (Case 3) developed transient auricular flutter after he had undergone glossopharyngeal section with the upper rootlets of the vagus.

Discussion

Compared with trigeminal neuralgia, glossopharyngeal neuralgia is relatively rare. Bohm and Strang (1962) showed an incidence of 1% in Olivecrona's material, and Harris (1937) an incidence of 0.57%. The corresponding figure for this neurosurgical unit is 0.75%.

The presence of a trigger zone is a rare finding, though there may be areas tender and sensitive to touch. One case in our series involved the tragus (Case 4). Harris (1926) remarked on the absence of trigger zones and thought it to be the main difference between glossopharyngeal and trigeminal neuralgia. However, cases with a trigger zone in the faucial region have been described (Dandy, 1927).

The location, distribution, and radiation of pain lie in the area of sensory supply of the glossopharyngeal nerve and of the auricular and pharyngeal branches of the vagus nerve—i.e., propharynx, concha of the ear, and deep to the angle of the jaw. Dandy (1927) implicated Jacobson's nerve in the radiation of pain to the ear, and described the radiation of pain to the angle of the jaw and concha as referred. Keith (1932) described pain in the regions of the upper part of the neck, the angle of the jaw, and the cheek, nose, and eyes, and regarded them as overflow phenomena. We think that pain deep to the angle of

Salient Features of Cases in Chronological Order

Case No.	Age and Sex	Duration of History of Pain Before Operation	Chief Site of Pain	Radiation	Aggravating Factor	Trigger Area	Treatment (Intracranial)	Duration of Follow-up	Results and Remarks
1	59 F	9 years	Deep in ear	Deep in side of neck	Swallowing. Washing concha		Division of 9th nerve and upper two rootlets of vagus	6 years	Section of 9th cranial nerve in neck 9 months previously. Pain-free since intracranial operation. Sensory depression faucial region and posterior part of tongue
2	50 M	7 „	Deep in ear	Throat and behind ear	Swallowing. Coughing			5 „	Pain-free. Sensory depression in concha
3	76 M	3 „	Faucial region	Angle of jaw	Swallowing. Talking			2 „	Death due to acute abdomen; pain-free for the period
4	57 M	10 „	Deep in side of neck at end of thyroid cartilage	Ear	Swallowing	Tragus		3 „	Pain-free. Sensory depression in concha
5	64 M	15 months	Deep in ear	Back of ear and angle of jaw	Swallowing	Tragus sensitive to touch		4 „	Pain-free. Sensory depression faucial region and soft palate
6	77 M	5 years	Deep in side of throat	Deep in angle of mandible and deep in ear	Swallowing. Coughing. Turning head to side of pain	Tragus sensitive		2 „	Pain-free. Sensory depression faucial region and posterior part of tongue
7	77 M	15	Tonsillar region	Nil	Swallowing. Coughing. Eating		Division of 9th nerve		Had section of 9th nerve in tonsillar bed 14 years before admission and remained pain-free for 12 years. Death on 11th postoperative day from bronchopneumonia and intestinal obstruction
8	32 M	2 „	Tragus	Deep to angle of mandible other side of throat	Swallowing. Talking. Brushing teeth	Tragus sensitive	Section of 9th nerve and upper two rootlets of vagus	4½ weeks	Did not turn up for follow-up. Pain-free postoperatively, but address unknown
9	61 M	2 „	Back of tongue		Rolling of tongue to side		Section of 9th nerve	18 months	Pain recurred in 3rd division of trigeminal; has remained pain-free after alcohol injection
10	73 M	4½ „	Faucial region	Back of tongue			Section of 9th nerve at another neurosurgical unit	3 „	Pain-free till suicide because of depression

the jaw, upper cervical region, and concha is due to involvement of the auricular branch of the vagus nerve. We did not observe overflow to the cheek, nose, or eyes. Bohm and Strang (1962) subdivided their series into two groups—oropharyngeal and aural—according to the main symptomatology, but patients usually present with pain in both zones concurrently. Typically there is no sensory impairment in the area of pain, as there usually is when tumours of the cerebellopontine angle or base of the skull are present.

The clinical picture of "idiopathic glossopharyngeal neuralgia" is so characteristic that diagnosis is seldom difficult. Glossopharyngeal neuralgia, however, may be confused with trigeminal neuralgia in patients with pain in the region of the tragus or deep to the angle of the jaw.

There is some evidence that glossopharyngeal neuralgia may be controlled by medication—for example, vitamin B complex, Tegretol (carbamazepine)—but no proof that the relief is lasting. Treatment of this neuralgia is essentially surgical. It has passed through various stages from dissection and avulsion of the glossopharyngeal nerve and pharyngeal branch of the vagus nerve in the neck to the intracranial section of the glossopharyngeal nerve alone or combined with the upper two rootlets of the vagus nerve. However, the avulsion of nerves in the neck has often been followed by recurrence of pain over a period of time—for example, Case 1—as has avulsion in the tonsillar fossa (Case 7). The treatment of choice remains the intracranial section of the glossopharyngeal nerve and upper two rootlets of the vagus nerve, as we feel that the latter nerve is also implicated. In skilled hands this operation carries a negligible mortality and can be performed on elderly patients.

Surgical Approach

This is essentially the approach by Dandy (1927), though nowadays it is facilitated by operating on the patient in the upright position. The legs should also be raised or bandaged in elderly patients to prevent postural arterial hypotension. The procedure is carried out through a small suboccipital craniectomy under endotracheal anaesthesia. Enough bone is removed to expose the lateral sinus above and the sigmoid sinus laterally—that is, about 3–4 cm. diameter. The dura is opened, with a small flap swung laterally over the sigmoid sinus. The cerebellopontine angle is opened up after the posterior fossa has been slackened either by slipping a retractor over the cerebellar hemisphere and opening the cisterna magna or by releasing a previously placed lumbar puncture needle. The rootlets of the ninth, tenth, and eleventh cranial nerves are seen arranged in a vertical column from above down. The ninth cranial nerve is a single filament normally separated from the multiple filaments of the tenth nerve by a dural isthmus as the nerves pass out through the jugular foramen. The ninth cranial nerve is hooked up and sectioned at this position, followed by section of the upper two rootlets of the vagus. In closing the craniectomy the dura is sutured back into position. The patient is usually sitting out of bed on the first day, and relieved of pain from the time of operation.

Summary

Ten cases of glossopharyngeal neuralgia have been studied and the literature has been reviewed. A more correct classification would be to describe the condition as "glossopharyngeal and vagal neuralgia." Evidence is given to support this view. Intracranial section of the glossopharyngeal nerve and the upper two rootlets of the vagus nerve is the operation of choice.

We wish to thank Mr. P. H. Schurr and Mr. J. J. Maccabe for permission to include their cases, and also our various neurological colleagues, particularly Dr. M. J. McArdle, for entrusting us with patients under their care.

References

Adson, A. W. (1924). *Arch. Neurol. Psychiat. (Chic.)*, **12**, 487.
Bohm, E., and Strang, R. R. (1962). *Brain*, **85**, 371.
Dandy, W. E. (1927). *Arch. Surg.*, **15**, 198.
—— (1945). Reprinted in 1966 as *The Brain*, p. 191. Hagerston, Maryland.
Harris, W. (1926). *Neuritis and Neuralgia*. New York.
—— (1937). *The Facial Neuralgias*. London.
Keith, W. S. (1932). *Brain*, **55**, 357.
Love, J. G. (1944). *Surg. Clin. N. Amer.*, **24**, 959.
Sicard, R., and Robineau, M. (1920). *Rev. neurol.*, **36**, 256.
Weisenburg, T. H. (1910). *J. Amer. med. Ass.*, **54**, 1600.
Wilson, C. P., and McAlpine, D. (1946). *Proc. roy. Soc. Med.*, **40**, 82.

Haemoglobin F Hull (γ 121 Glutamic Acid → Lysine), Homologous with Haemoglobins O Arab and O Indonesia

L. S. SACKER,* M.D., M.C.PATH; D. BEALE,† PH.D.; A. J. BLACK,‡ M.B., B.CHIR., D.OBST.R.C.O.G.
R. G. HUNTSMAN,‡ M.D., M.R.C.P., M.C.PATH.; H. LEHMANN,† M.D., SC.D., F.R.C.P., F.C.PATH.
P. A. LORKIN,† B.A.

Brit. med. J., 1967, **3**, 531–533

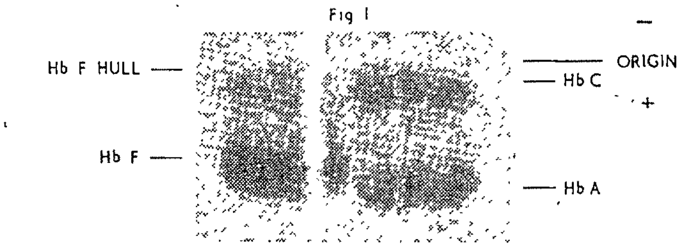
A haemoglobin variant is the result of an amino-acid substitution in one of the two pairs of polypeptide chains which constitute the haemoglobin molecule. Foetal haemoglobin (Haemoglobin F) has a pair of α-chains and a pair of γ-chains, and is denoted as $\alpha_2\gamma_2$. Variants of Haemoglobin F may thus be divided into two groups, those with abnormal α-chains and those with abnormal γ-chains.

An α-chain substitution gives rise not only to a variant of Haemoglobin F, but also to a variant of Haemoglobin A ($\alpha_2\beta_2$) and a variant of Haemoglobin A_2 ($\alpha_2\delta_2$) in the same individual. A γ-chain substitution, in contrast, can give rise only to a variant of Haemoglobin F. In the same way a β-chain substitution can give rise only to a variant of Haemoglobin A; most of the common haemoglobin variants—for example, Haemoglobins S, C, D, and E—are β-chain variants.

Few γ-chain variants have been described, and in only one case, that of Haemoglobin F Texas I, has the amino-acid substitution been identified (Schneider and Jones, 1965; Jenkins, Beale, Black, Huntsman, and Lehmann, 1967). We here describe a new γ-chain variant and define its amino-acid substitution. The variant, which is designated Haemoglobin F Hull, was first found as an electrophoretically slow component of the cord-blood haemoglobin of a normal baby of native English stock (Fig. 1). It made up 14% of the total haemoglobin, determined by the method of Marengo-Rowe (1965). It was found again in the cord blood of a subsequent baby born to the same parents, comprising 9% of the total haemoglobin. This baby was born after 30 weeks of gestation and died of prematurity after a few days. A third example of the variant was found in a healthy baby born to parents who are, so far as is known, unrelated to the first family, though both families live in the same town (Kingston-upon-Hull). The variant comprised 7% of the cord-blood haemoglobin of this baby. Although twice found in Hull families, the variant has not been observed again during a survey of 12,000 cord bloods in Britain.

---

* Consultant Haematologist, Hull A and B Groups of Hospitals.
† Medical Research Council Abnormal Haemoglobin Research Unit, University Department of Biochemistry, Cambridge.
‡ St. Thomas's Hospital Medical School, London S.E.1.



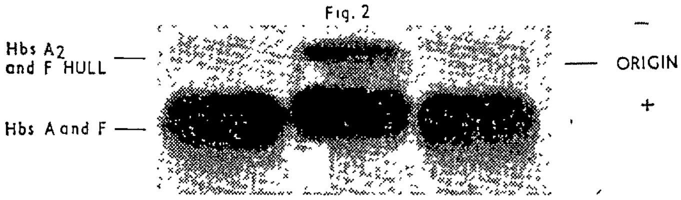


FIG. 1.—Haemoglobin electrophoresis on paper at *p*H 8.9 (barbiturate buffer). Left: cord blood containing Haemoglobin F Hull. Right: adult heterozygous for Haemoglobin C.

FIG. 2.—Haemoglobin electrophoresis on paper at *p*H 8.9 (tris buffer). Centre: cord blood containing Haemoglobin F Hull (near origin). Left and right; blood from the parents of this infant; Haemoglobin A_2 is shown near origin. The electrophoretic mobilities of Haemoglobins A_2 and F Hull are similar.

The abnormal haemoglobin was thought to be a variant of Haemoglobin F for the following reasons:

(1) It was absent from the blood of the parents (Fig. 2) in both families. An examination of the antigens of nine blood group systems in parents and children failed to provide evidence of aberrant paternity in any of the three cases.

(2) The ultraviolet spectrum of the isolated variant haemoglobin showed a clearly resolved tryptophan fine structure band at 289 mμ (Fig. 3). This is a characteristic feature of Haemoglobin F and its γ-chain variants.

(3) The amount of the variant present in the blood of the two surviving infants declined during the first few months of life.

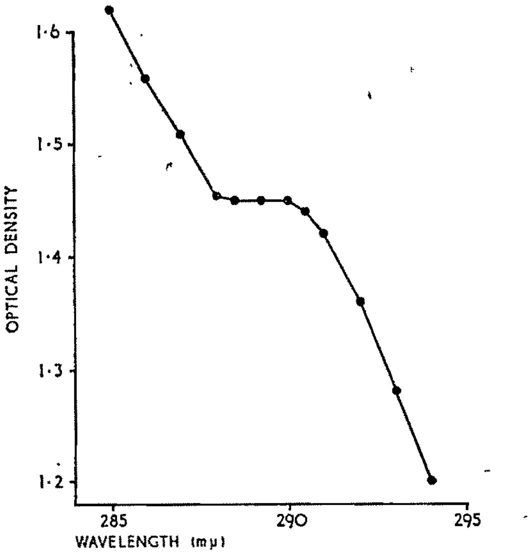


FIG. 3.—Ultraviolet spectrum of the isolated haemoglobin variant, showing the tryptophan fine structure band.

On paper electrophoresis at *p*H 8.9 Haemoglobin F Hull moved slightly more slowly towards the anode than Haemoglobin C (Fig. 1). The distance between the variant and Haemoglobin F was approximately the same as that between Haemoglobin C and A. If this difference in mobility is due to a single mutation it can be assumed that, as in Haemoglobin C, a positively charged amino-acid residue has taken the place of a negatively charged residue in each of the two abnormal polypeptide chains. The nature of the genetic code (Nirenberg *et al.*, 1965) is such that a charge change of this type is due to a substitution of glutamic acid by lysine (Beale and Lehmann, 1965).

In order to define the amino-acid substitution more fully, the haemoglobin was converted to globin, and peptide maps ("fingerprints") were prepared according to the procedures of Ingram (1958) and Baglioni (1961); these procedures have been described in detail by Beale (1966). Fingerprints of pure Haemoglobin F, isolated from normal cord blood by chromatography at pH 6 according to Huisman and Prins (1955), were prepared simultaneously with those of the variant.

Fingerprints of the variant when compared with those of Haemoglobin F (Fig. 4 A and B) showed that the spot corresponding to the thirteenth tryptic peptide of the γ-chain (peptide γTpXIII), marked 1 in Fig. 4 A and B, was absent in the variant. This peptide (γTpXIII) contains residues 121–132 of the 146 composing the γ-chain. Number 121, the first in this sequence, is a glutamic acid residue. Two abnormal peptide spots, which are marked 2 and 3 in Fig. 4, had appeared. Peptide 2 is positively charged, while peptide 3 is neutral. The abnormal peptides were eluted with constant-boiling HCl and analysed for their amino-acids (Spackman, Stein, and Moore, 1958). The results are shown in Table I. The abnormal positively charged peptide contains one extra lysine and one glutamic acid residue less when

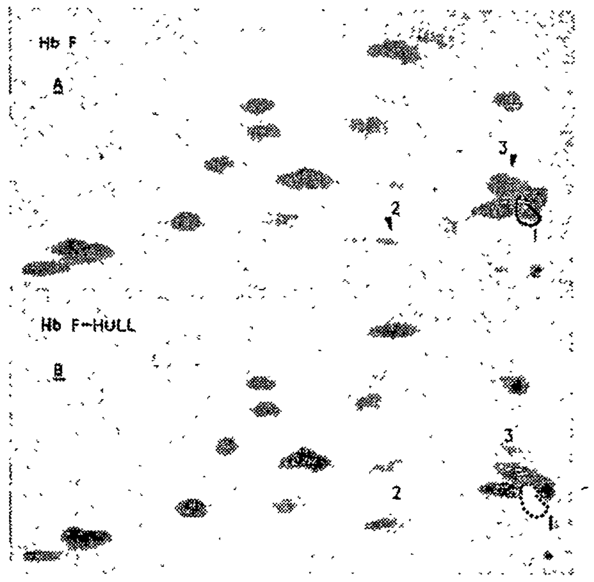


FIG. 4.—Fingerprints of (A) Haemoglobin F and (B) Haemoglobin F Hull.

TABLE I.—*Amino-acid Composition of the Hydrolysates of the Two Abnormal Peptides in the Fingerprints of Haemoglobin F Hull*

	Peptide 2 (Positively Charged)		Peptide 3 (Neutral)	
	μmole	Molar Ratio	μmole	Molar Ratio
Thr	0·015	1·2	0·012	1·1
Ser	0·021	1·3	0·015	1·4
Glu	0·049	3·0	0·030	2·7
Pro	0·014	0·9	0·014	1·3
Ala	0 016	1·0	0·013	1·2
Val	0·018	1·1	0·009	0·8
Phe	0·015	0·9	0·008	0·7
Trp	+	(1)	+	(1)
Lys	0·030	1·8	0·011	1·0
Total ..		12		11

TABLE II.—*Amino-acid Sequences of the Two Abnormal Peptides in the Fingerprints of Haemoglobin F Hull, Compared with the Normal Peptide γTpXIII of Haemoglobin F According to Schroeder, Shelton, Shelton, Cormick, and Jones (1963)*

γTpXIII	121 glu —	122 phe —	123 thr —	124 pro —	125 glu —	126 val —	127 gln —	128 ala —	129 ser —	130 trp —	131 gln —	132 lys
Peptide 2 (positively charged)	121 lys —	122 phe —	123 thr —	124 pro —	125 glu —	126 val —	127 gln —	128 ala —	129 ser —	130 trp —	131 gln —	132 lys
Peptide 3 (neutral)		122 phe —	123 thr —	124 pro —	125 glu —	126 val —	127 gln —	128 ala —	129 ser —	130 trp —	131 gln —	132 lys

compared with the peptide γTpXIII (Table II). This indicates that a glutamic acid→lysine substitution has occurred. The abnormal neutral peptide has one glutamic acid residue less than γ TpXIII. This can only be explained by a glutamic acid→lysine substitution at position 121 in the γ-chain. The presence of two abnormal peptides in place of γTpXIII indicates that tryptic digestion results in partial cleavage only between residues 121 and 122 of the variant haemoglobin.

Baglioni and Lehmann (1962) described two types of Haemoglobin O which they designated O Arab and O Indonesia. Haemoglobin O Arab bears a glutamic acid→lysine substitution at position 121 in the β-chain, while Haemoglobin O Indonesia bears a glutamic acid→lysine substitution at position 116 in the α-chain.

In a model of the haemoglobin molecule (Perutz, 1965) each polypeptide chain is divided into segments denoted by letters. The eight helical regions are lettered from A nearest the amino end to H nearest the carboxyl end, while the interhelical regions are lettered according to the adjoining helical regions—that is, AB, BC, CD, etc. The residues within each region are given numbers from 1 to n. By this notation the residues α116, β121, and γ121 are homologous, all three being designated GH4. Haemoglobins O Arab, O Indonesia, and F Hull are therefore variants of haemoglobin which bear identical substitutions at homologous positions in different polypeptide chains of human haemoglobin.

This is the first example of such a situation, and its interpretation is uncertain. It is possible that mutations affecting this position are unusually common; indeed, another haemoglobin variant, Haemoglobin D Punjab, has a glutamic acid→glutamine substitution at position 121 in the β-chain (Baglioni, 1962).

Summary

An identical variant of foetal haemoglobin was found in two unrelated families in Hull. It has not been seen again in a survey of 12,000 cord bloods in Britain. Haemoglobin F Hull differs from Haemoglobin F ($\alpha_2\gamma_2$) by the substitution of lysine for glutamic acid in position 121 of the 146 amino acid residues of the γ-chain. The same substitution occurs in the homologous position in the α- and β-chains of human haemoglobin, giving rise to Haemoglobins O Indonesia and O Arab respectively. The addition of glutamine in this position of the β-chain characterizes the common variant Haemoglobin D Punjab.

We are grateful to Mr. D. Irvine, Miss M. Joyce, and Miss P. M. Kynoch for technical assistance. Two of us (R. G. H. and A. J. B.) thank the Endowment Fund of St. Thomas's Hospital for financial support.

We gratefully acknowledge the co-operation of the nursing staff, obstetricians, and pathologists of the following hospitals who have sent us cord-blood samples: Copthorne Hospital, Shrewsbury; Coventry and Warwickshire Hospital; Dulwich Hospital, London; Guy's Hospital, London; General Lying-in Hospital, London; Hull Maternity Services; Lambeth Hospital, London; Lewisham Hospital, London; North Middlesex Hospital, Edmonton; Oldchurch Hospital, Romford; Plaistow Maternity Hospital; Queen Mary's Maternity Hospital, Hampstead; Royal Free Hospital, London; St. Alfege's Hospital, Greenwich; St. Andrew's Hospital, Bow; St. Bartholomew's Hospital, London; St. Thomas's Hospital, London; The Lister Hospital, Hitchin; The London Hospital, London; Victoria Maternity Hospital, Barnet; Waltham Maternity Hospital; Westminster Hospital, London; Wexham Park Hospital, Slough; Windlesham Maternity Hospital; Woking Maternity Hospital.

REFERENCES

Baglioni, C. (1961). *Biochim. biophys. Acta (Amst.)*, **48**, 392.

—— (1962). Ibid., **59**, 437.

—— and Lehmann, H. (1962). *Nature (Lond.)*, **196**, 229.

Beale, D. (1966). In Lehmann and Huntsman's *Man's Haemoglobins*, p. 299. Amsterdam.

—— and Lehmann, H. (1965). *Nature (Lond.)*, **207**, 259.

Huisman, T. H. J., and Prins, H. K. (1955). *J. Lab. clin. Med.*, **46**, 255.

Ingram, V. M. (1958). *Biochim. biophys. Acta (Amst.)*, **28**, 539.

Jenkins, G. C., Beale, D., Black, A. J., Huntsman, R. G., and Lehmann, H. (1967). *Brit. J. Haemat.*, **13**, 252.

Marengo-Rowe, A. J. (1965). *J. clin. Path.*, **18**, 790.

Nirenberg, M., *et al.* (1965). *Proc. nat. Acad. Sci. (Wash.)*, **53**, 1161.

Perutz, M. F. (1965). *J. molec. Biol.*, **13**, 646.

Schneider, R. G., and Jones, R. T. (1965). *Science*, **148**, 240.

Schroeder, W. A., Shelton, J. R., Shelton, J. B., Cormick, J., and Jones, R. T. (1963). *Biochemistry (N.Y.)*, **2**, 992.

Spackman, D. H., Stein, W. H., and Moore, S. (1958). *Analyt. Chem.*, **30**, 1190.

Paraplegia Caused by Spinal Metastasis from Thyroid Cancer*

K. E. HALNAN,† M.D., M.R.C.P., F.F.R.; P. H. ROBERTS,‡ F.R.C.S.

Brit. med. J., 1967, 3, 534–536

Paraplegia caused by metastases in the spine is a common and unfortunate incident in the natural history of many types of cancer. Even when the site of the primary tumour is known, treatment is too often symptomatic only, and when the primary is not known it is sometimes thought that energetic pursuit of the diagnosis is academic, and that the patient is better left to "die in peace." However, valuable time can also be wasted on extensive and sometimes fruitless searches for the primary tumour only to find that by this time the paraplegia is irreversible.

The striking complete success of treatment of a recent case of thyroid cancer, undiagnosed until eight months after the onset of spinal cord compression and two months after complete paraplegia, has prompted a review of nine cases seen at the Christie Hospital, Manchester, collected from about 700 new cases seen between 1945 and 1965.

Clinical Material

All but one (Case 9) of the patients had a history of thyroid disease, and in three (Cases 1, 4, and 5) thyroidectomy had been performed between three and nine years before in the belief that the lesion was benign (Table I). In these three cases, at least, it would seem that either dissemination or growth of metastases must have been very slow.

The presenting symptoms in four cases were related to the thyroid gland or neck and in the remainder to the spine. In only three cases was there a definite interval between the diagnosis of the primary tumour and the first signs of cord compression, this being three months and three and six years. However, in retrospect, if it is assumed that the apparently benign lesion had been malignant at the time of thyroidectomy, then the intervals between the appearance of the primary and the development of the spinal cord signs extend to three, six, and thirteen years.

In the seven cases for which full details are available paraplegia followed the first signs of compression in an average time of nine months and in all but one the paraplegia was complete (Table II). In the four cases showing recovery (Cases 1, 6, 8, and 9) the duration of the paraplegia was two months, two months, one month, and three weeks.

Full recovery was thought to have occurred when the patient had regained full bladder and bowel control and could walk without any external support.

Treatment of the paraplegia was by decompression in five cases (Nos. 1, 4, 6, 8, and 9), and in two of these the biopsy obtained was diagnostic (Cases 1 and 9). In three (Cases 2, 3, and 7) paraplegia was a terminal event and no attempt was made to decompress the cord. In the remaining case (No. 5) the biopsy was diagnostic, and, though some improvement followed treatment, death occurred six months later. Postmortem examination showed evidence of transverse myelitis at the level of the lesion which may have been due to irradiation.

TABLE I

Case No.	Age and Sex	Previous Thyroid History	First Signs of Malignancy	Time of Development of Spinal Signs from Diagnosis of Malignancy
1	51 M	Thyroidectomy 3 years before for "benign goitre"	Weakness of legs	0
2	70 F	Lifelong goitre. No treatment	Cervical lymph node metastases	3 months
3	55 M	Malignant goitre with cervical node metastases	Swelling in thyroid with cervical node metastases	Not known
4	54 M	"Benign" thyroidectomy 9 years before	Recurrent swelling of thyroid and metastasis. ileum	6 years
5	47 M	"Benign" thyroidectomy 6 years before	Pain and weakness in arm from spinal metastases	0
6	47 F	Swelling thyroid for 10 years	Weakness of legs, pain in neck, and paraesthesiae in arms	0
7	64 F	Goitre for 25 years, increased swelling for 5 years	Swelling in neck	Probably 4 years
8	54 M	Neck swelling for 2 years	Backache	0
9	66 F	None	Backache and sciatica	0

Abstracts of two cases are given.

Case 1

A 51-year-old man presented in January 1964 with a two-months history of weakness and numbness of the legs and urgency and increased frequency of micturition. A thyroidectomy had been performed in 1961 for a retrosternal goitre suggested histologically to be benign.

He was paraparetic with a sensory level at the sixth dorsal spinal segment. Radiographs showed a destructive lesion involving the

TABLE II

Case No.	Presenting Sign of Spinal Cord Compression	Time from First Sign of Cord Compression to Paraplegia	Duration of Paraplegia	Site of Lesion	Histology	Extent of Paraplegia	Treatment
1	Weakness of legs	8 months	2 months	D 6	Follicular	Complete	Thoracotomy. ^{131}I. *X*-ray treatment. Thyroxine
2	Not known	Not known. Terminal	Terminal	C 2	Not known	„	None
3	„ „	2 weeks. Terminal	2 weeks. Terminal	Lumbar spine	Hürthle cell	„	*X*-ray treatment to neck only
4	Backache	9 months	1 month	L 2. Later D 3–4	Not known	„	*X*-ray treatment. Laminectomy
5	Pain in the arm	6 months	7 months	D 1–2	Follicular	„	^{131}I
6	Weakness of legs	12 months	2 months	C 7. T 1	„	„	Laminectomy. *X*-ray treatment. ^{131}I. Thyroxine
7	Backache	14 months	Terminal	D 6–8. C 5–6. D 11–12	Anaplastic	„	*X*-ray treatment
8	„	6 months	1 month	D 7	Follicular	Incomplete	Thoracotomy. *X*-ray treatment. ^{131}I. Thyroxine
9	Backache and pain in legs	12 months	3 weeks	D 12. L 1. Later C 7	„	Complete	Laminectomy. *X*-ray treatment. ^{131}I. Thyroxine

---

* From the Christie Hospital and Holt Radium Institute, Manchester.

† Glasgow Institute for Radiotherapy, Western Infirmary, Glasgow W.1.

‡ Robert Jones and Agnes Hunt Orthopaedic Hospital, Oswestry, Shropshire.

sixth dorsal vertebra. No swelling was palpable in the neck and investigations failed to reveal a primary tumour.

He was admitted to hospital in August 1964, having been totally paraplegic for two months and unmanageable at home. Radiographs showed little change in the spine but a further metastasis in the ilium.

On 7 August a transthoracic anterior decompression of the spine was performed and the biopsy obtained showed a well-differentiated thyroid metastatic carcinoma. Radioiodine studies showed a 40% uptake in the neck and 9% in the region of the spinal metastasis. On 17 August 150 mCi of iodine-131 was given. By 30 August some movement had returned to the legs; he was walking between bars on 9 September and by 5 October with the aid of tripods only.

On 14 October tracer studies showed 2% uptake in the neck, 10% in the ilium, and 6% in the spine. A further dose of 200 mCi iodine-131 was given together with 4MV *x*-ray treatment of 1,500 rads skin dose each to the spine and the ilium. He was given 0.3 mg. sodium L-thyroxine daily by mouth from this time.

Rapid improvement continued so that by January 1965 he was able to walk a quarter of a mile (400 metres), ride a bicycle, and was laying concrete slabs in his garden. Bladder and bowel control was normal. Full motor power had returned to the legs. In February 1965 (after temporary cessation of thyroxine) 200 mCi iodine-131 was given, and in May radiographs showed regression and sclerosis of the spinal lesion.

He returned to work in August, and when last reviewed in May 1966 was completely well continuing the maintenance dose of thyroxine.

Case 6

A 47-year-old woman was admitted in July 1962 with a spastic paraplegia, having complained of weakness of the legs for 12 months and of a small goitre for 10 years.

At laminectomy a tumour was found in the seventh cervical and first thoracic vertebrae; histologically it was a poorly differentiated follicular thyroid cancer. During August four MV *x*-ray therapy of 3,000 rads skin dosage was given to the lesion over three weeks. By September there had been considerable return of power to the legs, and by January 1965 this was complete, together with normal bladder and bowel function.

In March 1965 the thyroid was ablated by 150 mCi iodine-131, followed two months later by a further 150 mCi. Maintenance therapy of 0.3 mg. sodium L-thyroxine daily was started.

In January 1966 the patient was completely well with normal gait and bladder and bowel function.

Cases Collected from the Literature

A search of the literature has produced histories of only four cases of paraplegia due to thyroid spinal metastases. Bradley Coley (1949) reported a case developing paraplegia 23 years after thyroidectomy for a "benign lesion" and 11 years after metastases had appeared. Full return of function followed decompression and *x*-ray treatment and the patient remained well for eight years. Outerbridge (1947) reported two cases. In one the paraplegia developed slowly over two years and recovery was only partial after decompression and *x*-ray therapy. In the other the onset was rapid, but the paraplegia was incomplete and complete recovery followed laminectomy and *x*-ray treatment. Barron, Hirano, Araki, and Terry (1959) reported a case of paraplegia of rapid onset showing complete recovery after decompression. Death occurred nine months later from widespread metastases.

Discussion and Review of Literature

Cancer of the thyroid is a rare disease, approximately 12 cases occurring per million population per year and accounting for 0.1% of all deaths from malignancy.

Metastatic spread from an apparently benign lesion of the thyroid was first described in 1876 by Cohnheim as "benign metastasizing goitre." Malignant change may not be apparent clinically and may not be recognized on histological examination. This occurred in three of our patients (Cases 1, 4, and 5) and in one of these the failure to recognize the possibility of malignant change resulted in an extensive and fruitless search for a primary tumour. The incidence of malignant change in non-toxic nodular goitre in three large series of cases was 7.6% (Hinton and Lord, 1945), 7.8% (Surridge and Kroger, 1961), and 8.5% (Fowler, Majarakis, and Cole, 1961).

Though spread to bone, in particular the vertebrae, is common in thyroid cancer (Halnan, 1965), the primary tumour itself is so uncommon that spinal metastases from the thyroid are rare in comparison with those from the bronchus, breast, and gastrointestinal tract. Reviewing metastases to the spine, Arseni, Simionescu, and Horwath (1959) found only two from the thyroid among 231 cases; Barron *et al.* (1959) found three among 127; Toumey (1943) two among 95; Alexander, Davis, and Field (1956) one among 15; Mullan and Evans (1957) one among 50; and Brice and McKissock (1965) none among 160. Collectively these series give an incidence of thyroid metastases causing paraplegia of about 1%.

Botterell and FitzGerald (1959) commented on the remarkably constant presentation of spinal metastases with local back pain sometimes together with nerve-root pain. This has been confirmed by Brice and McKissock (1965) in 90% of their cases, by Barron *et al.* (1959) in 82%, and by Arseni *et al.* (1959) in 86%. Back pain alone occurred in three of our cases, with leg pain in one, but in two others weakness of the legs alone was present.

The progress from the first signs of cord compression to paraplegia varies according to the source of the metastasis. Kennady and Stern (1962) found that in bronchogenic metastases the average time from local compression to paraplegia was four weeks, while in those from the breast it was 14 weeks. Prognosis is related to the rate of progress; the more rapid the rate the worse the prognosis. In our cases the progress was very slow, in two cases extending over a year and in two further cases between six months and one year.

Difficulty in diagnosis may occur when no evidence of bony destruction is seen on the radiographs, as occurred in 12% of the cases of Barron *et al.* (1959) and 10% of those of Brice and McKissock (1965). However, in thyroid cancer in all our cases and in those collected from the literature radiological bone changes were seen, and this may be related to the slow rate of growth. In thyroid metastases uptake of radioiodine is diagnostic but its absence is by no means exclusive. In 18% of cases extensive searches may fail to demonstrate a primary tumour (Arseni *et al.*, 1959).

Treatment should be by immediate decompression of the spinal cord, and if the primary tumour is unknown a biopsy will provide the diagnosis. Decompression is most commonly by laminectomy, but an anterior approach may often be better and leave the spine more stable.

The results of decompression of the spine in general are disappointing. Of 21 cases operated on by Mullen and Evans (1957) there were only two good results and one of these was from the thyroid. Arseni *et al.* (1959) noted improvement in 29% and complete recovery in 7.8% of cases; this series did not include any from the thyroid. Kennady and Stern (1962) noted worth-while improvement in sphincter control in 19 out of 59 cases. Brice and McKissock (1965) reported improvement in 30%.

In our series three cases were terminal, but of the remaining six complete recovery of the spinal cord lesion occurred in four (Cases 1, 6, 8, and 9) (Table III). In two cases recovery occurred in spite of the presence of paraplegia for two months. Full recovery has been maintained in two cases (Nos. 1 and 6) for 22 months and three and a half years after decompression.

In Case 8 the improvement has so far continued for six months after decompression. In Case 9 the paraplegia recurred four years later but there are now multiple metastases.

TABLE III

Case No.	Outcome	Length of Follow-up
1	Complete recovery	22 months
2	Death	
3	"	
4	Improvement following laminectomy for 2 years, when further metastases caused return of paraplegia, which was terminal	
5	Death probably due to radiation myelitis and not metastases. Temporary and partial improvement	
6	Complete recovery	3½ years
7	Death due to terminal quadriplegia	
8	Complete recovery	6 months
9	Complete recovery, but later on signs of further cervical cord compression were developing	4 years

The prognosis of thyroid cancer, particularly when well differentiated, may be surprisingly good, especially in the younger age groups (Halnan, 1966). Thus the presence of distant metastases may not be a terminal event even when paraplegia occurs, unless the latter itself is allowed to lead to death. Furthermore, bone metastases characteristically occur from follicular cancer with good uptake of radioiodine, as in all our cases that recovered. An optimistic and energetic approach seems justified in this type of case, quite different from the management of a patient with rapidly growing multiple metastases from undifferentiated carcinoma, whether originating in the thyroid or elsewhere.

Conclusions and Summary

Thyroid carcinoma is rare, but commonly metastasizes to bone, the well-differentiated variety sometimes spreading exclusively to bone.

Cases of paraplegia due to thyroid metastases are rare and few have been reported in the literature.

Metastasis to the spine causing cord compression should be treated as an emergency procedure and attempts to find the primary tumour should not delay this, particularly since in some cases no primary tumour may be found.

A thyroid tumour should always be considered as a possible origin of spinal metastases, and a history of thyroidectomy (even though apparently for benign disease) should add to rather than remove suspicion.

Though the results of surgical decompression for spinal metastases are often poor this should not rule out operation, since, even though life may not be prolonged, relief of the paraplegia is of considerable benefit. After thyroid metastases the extent and duration of recovery are significantly better than after most other tumours.

The duration of the paraplegia should not contraindicate operation. With thyroid metastases full recovery may occur even when two months have elapsed.

The first local treatment should be surgical, but this must be followed by treatment to both the primary and the secondary tumours; thyroidectomy is sometimes appropriate, but either or both radioiodine and *x*-ray therapy are almost always needed.

We are grateful to all colleagues at the Christie Hospital and elsewhere who have assisted in the care of these patients.

REFERENCES

Alexander, E., jun., Davis, C. H., jun., and Field, C. H. (1956). *Neurology (Minneap.)*, **6**, 103.
Aseni, C. N., Simionescu, M. D., and Howarth, L. (1959). *Acta psychiat. scand.*, **34**, 398.
Barron, K. D., Hirano, A., Araki, S., and Terry, R. D. (1959). *Neurology (Minneap.)*, **9**, 91.
Botterell, E. H., and FitzGerald, G. W. (1959). *Canad. med. Ass. J.*, **80**, 791.
Brice, J., and McKissock, W. (1965). *Brit. med. J.*, **1**, 1341.
Cohnheim (1876). *Arch. Path. Anat.*, **68**, 547.
Coley, Bradley L. (1949). *Neoplasms of Bone and Related Conditions.* New York.
Fowler, E. F., Majarakis, J. D., and Cole, W. H. (1961). *Arch. Surg.*, **82**, 925.
Halnan, K. E. (1965). *Brit. J. Surg.*, **52**, 736.
—— (1966). *Cancer (Philad.)*, **19**, 1534.
Hinton, J. W., and Lord, J. W., jun. (1945). *J. Amer. med. Ass.*, **129**, 605.
Kennady, J. C., and Stern, W. E. (1962). *Amer. J. Surg.*, **104**, 155.
Mullan, J., and Evans, J. P. (1957). *Arch. Surg.*, **74**, 900.
Outerbridge, R. E. (1947). *Ann. Surg.*, **125**, 282.
Surridge, R. C., and Kroger, W. P. (1961). *Arch. Surg.*, **82**, 910.
Toumey, J. W. (1943). *J. Bone Jt Surg.*, **25**, 292.

Medical Memoranda

Need for Clarity in Infant Feeding Instructions

Brit. med. J., 1967, **3**, 536–537

The danger of hypernatraemia occurring as a result of accidental salt-poisoning or excessive administration of solute is well recognized in infancy (Finberg and Harrison, 1955). The present report describes two cases admitted to the Royal Hospital for Sick Children, Edinburgh, within the past year with hypernatraemic dehydration resulting from parental failure to interpret correctly the manufacturers' instructions for reconstituting dried-milk formulae.

CASE 1

A 4-week-old male infant was admitted to hospital in January 1966 with a two-day history of irritability, refusal of feeds, and a high-pitched cry. He had been born in hospital at full term. This was the mother's first pregnancy and was uncomplicated. His birth weight was 4 kg. (8.8 lb.). There were no immediate neonatal problems, but on discharge from hospital on the fifth day of life his feeding was changed from half-cream milk to Ostermilk No. 2, reconstituted as follows: 6 measures dried-milk powder+3 tablespoonfuls water+1 teaspoonful of sugar, four-hourly. Despite the paste-like consistence of this mixture he had accepted feeds until two days before admission to hospital. When admitted he was dehydrated, with early peripheral circulatory failure. His cry was high-pitched and feeble. Neurologically he was generally hypertonic, with neck retraction, twitching of the eyelids, vertical nystagmus, and tremor of the limbs. His abdominal wall was doughy in consistency. Examination showed nothing else of note. Initial electrolyte values were—sodium 207 mEq/l., potassium 7.5 mEq/l., chloride 165 mEq/l., and calcium 7.2 mEq/l. His *p*H was 7.08, P_{CO_2} 71 mm. Hg, and standard bicarbonate 15.8 mEq/l. The blood urea nitrogen was 250 mg./100 ml.

He was treated as recommended by Harrison and Finberg (1964), being gradually rehydrated with a solution containing 20 mEq sodium per litre. Over the next three days he had repeated convulsive episodes, but gradually the serum electrolytes and blood urea nitrogen levels returned to normal. His subsequent progress has not been satisfactory and he is now severely handicapped mentally.

CASE 2

This 4-week-old female infant was admitted to hospital in October 1966, with symptoms and clinical features identical to those in

Case 1. She was the tenth-born in her family and weighed 2.75 kg. (6 lb.) at birth. She also was fed on Ostermilk No. 2, reconstituted as follows: 2½ measures Ostermilk No. 2+3½ *measures* water+ 1 teaspoonful of sugar, four-hourly. Her initial sodium level was 194 mEq/l., potassium 7.1 mEq/l., and chloride 156 mEq/l. The carbon dioxide combining power was 17 mEq/l., and the blood urea nitrogen was 198 mg./100 ml.

Treatment was carried out as in Case 1, and within 48 hours her electrolyte values had returned to normal. Convulsions occurred repeatedly throughout that period despite anticonvulsant therapy and the maintenance of normal blood sugar and calcium levels. She died suddenly at 51 hours, however, and necropsy permission was refused.

COMMENT

In both cases hypernatraemia was caused by excessive administration of solute in relation to fluid intake owing to improper reconstitution of dried-milk formulae. In Case 1 the mother had prepared feeds, using double the powder content recommended, but she believed that one tablespoon contained one fluid ounce of water. In Case 2 the initial feeding history obtained seemed quite normal. It only became clear on specific questioning that the mother used the dried-milk scoop for measuring fluid in the belief that each scoop contained a fluid ounce of water. The feeding instructions issued by the manufacturers of three commonly used dried-milk preparations—namely, Ostermilk No. 2, full-cream Cow and Gate, and full-cream National Dried Milk—would be quite clear to most mothers (see Table), but none of those instructions make it absolutely clear that the measure supplied is for dried milk and not fluid. The National Dried Milk instructions do indicate that one fluid ounce is approximately two tablespoons and for that reason are the most explicit. It is probably quite fortuitous that in both cases Ostermilk No. 2 was the dried milk powder used, but further errors could probably be avoided if feeding instructions were even more simple than at present. Thus it should be made clear that the measure supplied is for dried milk only and not fluid, and that one fluid ounce is approximately equal to two tablespoonfuls.

Comparison of Feeding-tables for Normal Babies of Normal Weight at 1 Month (Extract from Manufacturers' Instructions)

Preparation	Dried-milk Content	Fluid Content
Ostermilk No. 2	Level measures, 3½	Hot water, fluid oz. 4
Cow and Gate (Full-cream)	„ „ 3½	Make up with hot (boiled) water to 4 oz.
National dried milk (Full-cream)	Amount of milk powder for each feed (in level measures), 2½ or 3	Boiled water in ounces (1 oz. = 2 tablespoons approx.), 3½ or 4

We wish to thank Professor J. O. Forfar for his advice and criticism, and Drs. J. W. Farquhar and W. M. McCrae for permission to publish details of the above cases.

H. SIMPSON, M.B., CH.B.ED., M.R.C.P.ED., D.C.H.,
Lecturer, Department of Child Life and Health, University of Edinburgh.

J. O'DUFFY. M.B., B.S., M.R.C.P.ED.,
Registrar, Royal Edinburgh Hospital for Sick Children.

REFERENCES

Finberg, L., and Harrison, H. E. (1955). *Pediatrics*, **16**, 1.
Harrison, H. E., and Finberg, L. (1964). *Pediat. clin. N. Amer.*, **11**, 955.

Anaemia Due to Blood Loss from the Telangiectases of Scleroderma

Brit. med. J., 1967, **3**, 537–538

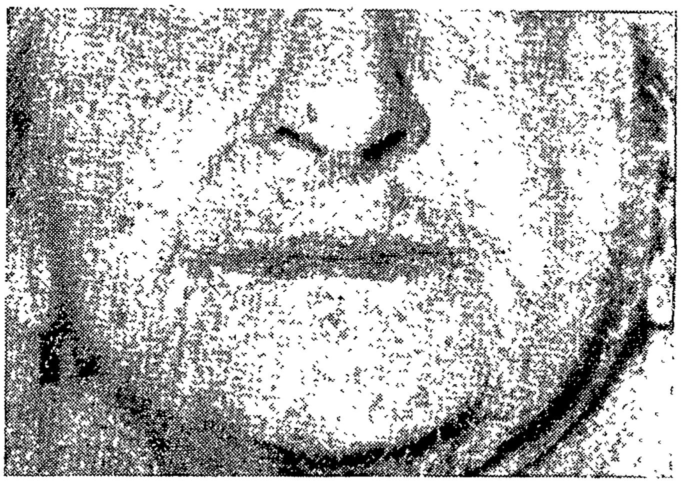
Telangiectases affecting the face, neck, oral mucous membranes, and extremities are not uncommon in scleroderma. In appearance they resemble closely those found in Osler–Weber–Rendu disease, though they are not hereditary (Verel, 1956; Winterbauer, 1964). However, it has been said that in contrast with Osler–Weber–Rendu disease the telangiectases of scleroderma rarely bleed and do not cause significant loss of blood (Winterbauer, 1964; Carr *et al.*, 1965). This report concerns two elderly women with scleroderma and telangiectases who have been gravely debilitated by severe hypochromic anaemia, for which the most likely explanation was gastrointestinal blood loss from telangiectases.

CASE 1

A 74-year-old widow was first seen elsewhere in 1958, when she complained of the symptoms of Raynaud's phenomenon for many years and the development of red blotches on the face. A diagnosis of scleroderma with telangiectases was made and as there was no evidence of systemic involvement a good prognosis was given. The blood was not examined, though two years previously her haemoglobin had been only 75%. Occasionally her nose had bled, but this had never been serious. None of her family had been troubled by anaemia or telangiectasia.

In October 1965 she was admitted to hospital because of increasingly severe symptoms of anaemia. She was pale, with striking telangiectasia affecting the face, lips, buccal mucosa, tongue, hands, and feet (see Fig.). The telangiectases varied in size up to a maximum of 5 mm. in diameter; they did not blanch on pressure. The skin of the fingers and toes was thickened and tense, with shortening of the terminal phalanges of some fingers. Elsewhere the skin was normal, but both normal and sclerotic skin was affected by telangiectasia. There were the signs of congestive heart failure. Blood pressure was 180/80 mm. Hg. Sigmoidoscopic examination was normal and mucosal telangiectases were not seen.

Investigations.—Hb 4.8 g./100 ml.; M.C.H.C. 24%; reticulocytes 5%; blood film—marked hypochromia; W.B.C. 13,200/cu. mm.; E.S.R. 14 mm./hour. Blood urea 65–59 mg./100 ml., plasma calcium 4.8 mEq/l., plasma proteins 6.6 g./100 ml., serum electrophoretic pattern normal. Antinuclear factor, gastric parietal cell, and thyroid antibodies negative. Urine normal. Faecal fat excretion 7.2 g./24 hours. E.C.G. normal. Radiological examinations: chest—marked cardiac enlargement, small pleural effusion on left side; hands—pronounced soft-tissue calcification affecting several digits; barium meal—dilated atonic oesophagus with impaired emptying, otherwise normal; barium enema—number of large saccules in sigmoid colon.



Case 1. Telangiectases affecting face and lips.

The principal cause of the congestive cardiac failure was judged to be the severe anaemia. She was treated with diuretics and carefully transfused. Two weeks later the haemoglobin was 13.8 g./100 ml.; she was feeling better and was no longer in heart failure. However, despite iron by mouth her haemoglobin fell during the next six weeks to 10.5 g./100 ml., but after a further six months her haemoglobin was 12.4 g./100 ml. (M.C.H.C. 32%, reticulocytes 3.2%), though she had had further bleeding from the nose necessitating cautery of small telangiectases in both nares.

CASE 2

A 73-year-old widow, first seen in May 1957, complained of pain and tenderness in the tips of the fingers of both hands which had developed suddenly one year previously. The skin was thin and atrophic and the hands were blue and cold. Radiological examination showed small erosions of the tips of the terminal phalanges. The haemoglobin was 13.3 g./100 ml. and the peripheral blood film normal.

A diagnosis of scleroderma was made. She was seen at frequent intervals with recurrent ulceration of the fingers and Raynaud's phenomenon. One year later telangiectases on the face, lips, and hands were noticed. None of her relatives had had similar lesions. A radiograph of the hands in 1960 showed calcification of the tip of one index finger. Barium study of the oesophagus with the patient in the prone position showed no peristalsis.

In January 1965 she was admitted to hospital because of shortness of breath on effort for six weeks and melaena for four days. She was pale and now had more numerous telangiectases on the face, lips, and arms; the buccal mucosa was spared. The hands showed marked sclerodactyly, the skin being thickened and atrophic with scarring of the fingers and wasting of the pulp. The skin elsewhere, notably on the face, was of normal texture. There were signs of mild congestive cardiac failure. Blood pressure was 120/60 mm. Hg. Sigmoidoscopic examination was normal.

Investigations.—Hb 7.5 g./100 ml.; reticulocytes 11.2%; blood film—hypochromia; M.C.H.C. 31%; W.B.C. 9,600/cu. mm.; E.S.R. 34 mm./hour; serum iron 6.8 μg./100 ml. Blood urea 39 mg./100 ml.; plasma calcium 5 mEq/l.; plasma phosphate 3.7 mg./100 ml. Plasma proteins 5.5 g./100 ml.; serum electrophoretic pattern normal. No L.E. cells detected; antinuclear factor, gastric parietal cell, and thyroid antibodies negative. Faecal fat excretion 2.2 g./24 hours. E.C.G. normal. Urine normal. Radiological examinations: chest—normal; hands—no soft tissue calcification; barium meal—normal stomach and small intestine; barium enema—numerous small diverticula throughout colon.

After blood transfusion and administration of iron the haemoglobin rose to 12.6 g./100 ml. Digitalis and diuretics were given in addition, and the signs of cardiac failure disappeared. Over the course of the next 14 months, despite oral and parenteral iron, the patient required blood transfusion on four occasions. Occult blood was detected in the stools repeatedly. Later the gastrointestinal blood loss during a 15-week period of study using ^{59}Fe and a whole-body counter (Callender *et al.*, 1966; Holt *et al.*, 1967) was estimated to be 1.5 litres per 100 days. Absorption of an orally administered dose of 5 μc. ^{59}FeCl was 90%, normal for a patient with iron deficiency. Frank bleeding from telangiectases on the inner aspect of the lips has since occurred.

DISCUSSION

Telangiectases occur most frequently in the variety of scleroderma that consists of sclerodactyly, Raynaud's phenomenon, and subcutaneous calcinosis in the absence of marked systemic involvement. It characteristically has a good prognosis (Tuffanelli and Winkelmann, 1961; Winterbauer, 1964; Carr *et al.*, 1965). Both the above patients had this variety of scleroderma, which would have caused them little trouble had they not been disabled by anaemia.

The most likely explanation for their anaemia was continuous bleeding from telangiectases in the gastrointestinal tract. The blood loss is just compensated for by oral iron in Case 1, but the second patient required periodic blood transfusion. Both patients had diverticulosis of the colon, but the nature of the blood loss made it unlikely that this was the underlying cause. It is of interest that in Case 1 the radiological features of the diverticula were those of scleroderma (Heinz *et al.*, 1963). Scleroderma may be associated with intestinal malabsorption (Sonneveldt *et al.*, 1962), and the faecal fat excretion in Case 1 was marginally raised. However, poor absorption of iron was unlikely to be a factor in the pathogenesis of anaemia in either patient, since iron given therapeutically in the first case was sufficiently absorbed to correct the anaemia, and in the second case absorption of ^{59}Fe was normal.

The telangiectases of scleroderma cannot be distinguished clinically from those occurring in the Osler–Weber–Rendu disease (Verel, 1956; Winterbauer, 1964). It is therefore surprising that stress has been laid on the apparent absence of a haemorrhagic tendency (Winterbauer, 1964; Carr *et al.*, 1965). There is no doubt that internal telangiectases occur in scleroderma as in Osler–Weber–Rendu disease, since two patients discussed by Winterbauer who suffered gastrointestinal haemorrhage were shown to have mucosal telangiectases in the stomach, and in one case in the large bowel also.

We believe it probable that the telangiectases of scleroderma can cause clinically significant blood loss. They occur mainly in a variety of scleroderma that is otherwise benign, and, as this usually affects elderly patients, iron-deficiency anaemia should be searched for frequently, since any symptoms of anaemia may be wrongly attributed to age and ignored.

Dr. H. R. Vickers kindly referred the second patient to us.

JOHN M. HOLT, M.D., M.SC., M.R.C.P.,
Lecturer in Medicine.
RALPH WRIGHT, M.D., D.PHIL., M.R.C.P.,
Clinical Assistant.
Nuffield Department of Clinical Medicine,
Radcliffe Infirmary,
Oxford.

REFERENCES

Callender, S. T., Witts, L. J., Warner, G. T., and Oliver, R. (1966). *Brit. J. Haemat.*, **12**, 276.
Carr, R. D., Heisel, E. B., and Stevenson, T. D. (1965). *Arch. Derm.*, **92**, 519.
Heinz, E. R., Steinberg, A. J., and Sackner, M. A. (1963). *Ann. intern. Med.* **59**, 822.
Holt, J. M., Mayett, F. G. H., Warner, G. T., and Callender, S. T. (1967). To be published.
Sonneveldt, H. A., van Leeuwen, P., and Blom, P. S. (1962). *Acta med. scand.*, **171**, 391.
Tuffanelli, D. L., and Winkelmann, R. K. (1961). *Arch. Derm.*, **84**, 359.
Verel, D. (1956). *Lancet*, **2**, 914.
Winterbauer, R. H. (1964). *Bull. Johns Hopk. Hosp.*, **114**, 361.

Current Practice

Transport of Invalids by Air

K. G. BERGIN,* O.S.J., M.A., M.D., D.P.H., F.R.AE.S.

General practitioners not infrequently are uncertain whether a patient is fit to travel by air. This article is based on a guide prepared to advise in general terms on the principal factors to be considered. The first guide was prepared some years ago, but it has since been revised on several occasions, the last time being by the Medical Committee of the Aerospace Medical Association.

Introduction

The number of persons travelling by air increases every year, and included in that total is an appreciable number of invalids suffering from illnesses of varying degrees of severity from the slightly indisposed to those near the end of a terminally fatal disease.

Sick persons, including those at both extremes of the age scale, tolerate modern flying conditions with very little, if any, discomfort. The number of invalids wishing to travel by air who have to be refused passage is steadily decreasing, and the great majority of cases benefit by the advantages air travel has to offer over surface travel, including speed, smoothness, and comfort. In many cases this form of transport is not merely desirable but actually life-saving.

Aircraft

Cabins.—All modern aircraft have pressurized cabins, the advent of which has greatly simplified problems of oxygen supply, though it has brought a number of other problems in its train. Briefly, the principle of pressurized cabins is to introduce air by means of a mechanically driven impeller, so that a controlled pressure is maintained in the cabin of the aircraft irrespective of the ambient atmospheric pressure. Aircraft design requirements make it necessary for the pressure in an aircraft to be slightly lower than the normal sea-level atmospheric pressure (14.7 lb. per sq. in.), and it is this factor which is chiefly responsible for the few specific contraindications to air travel. The slightly lowered air pressure means that the air density in the cabin is somewhat reduced, and that therefore a little less oxygen is present in the inspired air than is the case at sea level. In most modern aircraft the cabin air pressure is maintained at an equivalent of 6,000 ft. to 8,000 ft. (Table I).

TABLE I.—*Effects of Cabin Pressurization*

Aircraft	Concorde	Boeing 747	VC-10	Boeing 707	DC-8	Trident	Comet 4	BAC 111	Caravelle
Maximum differential pressure lb./sq. in.	10·7	8·9	9·0	8·6	8·77	8·25	8·75	7·5	8·25
Actual and cabin altitudes (ft.)									
60,000 ..	6,000								
40,000 ..	2,400	6,200	6,100	7,100	6,700	7,900	6,700	9,800	7,900
35,000 ..	1,000	4,700	4,500	5,400	5,000	6,100	5,000	8,000	6,100
30,000 ..	S.L.	2,700	2,600	3,400	3,000	4,100	3,000	5,800	4,100
25,000 ..		600	400	1,300	900	1,900	900	3,400	1,900
22,500 ..		S.L.	S.L.	S.L.	S.L.	700	S.L.	2,100	700
20,000 ..						S.L.		800	S.L.
17,500 ..								S.L.	
15,000 ..									

S.L. = Sea level.
It is normal practice to operate at cabin altitudes 300–500 ft. higher than those stated above in order to give smoother cabin altitude control.

Fig. 1 shows the fall in the oxygen tension in the lung alveoli as cabin altitude increases. Fortunately, the high affinity of haemoglobin for oxygen means that arterial oxygen saturation does not fall proportionately rapidly. As Fig. 2 indicates, a cabin altitude of 5,000 ft. leads to a fall in arterial oxygen saturation of only 3% below the ground-level normal of 96%. This slight degree of hypoxia may affect patients with significantly impaired cardiovascular or respiratory reserves, and such individuals should accordingly not travel by air without prior consultation with the medical department of the airline concerned, when special arrangements can be made to supply supplementary oxygen for individual cases.

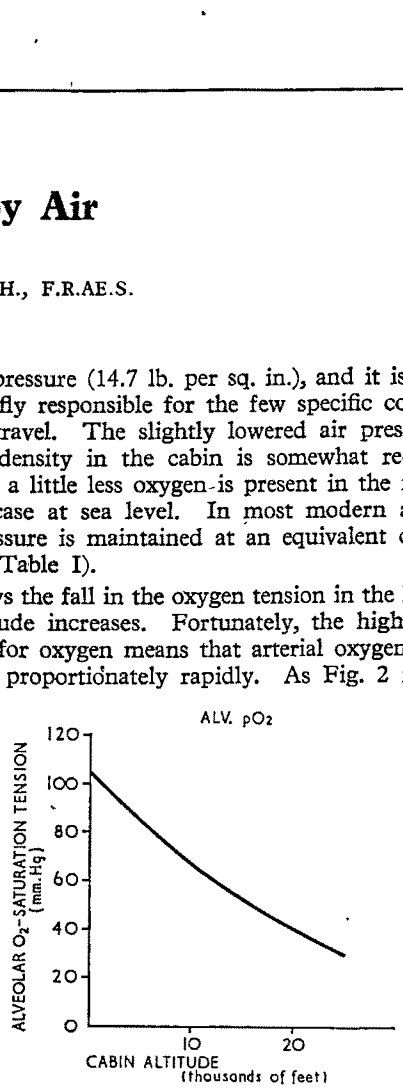


FIG. 1

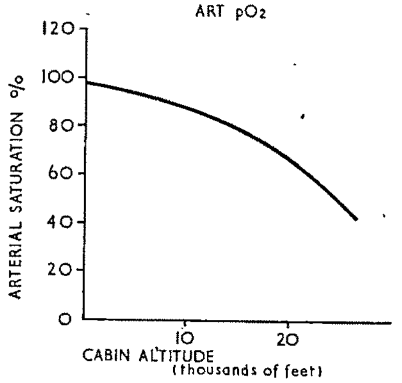


FIG. 2

Operational Characteristics.—It is sometimes helpful to know the operational characteristics of the aircraft in which the patient will fly—although nowadays conditions in the cabin are so regulated both as to actual conditions and rate of change

---

* Consultant in Aerospace Medicine, Air League and Guild of Air Pilots and Air Navigators; Lecturer in Aviation Medicine Oxford and Cambridge University Air Squadrons; late Director Medical Services, British Overseas Airways Corporation.

TABLE II.—*Typical Aircraft Comparative Data*

Aircraft	Boeing 707–436	Vickers Super VC10	Caravelle VIN	BAC 1-11 300	Trident I	Douglas DC-9-30	Concorde
Take off distance sea level (ft.)	11,000	9,050	6,200	7,150	7,900	7,300	9,650
Max. take off weight (lb.)	311,750	335,000	105,820	87,000	115,000	108,000	350,000
Take off speed at max. take off weight (m.p.h.)	183	181	153	146	164	—	230
Typical initial rate of climb (ft./min.) ..	2,500	2,500	2,500	2,500	2,900	3,000	3,300
Typical cruise speed (m.p.h.)	545	545	510	540	580	560	1,320
Normal operating altitude (ft.)	30/40,000	30/40,000	25/30,000	25/30,000	25/31,000	25/35,000	50/65,000
Typical average rate of descent (ft./min.) ..	1,500	2,000	2,400	2,000	2,100	2,000	2,400
Range, average statute miles	3,650	3,550	1,325	820	870	780	3,800
Average capacity (lb.)	44,600	43,500	17,100	21,600	19,000	24,300	25,000
Landing distance at max. landing weight (ft.)	7,800	6,250	5,300	5,560	6,260	4,850	8,450
Landing speed at max. landing weight (m.p.h.)	168	159	145	143	160	146	175
Max. passenger capacity	162	157	90	79	100	107	120
Cabin differential (lb./sq./in.)	8·6	9·0	8·1	7·5	8·25	7·46	10·7

that no doctor need fear for his patient's safety. As a matter of interest operational data of some current aircraft in common use are given in Table II.

An essential component of all large passenger aircraft is emergency oxygen equipment which comes into use automatically in the event of an emergency, when the cabin pressure falls for one reason or another. In addition, when a patient requires oxygen an invalid oxygen set can be put on board for his exclusive use. Fittings for stretcher cases are to be found on most large passenger aircraft.

All aircraft have seat belts, and seat backs and fittings are constructed so that in the event of an emergency landing or severe braking injury to passengers is minimized.

Finally, all airlines carry first aid kits for use should they be required.

Cabin Staff.—A proportion of air stewardesses are State registered nurses and all cabin staff have training in elementary first aid and care of the sick.

Consequences of Atmospheric Change

Apart from specific disabilities it is important to know of certain conditions which can be brought about by the changing physical environment of flight on ascent and descent. They may be of no concern to the passenger, or cause merely passing discomfort; in some cases they may produce disabling pain. The group heading under which the commoner conditions are included is known as dysbarism. The commoner manifestations met with in flying are described below.

Otitic Barotrauma or Barotitis Media.—This is cause by failure to equalize pressure in the middle and outer ear as atmospheric pressure rises when the aircraft descends, leading to tension and varying degrees of trauma to the tympanic membrane. It can vary from dull transient earache to severe disabling pain. It is brought about by lack of patency of the eustachian tube usually due to nasopharyngeal infection.

Sinus Barotrauma or Barosinusitis.—This condition is brought about by similar conditions, namely inadequate ventilation of a sinus resulting in a pressure gradient—the pain is caused by air trapped in the sinus expanding. It is very sharp and sudden in onset and has been likened to a blow on the head with a hard instrument.

Aeroembolism.—This is very rarely met with in pressurized cabins. Pain in the joints is caused by release of nitrogen into the tissues. It is relieved by the administration of oxygen.

Aerodontalgia—is toothache brought on by expansion of gas in a badly filled cavity. It is rare.

Expansion of gases—whether in the gut or the thorax can lead to discomfort and in some cases severe pain. It is usually of no clinical significance, but in the thorax it can lead to serious conditions such as mediastinal shift (Figs. 3 and 4).

Hypoxia.—As stated earlier, pressurized cabins maintain an atmospheric pressure approximately equivalent to 8,000 feet at whatever altitude the aircraft may be flying. There is therefore a small degree of hypoxia. Any patients with a decrease of the pulmonary ventilating area or coronary deficiency may experience exaggerated symptoms for which personal emergency oxygen should be provided.

Motion Sickness.—This is very rare in modern jet flying, which is usually above bad weather—but there are three occasions when it may occur, namely clear air turbulence, when descending through bad weather to airports, or when delayed in the airport circuit while other aircraft are landing. Such transient sickness can be effectively dealt with by well-known remedies with a hyoscine content, in addition to such measures as loosening constrictive collars, lying in the recumbent position, and avoidance of overheating. Severe attacks must be carefully watched in the case of diabetics or recent peptic perforation, but such episodes are very rare.

Assessment of the Patient

General basic principles should be considered before a patient flies.

(a) Is he fit to travel by any means of transport? If the answer is "no," further consideration of air travel can be ruled out.

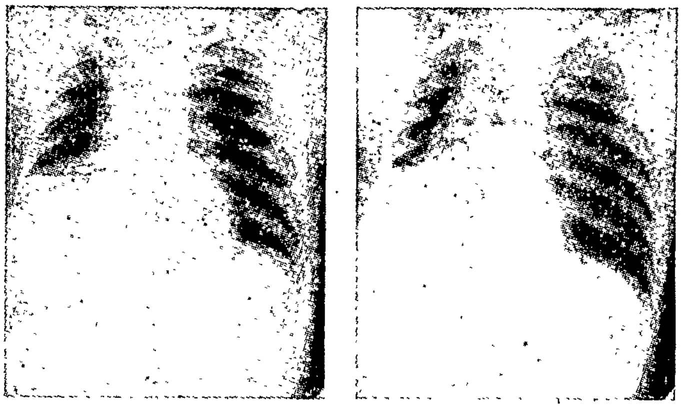

A B

FIG. 3.—Radiographs showing pneumothorax at 1,000 ft. (A) and 10,000 ft. (B) respectively.

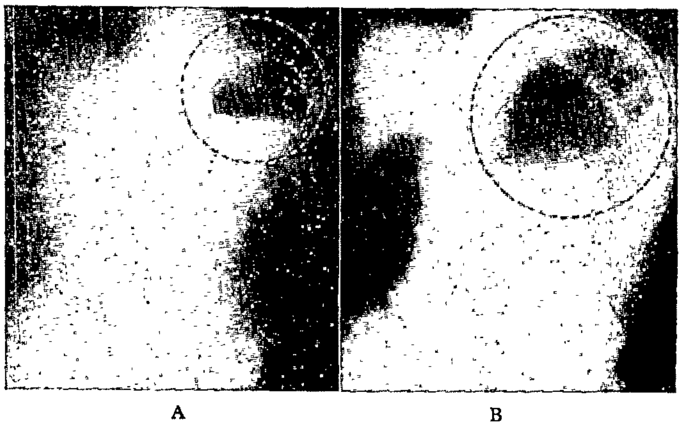

A B

FIG. 4.—Radiographs showing expansion of intestinal gases under lowered conditions of atmospheric pressure. A, Ground level; B, 40,000 ft.

(b) Is he fit to travel with other members of the public? There are certain cases which for reasons of public policy cannot be carried in a public transport vehicle. In public transport aircraft aesthetic considerations and the comfort of the other passengers demand that a patient should look and smell normal and behave normally. If these requirements cannot be met a private charter aircraft should be considered. The first type of case of this sort which cannot be carried is that which either in appearance or odour is objectionable to fellow passengers. Such cases include open wounds or lesions of exposed parts, such as the face, a colostomy over which the patient has little or no control, grossly disfiguring conditions, or incontinence of urine or faeces. It should be remembered that a colostomy over which an individual has control at ground atmospheric pressure may well become uncontrollable in conditions of lowered pressure. Patients with carcinoma at times have an extremely unpleasant smell and in the confined space of an aircraft cabin can be most objectionable. Secondly, cases should be refused which by reasons of their behaviour are objectionable to other occupants of the aircraft. Such cases would include those prone to extreme noisiness, peculiarities of habit, incontinence, or major epilepsy, and cases of mental illness when not accompanied by an attendant or suitably sedated.

(c) The stability of the patient's condition should be considered. It should be ensured as far as possible that there is not likely to be a medical crisis en route necessitating diversion of the aircraft from its prescribed course. Apart from the great inconvenience and cost caused it can in certain cases, as for example long trans-oceanic flights, imperil the safety of the aircraft. It should be possible to ensure against the likelihood of this with a fair degree of certainty.

Contraindications for Acceptability

Cardiovascular

Cases of uncompensated heart disease and severe angina pectoris should not travel by air unless special arrangements are made and extra supplies of oxygen are available. Unhealed coronary thrombosis is a contraindication to air travel. At least two to three months should have elapsed since the acute episode, and if there are residual symptoms the medical department of the airline should be consulted.

Cases of controlled hypertension will normally be accepted without restriction, but the value of a sedative before flight should be remembered. Where there is evidence of cardiac, ocular, or renal complications, the airline medical department should be advised.

Persons who exhibit cyanosis, severe disturbance of rhythm, persistent arrythmias resulting in recurrent prostration, syncope, or shocklike conditions, those with markedly enlarged hearts, extreme valvular stenosis, convalescent myocardial infarction, marked exertional angina, severe hypertension and hypertensive encephalopathy, or any other condition which restricts the cardiac reserve to such an extent as to render the patient unable to climb one flight of stairs without production of symptoms or severe dyspnoea should be carefully evaluated before they are advised that air travel is safe for them.

A patient with a history of thrombotic or venous disease should be instructed against remaining immobile for long periods during air flight. Immobility and the associated venous stasis in the limbs are believed to be important factors in the development of "passenger phlebitis," which may result in pulmonary infarction.

Blood Dyscrasias

Flying is contraindicated in blood dyscrasias where the red cell count is less than 2.5 million/mm., or the haemoglobin less than 50%. If a blood transfusion is given, the aim should be to raise the haemoglobin to over 60% before flight. All cases of blood dyscrasia other than simple mild anaemias should be referred to the airline medical department because of their known liability to symptoms from minor degrees of oxygen lack. Acute leukaemias which have recently been treated with *x* rays constitute a contraindication to air travel on account of the possibility of haemorrhage under conditions of lowered oxygen tension.

Respiratory

Acute upper respiratory tract infections.—The common cold, sinusitis, and pharyngitis may cause blockage of eustachian tubes and sinus foramina. Inability to ventilate the middle ears and sinuses to compensate for pressure changes during climb and descent may cause severe pain, and patients with these disorders should postpone their flight until the condition has subsided. It should be remembered that chronic naso-pharyngeal conditions in which the patency of the eustachian tubes is impaired can give more trouble than the acute phase when congestion is not so marked.

Asthma and bronchitis.—Sufferers from asthma, chronic bronchitis, and emphysema should be assessed for the degree of respiratory embarrassment present, and the value of a sedative should be remembered. The uncontrolled coughing and copious offensive sputum which may be produced in cases of severe bronchiectasis may make patients with the condition unacceptable in spite of reasonable respiratory efficiency.

Tuberculosis, Pneumothorax, etc.—Respiratory disorders affecting exercise tolerance should be considered in a similar manner to cardiovascular diseases, and where there is any doubt the attending physician should make special arrangements with the airline medical department. Cases of active pulmonary tuberculosis must be considered to be potentially infective under conditions of reduced air pressure and cannot therefore be accepted. Quiescent or healed cases may travel without restriction. If an artificial pneumothorax is present, seven days must have elapsed since the last refill and the lung must be at least three-quarters expanded, because of the effects of reduced pressure on trapped gas.

Apart from the question of reduction in the available area of lung tissue, another important factor is the possibility of mediastinal or diaphragmatic shift (Fig. 3) as a result of operation or disease. Such a condition would be aggravated under changed conditions of pressure, and where such a liability exists flying should be avoided.

Persons whose vital capacity is 50% or less do not do well in unpressurized aircraft unless a flight altitude of less than 5,000 feet is maintained. Pulmonary function and reserve should be evaluated in order to determine whether persons with pulmonary emphysema or severely limited ventilation, arising from pulmonary fibrosis, should travel by air.

Gastrointestinal

The reduced cabin air-pressure allows intestinal gas to expand. Resulting distension means that flying is contraindicated in patients who have recently undergone abdominal operations—10 days post-operation being the minimum acceptable time after uncomplicated appendicectomy, etc. The risk of perforation and haemorrhage from this cause in patients with active peptic ulceration means that the airline medical department must be consulted in these cases prior to flight. Trained colostomy patients may fly provided that they are well acquainted with measures for the control of their colostomy, which is likely to be more active in the air. In all such cases any increased tendency to vomit must be watched and control measures taken.

Infection

Cases of infectious diseases, including poliomyelitis and trachoma, cannot of course travel in public transport aircraft. Special arrangements can usually be made for the carriage of poliomyelitis cases after the acute and infectious stages have passed.

Neuropsychiatric

The safety of the other passengers and crew should be evaluated when a person with a psychiatric disorder is being considered for travel by air. Persons manifesting unpredictable behaviour or those who require heavy sedation or restraint should not fly on commercial transports. However, the judicious use of medication should reduce the incidence of neuropsychiatric problems.

Age

Old people with well-compensated cardiovascular and respiratory systems tolerate air flight excellently. There are no contraindications to flying based on advanced age alone. Equally, the newly born tolerate air travel well and there are no lower limits to such cases.

Central Nervous System Disorders

Most of these cases are covered by the "look and smell normal, and behave normally" rule. Uncontrolled epilepsy and faecal or urinary incontinence would therefore be absolute contraindications to travel in public transport aircraft. It must be remembered that epilepsy is aggravated by mild hypoxia and hyperventilation. Cases of Parkinson's disease, for example, could be carried by special arrangement, and cases of mental disorder might be accepted under sedation, or if accompanied by an attendant.

Patients who have had poliomyelitis are acceptable for air travel provided one month has elapsed since the onset of the disease, the disease generally being considered to be non-infectious after such a period. If the patient is not ambulatory a special attendant is required. Occasionally special arrangements can be made with some airlines to transport persons recovered from the bulbar type of poliomyelitis. In this type of case preparation must be made by the airline concerned to have the proper power supply (correct voltage and wattage) for activation of the portable respirator, if this apparatus is required.

Metabolic Disorders

Diabetes is not a contraindication to air travel provided the patient is well stabilized, severe cardiovascular disease is absent, and the individual is instructed concerning the importance of feeding at physiological intervals rather than being guided by local times, which can change by several hours in flying. Oxygen should be available in these cases, because they are particularly sensitive to hypoxia. Appropriate preventive measures should be taken if the patient is liable to motion-sickness.

Airsickness is, however, rare nowadays in aircraft which fly at high altitudes, because less turbulence is encountered. It has been found by experience that remedies containing hyoscine in a dosage of 1/100 gr. (0.6 mg.) constitute the best routine prophylactic for adults.

Pregnancy

The majority of international airlines carry pregnant women up to and including the 32nd week of pregnancy, and this may be extended on domestic services. The restriction is introduced in order to avoid, as far as possible, the risk of birth while airborne. If a passenger is known to be prone to abortion flying may be contraindicated up to the third month of pregnancy. In this connexion it should be remembered that though weather conditions may be good at the beginning of a flight they may deteriorate en route and extreme turbulence may occasionally be encountered. This might result in premature and precipitate labour.

Terminal Stage of Life

There is no contraindication to patients near to death flying, but patients *in extremis* should not be accepted for air travel because of the difficulties associated with deaths en route.

TABLE III.—*Summary of Restrictions on the Carriage of Invalids*

Condition	Limiting Factors	Restrictions and Precautions
Anaemias Blood dyscrasias Reticuloses	Red cell count below 2½ million per cu.mm. Haemoglobin below 50% Severe involvement of mediastinal lymph glands Severe constitutional upset Radiation sickness Tendency to haemorrhage	Airline medical department must be consulted Haemoglobin should preferably be raised to 60%, by transfusion if necessary Oxygen must be available
CARDIOVASCULAR DISEASES		
A. Angina pectoris Compensated heart disease	Reasonable threshold for exercise without symptoms	Airline medical department should be notified Oxygen must be available
B. Uncompensated heart disease	Evidence of failure	Each case must be considered on its merits
C. Coronary occlusion	Minimum of 8–12 weeks post-occlusion. If residual symptoms are present, case must be treated as A or B above	As A or B above
D. Hypertension:		
(i) Controlled and asymptomatic		Sedative may be indicated. Airline should be notified
(ii) Complicated	Impairment of cardiac, renal or C.N.S. function	Airline medical department must be consulted Oxygen must be available
RESPIRATORY DISEASES		
A. Acute upper respiratory tract infections	Eustachian or sinus catarrh	Air travel temporarily contraindicated
B. Asthma, bronchitis, emphysema, and non-infectious fibrotic diseases	Exercise tolerance only moderately impaired	Airline medical department should be notified Oxygen must be available If exercise tolerance is severely impaired, special arrangements must be made
C. Pulmonary T.B.		
(i) Active	Tubercle bacilli in sputum	Cannot be carried while regarded as infectious
(ii) Quiescent or healed	Degree of impairment of function	As B above. Seven days must have elapsed since refill of artificial pneumothorax or pneumoperitoneum. Lung must be ¾ expanded
D. Pneumonia	Must be resolved. Residual impairment of function	As B above
E. Bronchiectasis	(i) Impairment of function	As B above
	(ii) Copious offensive sputum	Cannot be carried, except by special arrangement
GASTROINTESTINAL DISEASES		
A. Peptic and bowel ulceration		
(i) Active	May bleed or perforate under reduced pressure, or be aggravated by motion sickness Should not travel within 3–4 weeks of haematemesis or melaena	Air travel contraindicated except in emergency Airline medical department must be consulted
(ii) Healed		
B. Post-operation	Distension of bowel under reduced pressure	Airline medical department must be notified Minimum of 10 days should have elapsed since operation Hyoscine to prevent airsickness if necessary
C. Colostomy	Overactivity and poor control	Airline medical department must be consulted
RENAL DISEASES		
A. Calculus	Frequent attacks of colic	Normally no restriction Hyoscine to prevent airsickness
B. Other	Degree of impairment of function	Airline medical department should be consulted

(Continued on next page)

TABLE III.—*Continued*

Condition	Limiting Factors	Restrictions and Precautions
C.N.S. DISEASES		
A. Epilepsy	Frequent seizures	Special arrangements must be made if fits are uncontrolled
B. Mental disease	Behaviour must be normal under mild stress	Special arrangements, including sedation and an attendant normally required
C. Faecal or urinary incontinence		Cases will not normally be be carried
INFECTIOUS DISEASES	Infectious phase	Will not be carried
METABOLIC DISEASES		
A. Diabetes		
(i) Stable and uncomplicated	Patient must understand his own case, and be able to administer his own insulin etc.	Time changes must be taken into account Airline medical department should be notified and hyoscine given if necessary
(ii) Unstable or complicated		Special arrangements must be made
B. Liver diseases	Ascites or severe impairment of function Possible rupture of abscesses	Airline medical department must be consulted
ELDERLY	Respiratory and cardiovascular function must be adequate. Bowel and bladder control must be normal	None, unless patient is not fully ambulant, when special arrangements should be made
PREGNANCY		
(i) First trimester		History of abortion is relative contraindication Hyoscine to be given if necessary
(ii) 12–32 weeks		None if normal. Airline medical department to be notified Oxygen to be available
(iii) Beyond end of 32nd week		Will not normally be carried on international flights

Queries

In the majority of the larger airlines there are specialist medical officers who have a great deal of experience in problems of the carriage of invalids by air, and there is a department which deals with the care and transport of such passengers to which all such inquiries should be addressed. Application should be made to the airline concerned, when usually a questionary will be sent to be completed by the patient's private doctor. This will then be considered by the medical department, and a decision will be made on whether the patient is acceptable for air travel. If the answer is in the affirmative a briefing form is completed alerting the airline officials en route of the special services which will be required and setting in train the provision of such requirements from the port of departure through to the final destination. These arrangements may include the attendance of doctors, or the administration of drugs en route, the provision of certain items of medical equipment and oxygen sets, nursing facilities, or ambulance requirements.

Conclusion

Experience has shown that increasing numbers of seriously ill patients can be carried by air, and many of course benefit from the availability of this form of transport. The advantages offered by rapid transit, smooth flight at high altitudes, controlled atmospheric conditions within the cabin, coupled with the medical facilities available in flight such as emergency oxygen supplies, make air travel a most useful form of transportation for the seriously ill person who wishes to travel with a minimum of physical upset or discomfort.

The author is grateful to the Editor of the *Journal of the Aerospace Medical Association* for permission to quote, and to the other authors to whom reference is made in the bibliography. Figures 3 and 4 are reproduced from Bergin, K. G., *Aviation Medicine*, John Wright and Sons, 1949, by permission of the publishers.

BIBLIOGRAPHY

(1961). *Medical Criteria for Passenger Flying.* Aerospace Medical Association.

Armstrong, H. G. (1950). *Air Travel and the Ambulatory Patient.* International Forum 4. No. 1.

Bergin, K. G. (1949). *Aviation Medicine.* Chapt. 26. Bristol.

—— (1956). Contraindications to Air Travel. *British Encyclopaedia of Medical Practice.* Interim Suppl. No. 167, p. 6.

—— 1960). *Transport of Invalids by Air.*

Berry, C. A. (1958). *Tex. St. J. Med.*, 54, 11.

McFarland, R. A. (1953). *Human Factors in Air Transportation: Occupational Health and Safety.* New York. p. 726.

ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

"Arc Eye"

A.—*What is the best topical application for "arc eye"?*

A.—Local anaesthetic drops may be necessary for examining an eye after exposure to ultraviolet radiation, but their continued use is inadvisable. Adrenaline eye-drops are helpful in mild cases and cold compresses produce some alleviation of symptoms. Light should be excluded by bandaging the eyes.

Oral Contraceptives and Mitral Stenosis

Q.—*Is there any evidence that oral contraceptives might increase fibrin deposit on the mitral valves in cases of mitral stenosis?*

A.—It is very unlikely that thrombosis as such plays any part at all in the fibrotic narrowing of the mitral valve which leads finally to mitral stenosis. Therefore oral contraceptives should not have any effect whatsoever on the rheumatic mitral valve.

Treatment of Barbiturate Poisoning

Q.—*What are the main points in the treatment of barbiturate poisoning, and what are the indications for the administration of bemegride?*

A.—Bemegride, though introduced as an antidote for acute barbiturate poisoning,[1] is an analeptic with no specific action against barbiturates. It and other analeptics have no place in the treatment of barbiturate poisoning.[2]

Since there is no antidote, the treatment consists in the maintenance of vital functions. Respiration has to be safeguarded by keeping the airway clear, and, if necessary, by applying oxygen and artificial respiration. Shock will require vigorous management, the blood pressure being maintained with metaraminol. Hypothermia, hydration, and acid–base balance may all require active attention. Intensive nursing care is most important. These measures alone will be successful in 95% of cases. Gastric aspiration and lavage should be undertaken only within four hours of the ingestion of the tablets and if the lungs are protected by an adequate cough reflex or a cuffed endotracheal tube.[3]

Forced diuresis and peritoneal- and haemodialysis should be used only in exceptional circumstances—for example, when the condition deteriorates despite intensive measures to support vital functions. Treatment will not be complete unless the psychiatric aspects of the case are investigated and dealt with.

REFERENCES

[1] Shaw, F. H., *Med. J. Aust.*, 1955, 2, 889.

[2] Matthew, H., and Lawson, A. A. H., *Quart. J. Med.*, 1966, **35**, 539.

[3] Matthew, H., Mackintosh, T. F., Tompsett, S. L., and Cameron, J. C., *Brit. med. J.*, 1966, 1, 1333.

Clinicopathological Conference

A Case of Hypertension, Anuria, and Uraemia

DEMONSTRATED AT THE ROYAL POSTGRADUATE MEDICAL SCHOOL

Clinical History

DR. O. WRONG: The patient (Case No. 300365, P.M. No. 11312) was a married woman aged 39 at the time of her death from uraemia. There was no known history of hypertension or renal disease. In 1950 and 1952 she had had pregnancies which were apparently uneventful. In 1953 and 1955 further pregnancies were complicated by hypertension—noted at 37 and 12 weeks, respectively—but she went to term successfully. In 1957 her fifth pregnancy was also complicated by hypertension, and she prematurely delivered a living child at 36 weeks.

After the fifth pregnancy she was found to have persistent hypertension, which was investigated in New Zealand. Her fundi were said to show grade III retinopathy, while an intravenous pyelogram showed no abnormality. Her hypertension was thought to be essential in type, and treatment with hypotensive drugs was started. In 1963 she became pregnant again, and in March 1964 this sixth pregnancy was terminated at 29 weeks because of a blood pressure of 210/130, which persisted despite treatment with guanethidine and polythiazide. The blood-urea concentration was 48 mg./100 ml. and the haemoglobin level 10 g./100 ml. Subsequently she was well enough to resume domestic chores, look after her children, and play an occasional round of golf. She continued to take drugs for her hypertension. In February 1965 she had a short illness with back pain, fever, and slight urinary frequency. From that time on she had nocturia and frequent nausea and anorexia. In April she stopped taking her guanethidine because of this nausea.

Progress

By the end of April she was more nauseated and noticed that her urinary output was scanty. On 6 May she became breathless and was admitted to her local hospital with pulmonary oedema and a blood-urea level of 330 mg./100 ml. She was treated with digoxin, methyldopa, guanethidine, and ampicillin, being transferred to Hammersmith Hospital on the following day. Here she was found to be pale and confused, with a pyrexia of up to 39° C. There were multiple bruises on the skin. The jugular venous pressure was raised, but there was no ankle or sacral oedema. Her blood pressure was 170/105 mm. Hg, and the optic fundi showed scattered haemorrhages and exudates but no papilloedema. There was evidence of moderate cardiac enlargement and a left pleural effusion, and widespread rhonchi were heard. The kidneys could not be felt, and she was unable to pass urine.

The blood urea was 350 mg./100 ml., serum sodium 130, potassium 5.8, and bicarbonate 24 mEq/l. The serum albumin was 3.5 g. and the globulin 1.9 g./100 ml., with a normal electrophoretic pattern (one month later the albumin was 2.3 and the globulin 5.5 g./100 ml., with an increased gamma-globulin fraction). A radiograph of the chest showed appearances consistent with a left pleural effusion and consolidation or oedema of both lower lobes; the right kidney appeared rather small in the abdominal *x*-ray film, but neither kidney could be clearly seen; a radiograph of the hands was normal. The haemoglobin level was 6.3 g./100 ml. (M.C.H.C. 28%) and the stained film showed fragmented and crenated red cells. The platelet count was 171,000/cu. mm. The antistreptolysin-O titre was 50 units/ml. An electrocardiogram showed left ventricular hypertrophy and non-specific T-wave changes; at a later date she was found to have auricular fibrillation.

Her uraemia was controlled with peritoneal dialysis and her hypertension treated with methyldopa. Details of the clinical course are shown in Fig. 1. She remained almost totally anuric for the rest of her life, the few drops of urine she did pass containing many red cells and 5 grammes of protein per litre but only scanty granular casts. Despite aspiration of her left pleural effusion and various antibiotics she repeatedly showed evidence of pulmonary consolidation with fever and purulent sputum.

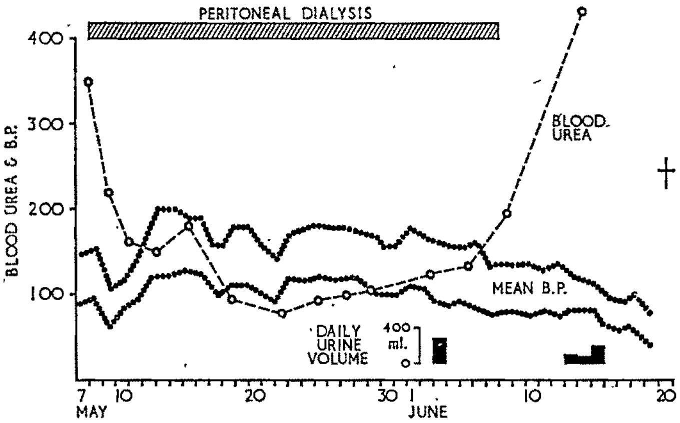


FIG. 1

On 15 May *Klebsiella* was grown from the peritoneal fluid, and she had slight abdominal pain and tenderness. Kanamycin was given, its dosage being controlled by blood levels. A renal biopsy on 25 May showed evidence of benign hypertension only, without either glomerulitis or the characteristic changes of malignant hypertension. Because of the failure to explain adequately her anuria a retrograde pyelogram was performed on 4 June, but showed no abnormality. Corticosteroid therapy was also started on that day (prednisone 60 mg./day) on the remote chance that she had a polyarteritis that was not revealed by the renal biopsy. Over the next few days peritoneal dialysis became increasingly difficult, with repeated growth of *Escherichia coli* in the fluid and occasional

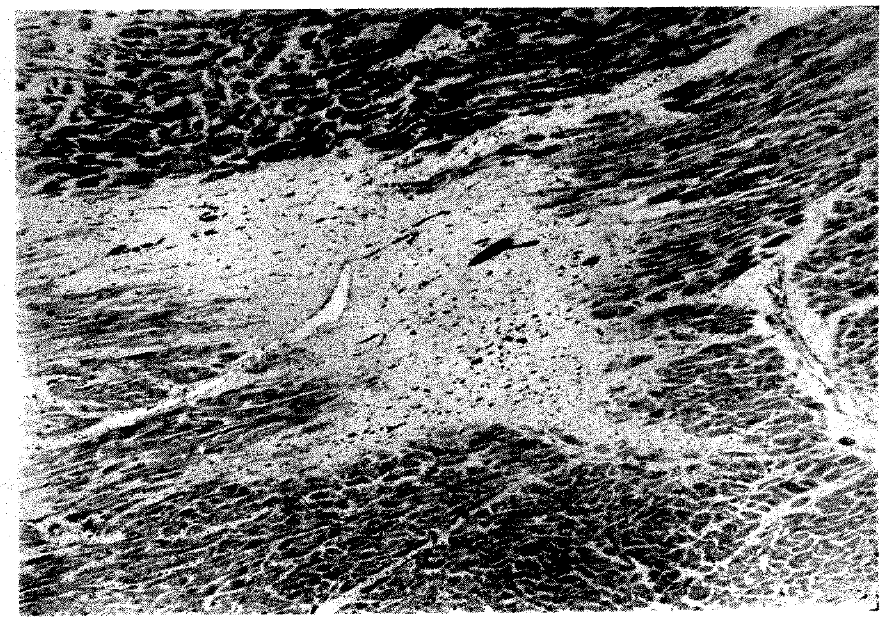


FIG. 2.—Myocardium of left ventricle showing a focus of recent necrosis. (H. and E. ×40.)

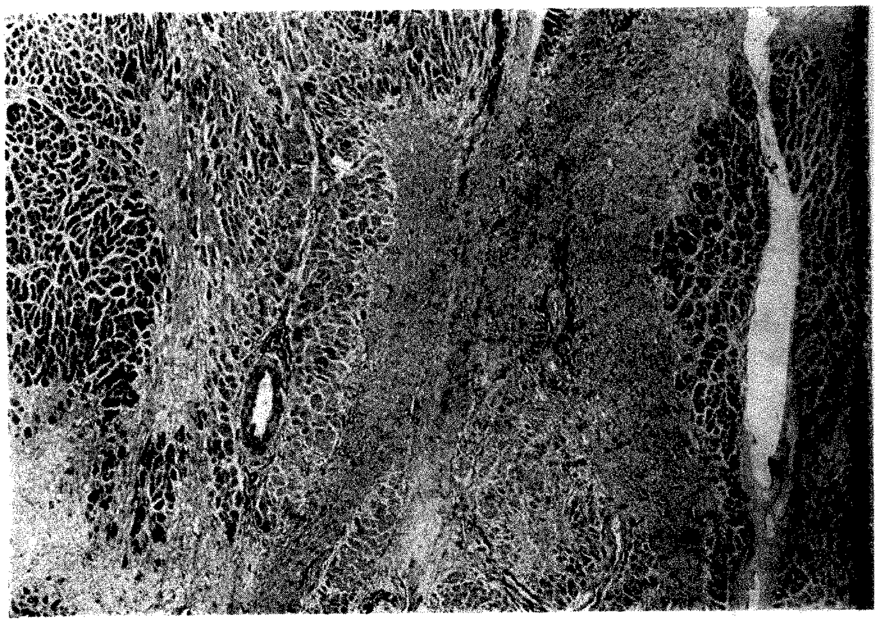


FIG. 3.—Myocardium of left ventricle showing organization of an older necrotic region. (Picro-Mallory. ×40.)

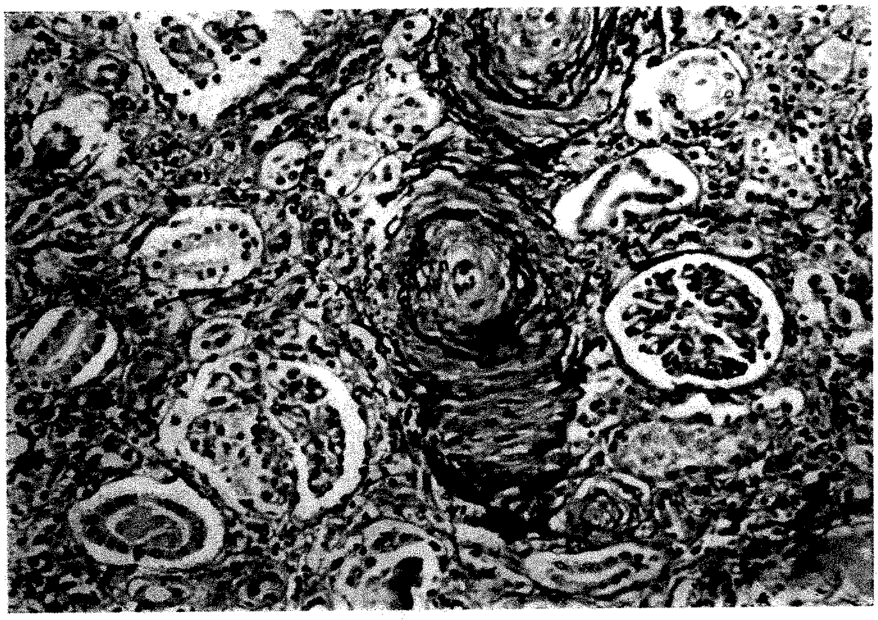


FIG. 4.—Renal cortex with relatively normal glomeruli, a few atrophic tubules, and an afferent arteriole with its lumen almost obliterated by intimal thickening. (Elastic-van Gieson. ×190.)

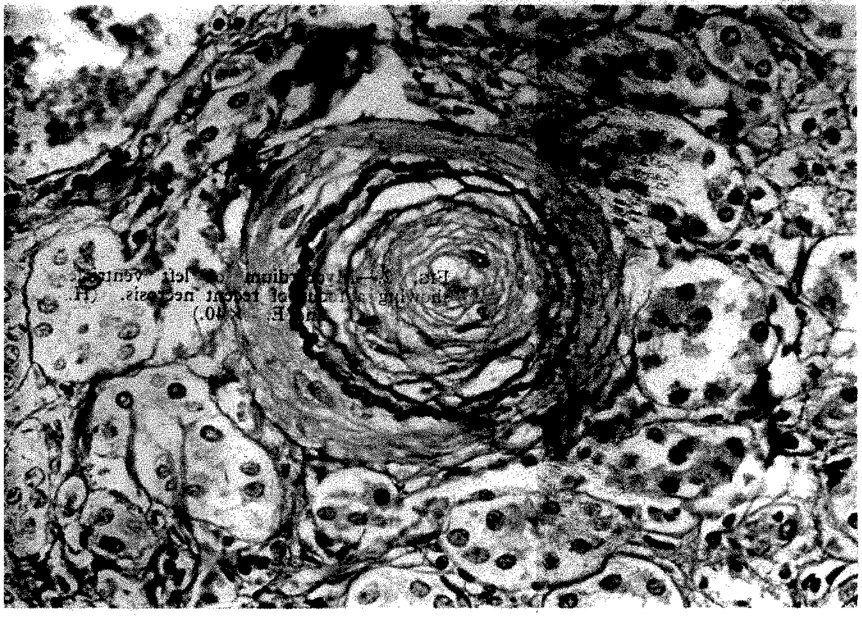
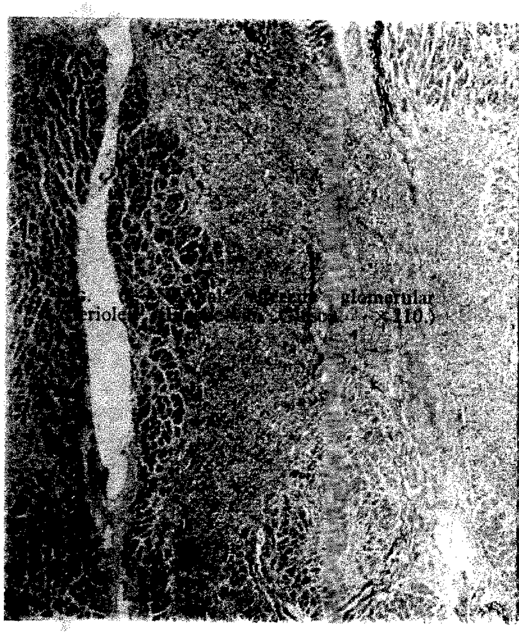
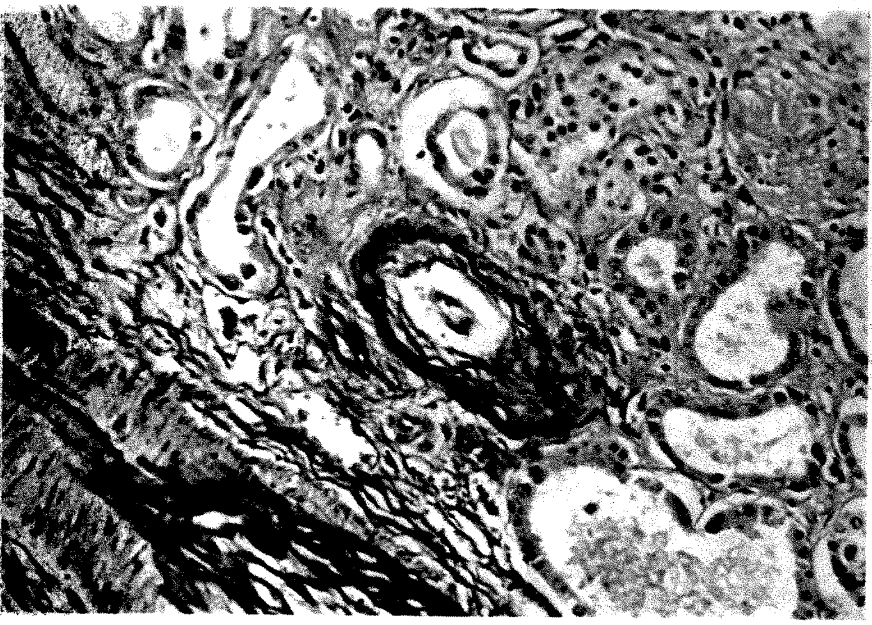


FIG. 5.—Afferent glomerular arteriole with its lumen almost completely occluded by the typical " onion skin " intimal proliferation of malignant hypertension. (Elastic–van Gieson. ×400.)





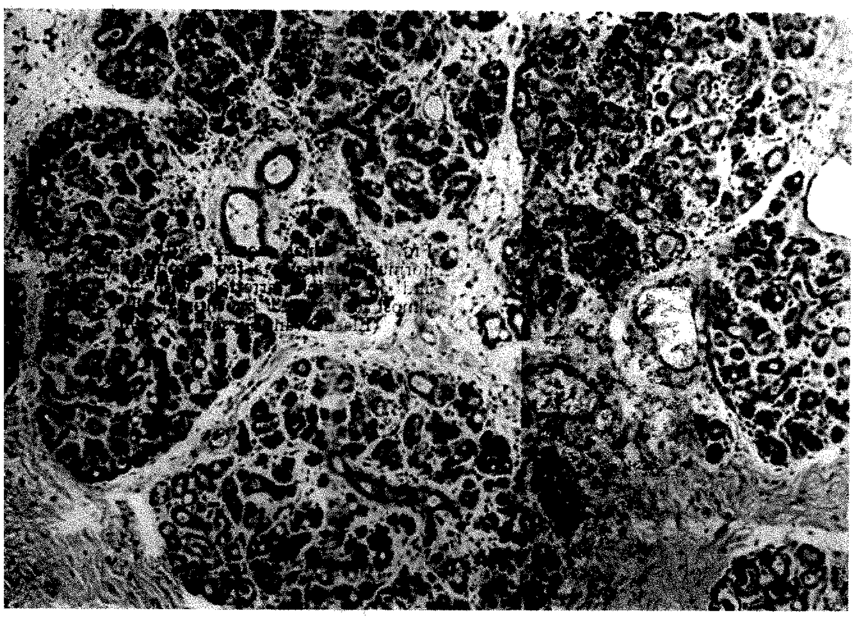


FIG. 7.—Breast tissue showing secretory changes, probably due to chlorpromazine treatment. (H. and E. ×55.)

Pseudomonas pyocyanea, and had to be abandoned on 7 June. She died in uraemic coma on 20 June, six weeks after admission.

Clinical Diagnosis

(1) Oliguric renal failure, with uraemia resulting from either (*a*) malignant hypertension (? essential) or (*b*) polyarteritis nodosa.

Post Mortem Findings

Dr. E. D. WILLIAMS: The body was that of a thin middle-aged woman with a few purpuric spots on the arms and abdomen and slight oedema of the lower legs. There were peritoneal dialysis incisions below the umbilicus and in the left iliac fossa.

The heart weighed 400 g. (normal for patient 286 g.). The pericardium was normal. The left ventricle showed hypertrophy, being 21 mm. thick (normal 15 mm.), but the right ventricle was of normal thickness. All the valves were healthy and valve rings were of normal size. The coronary arteries showed only minimal atheroma without appreciable narrowing. In the basal half of the myocardium of the left ventricle there were numerous small foci (1–3 mm.) of grey tissue replacing the muscle. These were scattered indiscriminately around the circumference. Microscopically these were foci of muscle necrosis (Fig. 2) with fibrous replacement, which varied in age from early organization to full fibrosis (Fig. 3). In some of these foci the microscopic branches of the coronary arteries were occluded by fibrosis, usually together with partial or total destruction of the media. The aorta showed only mild atheroma in the form of fatty streaks and isolated plaques covering less than one-quarter of the surface. The renal arteries were normal, as were the other branches of the aorta.

The *right kidney* weighed 105 g., the *left* 95 g. (normal 115–155 g. each). Their surfaces were smooth, while the cortex was slightly thin and blotchy in colour. There was a small cortical adenoma in the right kidney. Histologically neither of the renal biopsy specimens (Fig. 4) showed more than a few glomeruli, and these were free from any sign of nephritis. There was some evidence of tubular atrophy. The interlobular arteries showed fibroelastosis, while the arterioles showed hyaline change and necrosis. The "onion-skin" intimal thickening of malignant hypertension was not seen. Histological examination of sections of the kidneys taken at necropsy confirmed the presence of tubular atrophy. The glomeruli were free from signs of nephritis and the arteries and arterioles showed the same changes as seen in the biopsy specimens, but in addition a number of arcuate and interlobular arteries did show typical "onion-skin" intimal fibrosis (Figs. 5 and 6). This finding, the lack of renal scarring and shrinkage, and the history of acute hypertensive treatment are consistent with a diagnosis of essential malignant hypertension. Microscopical examination of other arteries showed hyaline sclerosis with occasional points of necrosis in arterioles in the suprarenal, the pancreas, and the heart.

In the abdomen there were fibrinous adhesions between loops of intestine and the omentum, and layers of fibrin over the liver and in the pelvis. Microscopically these showed organizing fibrinous exudate, but few polymorphs and no organisms were seen. The appearances suggested a peritonitis that had been successfully treated. The *parathyroids* were within normal limits, and the *bones* were free from secondary osteitis fibrosa.

Other incidental findings included a few foci of acute pancreatic necrosis, and a few foci of pulmonary alveolar exudate that appeared to be treated bronchopneumonia. There were six mixed gallstones. The *breast* showed lobular hyperplasia and signs of secretion (Fig. 7), possibly due to the administration of chlorpromazine.

Pathologist's Diagnosis

(1) Treated essential malignant hypertension.
(2) Uraemia.
(3) Treated peritonitis with persisting fibrinous exudate.
(4) Focal myocardial necrosis, probably of vascular origin.
(5) Gallstones.
(6) Focal pancreatic necrosis.
(7) Hyperplasia of breast due to drugs.

Discussion

Dr. O. WRONG: One of the chief reasons why we thought she had the histology of malignant hypertension is that in the course of a year she had gone from a stage when her blood-urea level was 48 mg./100 ml. to total anuria with death in uraemia. It is quite likely that at some time during this period she went through a phase of papilloedema with a higher diastolic blood pressure than any we have recorded—particularly in the last month before admission, when she was already ill and stopped treatment. Obviously there must be patients with a condition intermediate between what one would accept as benign nephrosclerosis, on the one hand, and malignant nephrosclerosis, on the other—and she was in this no-man's land, though perhaps more at the benign end of the spectrum histologically, and more at the malignant end clinically.

In the last two years we have had several patients with severe hypertension, progressive renal failure, and the histological features of malignant hypertension who have *not* had a papilloedema. We presume that the malignant hypertension is so rapid that they develop the lesions in the kidney causing uraemia without developing the papilloedema which is usually an accompaniment of the arteriolar lesions. Patients with histological malignant hypertension don't always have papilloedema. I see that Dr. Kincaid-Smith is here today, and I would remind you that in her series of over 200 patients with histological malignant hypertension[1] 3% did not have papilloedema.

Dr. P. KINCAID-SMITH: Yes, I agree.

Dr. WRONG: So we can make a diagnosis of malignant hypertension in a patient who doesn't have papilloedema, particularly if he has got worse rather rapidly. At the moment we have a patient with this syndrome who has actually recovered some renal function after six weeks of dialysis and hypotensive drugs, and has been able to go out of hospital with a blood-urea level of about 200 mg./100 ml. With the patient we are discussing we were not able to persist with treatment for as long as this. I wish we could have gone on longer. Intermittent haemodialysis is probably the best way of treating someone with kidney disease who might have a chance of eventual recovery, but at the time we were not able to squeeze another patient on to our haemodialysis programme, and therefore had to use peritoneal dialysis.

I'm reassured that the infective complications of dialysis were not as bad as we thought they were, but we must do all we can to improve our technique of peritoneal dialysis, in which, at the moment, infection is a limiting factor, as it was here. In this hospital—at least in our unit—we have not so far managed to keep a totally anuric patient alive for more than four months by peritoneal dialysis, because of the technical difficulties caused by low-grade infection. I do find it surprising that this patient had anuria. The glomeruli looked pretty normal, so I presume the blood vessels had closed up completely.

Professor C. C. BOOTH: I find it equally puzzling, frankly, why this patient should have died in oliguric renal failure. I wonder, Dr. Kincaid-Smith, if you would like to comment?

Dr. KINCAID-SMITH: I don't really have much difficulty in understanding the case. I think she had "malignant" hypertension. I believe that she had the lesions in the blood vessels, which I would call treated malignant hypertension; she then blocked off these vessels when she stopped treatment, and became anuric. This used to be fairly common in the course of malignant hypertension—particularly in the days before treatment—and we've seen quite a number of them since treatment has been available. This usually occurs in a patient like this—one who stops treatment, or one who has never been treated. We have done renal biopsies in 80 patients who have been admitted to hospital with acute renal failure and in whom we've expected some sort of irreversible cause; 14 of these have had the vascular changes of malignant hypertension. There are two types of change which are associated with oliguria. The first is the "onion-layering" changes in interlobular arteries. If you follow a particular vessel along they may show definite narrowing in one area and little or none a bit further distally. The second type of change is that the arterioles are quite often occluded by little plugs of thrombosis. This is, I think, thrombotic thrombocytopenic purpura associated with malignant hypertension, and which I think may cause the anuria. I'm very intrigued by the vessels in the heart. I wonder if this had something to do with uraemia rather than hypertension, or whether it couldn't be polyarteritis treated by corticosteroids?

Professor BOOTH: Professor Doyle?

Professor AUSTIN DOYLE: There are one or two things that did occur to me. Dr. Kincaid-Smith has made the statement that if you follow these vessels along you may find obstruction—as far as I know this hasn't been looked for in much detail in this case. Certainly in this kidney there is evidence of ischaemic atrophy. Is it necessary to talk about essential hypertension or benign hypertension? It doesn't seem to me to be a very useful distinction to make. Clearly there are all degrees of involvement of arteries, and clearly this is a patient who has some of the features pathologically of malignant hypertension and some of the features of benign hypertension, but blocked arteries have resulted in her death. I think it is rather uncommon to find these blockages occurring in treated patients, though, as Dr. Kincaid-Smith has said, if treatment is stopped this may happen rather quickly and startlingly.

Dr. C. T. DOLLERY: There are two points worth making. Firstly, the kidney is an organ which requires a high perfusion pressure, so a given degree of arteriolar obstruction will impair the function of the kidney more than other organs. Secondly, I agree with what Professor Doyle has said about the distinction between malignant and benign hypertension. Our work on the retinopathy of Grade III hypertension shows focal damage to the wall of small arterioles, and many people take that as the stigma of malignant hypertension. There is some point perhaps in using the term "accelerated hypertension" to describe this kind of disease. The distinction between grade III and IV retinopathy is still worth while from the clinical point of view, because patients with papilloedema who are treated do a lot worse than those who have only cotton-wool spots.

Professor BOOTH: Why did she get hypertension, then? Were her kidney lesions the primary cause?

Dr. KINCAID-SMITH: Oh no, they were the result.

Dr. WRONG: Why did she get hypertension, then?

Dr. KINCAID-SMITH: I suspect she had it in her genes.

Dr. WRONG: You wouldn't argue that she had toxaemia of pregnancy and became hypertensive on the basis of repeated pregnancies?

Dr. KINCAID-SMITH: She wasn't hypertensive in her first two pregnancies?

Dr. WRONG: Not as far as we know.

Professor BOOTH: Was there any evidence, Dr. Wrong, that this lady had toxaemia in the pregnancy when she *was* hypertensive; did she have proteinuria?

Dr. WRONG: Our evidence is very scanty—we never had any information from New Zealand.

Professor BOOTH: I think it has been suggested that toxaemia of pregnancy may damage the kidney and lead later to malignant hypertension.

Dr. KINCAID-SMITH: Certainly ours would support this—that toxaemic changes may leave permanent damage. I don't know how good the evidence is that it can cause hypertension, because we never really know which came first.

Dr. DOLLERY: Pollock in Chicago has some very convincing serial renal biopsies in a patient who had severe toxaemia. The lesions of the small arterioles have persisted—and even seem to be progressing—though the patient is not hypertensive. It makes one think that hypertension may develop in future.

Dr. C. OAKLEY: Isn't this very unlike toxaemia if she didn't have toxaemia in the first pregnancies? The presence of hypertension in the subsequent ones sounds more like hypertension complicated by pregnancy.

Professor BOOTH: More like a pregnant patient who happens to have hypertension. We are back to Dr. Kincaid-Smith's genes.

Professor J. GOODWIN: Could we come back to the heart again? I would like to ask Professor Harrison whether the vascular changes could possibly resemble in any way the changes described by Saphir and his colleagues[2] in old people who have been given various drugs such as noradrenaline. (I believe this patient had noradrenaline.) They attributed the changes in the myocardium to some sort of hypersensitivity angiitis leading to necrosis. I wonder if this is a possiblity in this patient or whether there were any drugs given that might have done this?

Dr. WRONG: I am afraid I have no information about this. The electrocardiograms showed left-ventricular hypertrophy and non-specific T-wave changes. I'm sorry I can't give you more information.

Professor GOODWIN: Was there left-axis deviation, which might suggest fibrosis of the myocardium?

Dr. WRONG: I don't know.

Professor HARRISON: It is a bit difficult answering this. These changes, where you get a loss of muscle, a falling together of connective tissue, and finally fibrosis are found in patients with aortic regurgitation, or in patients who have had a prolonged period of low cardiac-output failure. The isolated change is common; what is so remarkable in this patient is the enormous number of them clustered together, and of a size that we could see with the naked eye. This is extremely unusual. The next point is the correlation between these and the vascular change accompanying them. Who can tell which is cart and which is horse? If you occlude the vessel surely you might get necrosis of the muscle. If you have dead muscle here are you not in danger of causing thrombosis of the local vessel? I don't know.

Professor GOODWIN: Patients who have massive myocardial fibrosis or necrosis from cardiomyopathy tend to have normal vessels, so I'd have thought the vascular change came first.

Professor HARRISON: That is why I suggested it, but it is impossible to prove it.

Professor BOOTH: Now these vascular changes are thought to produce changes in the red cells. Professor Dacie, would you like to comment on this?

Professor J. V. DACIE: Uraemic patients are often very seriously anaemic. Azotaemia and perhaps infection probably both result in anaemia by diminishing the life-span of the red cells and also by inhibiting erythropoiesis. On top of this we see in some patients—in particular, in those who are suffering from progressive and severe renal failure, often with anuria—a florid haemolytic picture. These patients have a raised reticulocyte count and show fragmented red cells in their blood films. It looks as if a superimposed haemolytic mechanism is active. At necropsy a characteristic finding is disease of small blood vessels of the sort we've seen in the patient we are now discussing. Why the red cells are destroyed is really anybody's guess, but one hypothesis is that they are destroyed in some way by contact with the damaged vessels. Whether this is a result of contact with necrotic tissue, or as the result of intimate contact with fibrin deposited in the vessels, we don't know.

Professor BOOTH: Does this imply that when you see crenated and damaged red cells in the peripheral blood there is fibrinoid necrosis, and that you're therefore dealing with severe hypertension, or accelerated hypertension, or malignant hypertension, or whatever you call it ?

Professor DACIE: We believe this is so, but there are many other causes of this blood picture than malignant hypertension. One such cause is thrombotic thrombocytopenic purpura—or Moschcowitz's disease—where the blood-vessel changes are widespread and not confined to the kidneys. We see, too, a similar picture in cases of carcinomatosis where carcinoma cells are growing in the blood vessels or in the spleen or bone marrow.

Dr. DOLLERY: May I ask a question of our visitors ? What do they think is the difference between benign and accelerated hypertension. If you compare two people with similar pressure levels, one of them may destroy his small arterioles and die with uraemia, while the other goes on for years without suffering severe damage to small blood vessels.

Professor DOYLE: This is a very difficult question to answer There is a good deal of evidence to suggest that the higher the blood pressure the more likely you are to find fibrinoid change and thrombosis in the blood vessels. Another factor is the speed at which these changes develop ; changes rather like this occur rapidly in acute nephritis and in eclampsia. The more rapidly the disease process progresses the more likelihood there is of vascular damage. There is some evidence that it is possible to render blood vessels more sensitive to the changes of high blood pressure. Asscher and his colleagues[3] irradiated the arteries of rats and found increased sensitivity. I don't think an autoimmune factor is beyond the realms of possibility. Evidence for this at the moment is not strong.

Professor BOOTH: Well, I think that's a very clear statement of the present problem.

We are grateful to Professor J. P. Shillingford and Dr. E. D. Williams for assistance in preparing this report, and to Mr. W. Brackenbury for the photomicrographs.

REFERENCES

[1] Kincaid-Smith, P., McMichael, J., and Murphy, E. A., *Quart. J. Med.*, 1958, 27, 117.

[2] Kline, I. K., Kline, T. S., and Saphir, O., *Amer. Heart J.*, 1963, 65, 446.

[3] Asscher, A. W., Wilson, C., and Anson, S. G., *Lancet*, 1961, 1, 580.

NEW APPLIANCES

A Means of Speaking for Patients with Cuffed Tracheostomy Tubes

Dr. R. M. L. WHITLOCK, formerly registrar, Acute Respiratory Unit, Auckland Hospital, Auckland, New Zealand, writes: Cuffed tracheostomy tubes are used to protect the lower airways in conditions complicated by bulbar paralysis and to facilitate prolonged intermittent positive-pressure respiration (I.P.P.R.) in the treatment of respiratory failure. Patients with these conditions are often unable to write because of paralysis or limb injuries and few people are skilled at lip reading. Because of the need for another means of communication a simple tracheostomy-tube attachment has been developed.

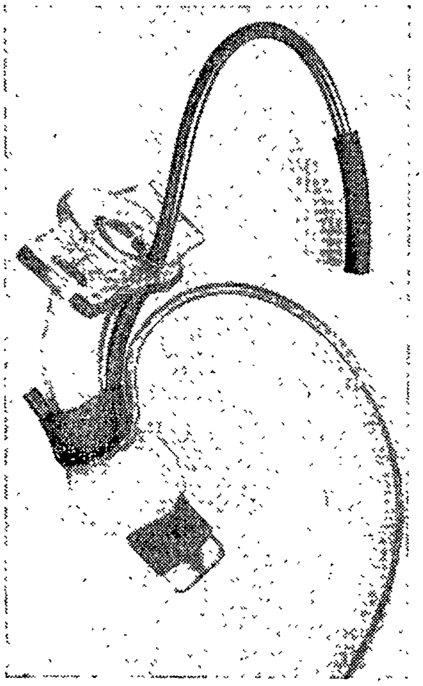


FIG. 1

The attachment (Fig. 1) consists of an F.G. 8 or 10 disposable plastic suction catheter through which air or oxygen is passed to blow on to the vocal cords. The catheter passes through a hole bored in the lower edge of the flange of a Portex plastic tracheostomy tube (Portland Plastics, Great Britain) which has a detachable inflatable cuff at the distal end. It then runs below the tube until it curves round one side to direct the tip upwards towards the vocal cords. Its curved portion is held in position by the edge of the cuff. With the catheter in the correct position (Fig. 2) a gas flow of 5 litres per minute is sufficient for distinct speech in the average adult without discomfort. The supply can be from a small air compressor or an oxygen cylinder with a pressure-reducing valve. To avoid drying of the mucosa and discomfort to the patient it is preferable to warm and humidify the gas, especially if oxygen is used. A pressure-relief valve somewhere in the supply line is a desirable safety measure. The gas supply should not run continuously but only when the patient wishes to speak. If a small electrical air compressor is used the flow rate can be pre-set and the compressor switched on by a microswitch which can be operated by any movable part of the patient's body. Alternatively a nurse may switch on the gas supply.

This attachment is cheap and of simple construction, and does not interfere with tracheostomy management or I.P.P.R. It allows speech throughout the whole of the respiratory cycle, does not rely on I.P.P.R., and has no moving parts. (A specially constructed tracheostomy cannula that uses the patient's exhaled air through a sliding valve for speech has been described elsewhere,[1] but it can be used only for patients on a Bird respirator.)

A delay of three days after tracheostomy is recommended before attempting to use the attachment. This interval allows time for the tracheostome to become sealed by granulation tissue, thus preventing escape of air around the tracheostomy tube or, worse, into the tissues of the neck and mediastinum.

Clinical trials on seven patients have been encouraging with six successes, though one of these found the flow of air too uncomfortable after a successful trial. The failure occurred in a patient with a tracheostome larger than usual which allowed the air to flow out round the tracheostomy tube more readily than through the vocal cords.

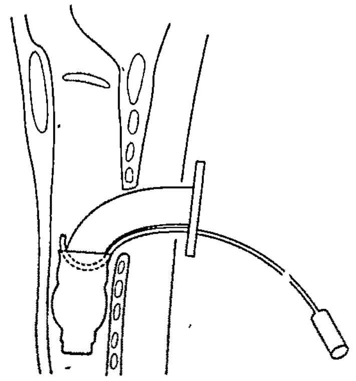


FIG. 2

This speaking-aid not only makes communication easier but also relieves the patient from the frustration and fear of not being able to make his requirements known. There have been no complications from its use.

I thank Dr. M. Spence, medical officer in charge, Acute Respiratory Unit, Auckland Hospital, for permission to develop this device and for advice on its use.

REFERENCE

[1] Hessler, O., Rehder, K., and Carveth, S. W., *Anesthesiology*, 1964, 25, 719.

Book Reviews

Conditions Causing Headache

Research and Clinical Studies in Headache. Vol. 1. Edited by Arnold P. Friedman, M.D. (Pp. 221; illustrated. sFr./DM. 41.50.) Basle and New York: S. Karger. 1967.

Interest in the subject of headache has greatly increased in the last decade as research activities move rapidly into the sphere of chemical investigation rather than clinical description, but the literature is so scattered that the average physician finds difficulty in keeping up to date. This book is said to be the first of a series intended to bring together under one cover authoritative reviews on different facets of the problem, and edited by a distinguished physician well known for his own work in this field the series has certainly made a good start. The contributors are drawn from widely separated parts of the world—Europe, Australia, and America—and are recognized authorities on the subjects they discuss. Though any book drawn up in this manner is bound to have a lot of repetition in it, this has been reduced to an acceptable minimum.

The introduction by E. C. Kunkle forms a philosophical prelude, stressing the need to look at the "whole" patient, and often to temper one's therapeutic enthusiasm with sound common sense. It includes a number of classical quotations which will no doubt be a boon to speakers looking for an opening or closing sentence to their discourse on headache. There then follows an extensive review by F. Sicuteri on vasoneuractive substances and vascular pain. This is a valuable article, with 163 references, tracing the development of thought and work on this aspect, and goes well beyond the action of methysergide, the drug with which its author's name has been so closely connected. The clinical use of methysergide is later dealt with by D. A. Curran, H. Hinterberger, and J. W. Lance, from Sydney, who review its development, trials, indications and limitations, and its dosage schedule. It is of course a drug not without dangers, and its most alarming side-effect—retroperitoneal fibrosis—has a chapter to itself written by J. A. Graham and his colleagues from Boston. They analyse 27 cases of this curious condition, which of course also occurs in patients without any such precipitating cause; they consider it in conjunction with other types of inflammatory fibrosis (for example, pleuro-pulmonary fibrosis) occurring during methysergide therapy and think the drug uncovers rather than causes a predisposition to collagenosis in susceptible individuals. They suggest further that more attention might be paid to a possible link between migraine and the collagen disorders.

A very useful clinical chapter on migraine variants is contributed by J. D. Carroll, but this is marred a little by some unfortunate phraseology and even some inaccuracies. The statement that in recurrent attacks of unilateral headache followed by a third nerve palsy, or sometimes a total unilateral ophthalmoplegia, arteriography has always failed to show any abnormality could be very misleading to many readers, and this is not helped by the later statements that the most common sites for aneurysms causing the ophthalmoplegic variety of migraine are the main trunk of the internal carotid artery or its junction with the posterior communicating artery. Most neurologists and neurosurgeons will know what the writer means by these apparently contradictory statements, but there are many others who are going to read this book. This section also quotes another author as holding views on certain arteriographic appearances in "ophthalmoplegic migraine" which are exactly the opposite to those which he has published, and it is a pity that this has been allowed to creep into a textbook.

There is a chapter by R. Greene on menstrual headache, and a justifiably rather indefinite chapter by P. F. A. Hoefer on the electroencephalogram in headache. The book ends with two chapters from the Mayo Clinic by M. J. Martin, H. P. Rome, and W. M. Swenson on that most common of all chronic headaches—the muscle tension headache—which is so often glossed over in a few sentences in textbooks. Here it is looked at symptomatically, aetiologically, and therapeutically. The optimism of two of the authors in the results of treatment will not be shared by many, and it is important not to confuse relief from the headache with relief from the patient's complaints about it. However their emphasis on looking at the patient as a whole brings us back to the introduction and so rounds off a most informative book, which will be a source of reference of great value to anyone trying to understand the wide spectrum of the conditions causing headache.

EDWIN R. BICKERSTAFF.

Philosophical Approach to Learning

An Introduction to Gynaecology and Obstetrics. By Philip Rhodes, F.R.C.S. (Eng.), F.R.C.O.G. (Pp. 278+viii; illustrated. 21s.) London: Lloyd-Luke. 1967.

The plethora of small books on obstetrics and gynaecology which have been added to the collection of new editions of old-established small textbooks of the "crammer" type in recent years would seem to make it very difficult to justify the production of yet another. This is a textbook with a difference, as it approaches the subjects in a novel fashion and is obviously not intended as a book for quickly memorizing a few essential facts before an examination as are so many of the other small textbooks.

The author deals with the subject in an almost philosophical fashion, and has tried, with success, "to show something of the background ideas which inform the practice of gynaecology and obstetrics." He has also succeeded in bringing into perspective the relationships between obstetrics and gynaecology and the other disciplines of medicine. This has been difficult to achieve in the compass of the small size of this book while still introducing all the essential factual elements of obstetrics and gynaecology. It is not intended to replace a full textbook, but a student reading this book would be able to grasp the wider concept which Professor Rhodes has been trying to convey. When a student comes to reading any of the present large textbooks, particularly if they are being used only for reference, after reading this small book he will be able to see any of the conditions found in obstetrics and gynaecology in its true context in relation to medicine. In any new venture there are bound to be some parts which are not universally acceptable; for example, it might have been preferable to deal with the treatment of each condition as it occurred rather than to leave the whole treatment in gynaecology to one chapter. This is a small criticism of a book which is otherwise very attractive, both from the point of view of what it is aiming to do and for the way in which the author expresses his undoubted literary ability.

This book can certainly be recommended to students in preference to all the other books on obstetrics and gynaecology which some students rely on without reading one of the large textbooks, because this book, while small, does not attempt to provide more than a framework but does convey an impression of the width and scope of the subjects of obstetrics and gynaecology.

IAN MACGILLIVRAY.

Human Extracellular Proteins

Molecular Biology of Human Proteins. Vol. 1. Nature and Metabolism of Extracellular Proteins. By H. E. Schultze and J. F. Heremans. (Pp. 904+xii; illustrated. £15.) Amsterdam, London, and New York: Elsevier. 1966.

On opening a book of this size one expects to find a collection of articles lacking coherency and of varying quality that have been contributed by a group of authors. It is a refreshing surprise to discover that this massive book has been compiled by two authors, that it possesses many of the desirable qualities which should be associated with single- or dual-authorship, and that it contains a critical, concise, and comprehensive account of interwoven topics.

This volume represents the first half of a treatise on the soluble proteins of human plasma and other extracellular fluids, and in particular on the understanding of. their physiological activities in terms of their molecular structures. The title of the treatise is, however, somewhat optimistic, since the relationships between the structures of the majority of the proteins which are discussed and the functions of these proteins in health and disease have yet to be elucidated. The book is divided into four sections: (1) a survey of protein structure and of physical, chemical, and immunological methods of analysis; (2) tables of the properties of thirty-four purified plasma proteins and a survey of the methods which are used to fractionate plasma proteins; (3) an account of the biosynthesis and metabolism of plasma proteins, including the exchange of the proteins between mother and child; and (4) a description of the nature and properties of the proteins of extravascular secretions. The text is supported by extensive tables, over 400 illustrations, numerous references, and a subject index. Although much of the information presented in the first section is available elsewhere in greater detail, the remaining sections contain material which has not previously been published collectively in such detail. Each topic is developed historically from the first significant observations to the beginning of 1965.

However, science does not stand still while books are printed, and much new information on, especially, the structure of proteins and, in particular, of the immunoglobulins has appeared since this volume was written. But, in spite of some of the topics being a little behind the times, this book will be invaluable to all who are interested in the nature, biosynthesis, and metabolism of the proteins of human extracellular fluids.

M. J. Crumpton.

Systems of Medical Care

Medical Care. Social and Organizational Aspects. Edited by Leslie J. DeGroot, M.D. (Pp. 538+xiv. $16.50.) Springfield, Illinois: Charles C. Thomas. 1966.

This book is chiefly a collection of papers on medical care in the United States which appeared in the *New England Journal of Medicine* from 1963 to 1964. New information has been added, together with several additional papers.

Of the 36 chapters 35 are contributed by American experts. Chapter 23, on the regionalization of hospitals in the United Kingdom, which is written by Dr. John R. Ellis, secretary of the Association for the Study of Medical Education, is useful for comparison with American systems.

The first chapter, "Twentieth Century Attitudes towards Health," quotes a nation-wide survey which concluded that "the overwhelming majority of Americans seem to have a deep respect for the personnel, facilities, and services provided by modern medicine."

It is interesting to note that, as in Britain, in the 1930s the support of hospitals by private wealthy donors ceased in America. These are now chiefly supported by private repayment insurance and grants from governmental bodies. More persons obtain medical care, and there is an increasing demand for good care. Chapters 2 to 8 discuss selection of medical students, undergraduate and post-graduate medical education, and integration of education with medical research. Chapters 9 to 15 deal with community, university, and voluntary teaching hospitals and nursing-homes in their various aspects and their relation to social medicine. Chapter 16 critically compares health-service systems in the United States with those of other countries, especially Sweden and Great Britain. Chapters 17 and 18 are concerned with the general practitioners and group medical practice. Chapters 19 to 27 touch on many problems of hospital and health planning and medical care. Chapter 26, on public medical care for the needy, indicates that the provision is uneven, and still is based on the Poor Law principle, which Great Britain began to abandon in 1929. Chapters 28 to 35 are devoted to further medical organizations and features of medical care. In Chapter 30 there is an excellent account of the aims and work of the American Medical Association. As is well known, the administrative organization of American public health is of a high standard (see Chapters 25 and 28). Several of the contributors to this book suggest that it should be more closely integrated with the clinical medical services.

Finally, in Chapter 36 the editor, Dr. L. J. DeGroot, considers that in the future the Federal Government will organize medical care on a comprehensive scale. It may well be so, but in so vast a country as America, composed of a number of States with their own laws and regulations, often differing from one another, it will be a gradual and prolonged process.

Dr. DeGroot has essayed a difficult and controversial subject for this book. He and his contributors have done it well, though inevitably there is much repetition and overlapping and some disagreement in so wide a symposium.

Arthur S. MacNalty.

Blood Groups

Lehrbuch der Menschlichen Blut- und Serumgruppen. 2nd edition. By Professor Otto Prokop and Dr. Gerhard Uhlenbruck. (Pp. 924+xvi; illustrated. £6 13s. 7d.) Leipzig: Georg Thieme. 1966.

In the introduction to the first edition of this textbook on blood and serum groups the authors stated that they were closing some gaps by adding to the discussion of blood groups in general a more detailed account of the modern serum groups and of the chemistry of blood group substances. A second edition became necessary within less than three years, and this has now become a handbook rather than a mere textbook. It has become impossible to cover the whole field because it now includes molecular biology, immunochemistry, and serological genetics. It helps, therefore, that at the end of this second edition there is a list of international addresses of experts in many fields. There are several hundred names, but only for some of them do the addresses indicate the expert's special interest. Many of the names, of course, speak for themselves, but nevertheless it is often not easy to know what kind of help the person indicated may render. There is also an enormous list of references, 142 pages with some 30 references per page. Another interesting feature is a table giving the dates of the discovery of 82 blood group systems, with the names with which they are associated, beginning with the ABO groups discovered by Landsteiner in 1900. It ends with three blood groups discovered in 1965: Kamhuber, A_{hel}, and Do^a.

The blood groups themselves are described and the preparation of antisera in various animals is discussed. There is an excellent and detailed chapter on the chemistry of blood group substances. Haptoglobins are described, and methods for their recognition such as starch electrophoresis using various buffer systems are given in detail. The pre-albumins, the Gm and the Gc and the Ag serum groups, as well as the cholinesterases, are given a chapter each, and there are chapters on the qualifications of blood group experts for law cases and on the probability calculations for eliminating paternity. There is a very detailed description of the present position of the association of blood groups with diseases. This is an excellent book, but it will be appreciated only by readers who are fully familiar with the German. However, even those who may find the language occasionally difficult may learn from its unique collection of references.

H. Lehmann.

Value of Group Treatment

The International Handbook of Group Psychotherapy. Edited by J. L. Moreno, M.D. (Pp. 747. 84s.) London: Peter Owen. 1966.

In July 1963 the Third International Congress of Group Psychotherapy met in Milan. One hundred and twenty-four papers were read in five different languages. All the papers have been collected and are presented in this voluminous tome in their original language and usually in highly abridged form.

The master mind behind the Congress and the main editor of the book is J. L. Moreno. He does not let this opportunity slip without reminding us, once again, of his unique contributions to the initiation and development of the theory and practice of group psychotherapy. He confides that he began it all in 1913 with some prostitutes in the sexual ghetto of Vienna. Since then he has come to see in group therapy a "third psychiatric revolution" whose "ultimate goal is a therapeutic society, a therapeutic world order." Moreno believes that it is his role to spread the gospel of group treatment. He is supported in this belief by his wife, who contributes the longest paper to the book. She disavows "misplaced modesty," and says of her husband: "Like a modern St. Paul, Moreno . . . carried the message everywhere." This book is certainly a monument to his achievement in establishing an international group therapy movement.

To those in search of evidence of the value of group treatment, or of the differential merits of particular modifications of it, this book has little to offer. But those who need no further convincing will find a rich feast in it of theoretical formulations, technical variations, diversities of applications, and range of methods used in the teaching and training of novices. It is indeed remarkable to see how much thought and ingenuity have gone into the interpretation of group processes, the development of new practices, and the discovery of new fields of usefulness.

F. KRÄUPL TAYLOR.

Life Insurance

Annals of Life Insurance Medicine. 1967. Vol. 3. Edited by Swiss Reinsurance Co., Zurich. (Pp. 272; illustrated. DM. 42.) Berlin, Heidelberg, and New York: Springer. 1967.

The title of this book might lead one to believe that it is of interest only to actuaries and medical advisers to life insurance offices, and the first article, which is concerned with the interpretation of survival rates, and which contains a liberal sprinkling of mathematical symbols, certainly confirms this impression. But the persistent reader will eventually be rewarded by finding something of interest among the remaining 14 articles which make up the book.

There is, for example, an interesting chapter on variations in mortality rates and causes of death in different parts of the world. This is followed by a well-documented article on the antecedents of disease based on the records of a number of North American life insurance companies. By relating the results of medical examination of persons accepted for life insurance to their subsequent survival these studies provide some assessment of the significance of variations in body build and blood pressure and of such abnormalities as heart murmurs and arrhythmias, chest pain, albuminuria, and glycosuria. Some of these points are developed by other authors, who contribute articles on the value of the electrocardiogram, the prevalence of silent coronary disease, and the significance of heart size and of proteinuria.

Most of the rest of the book deals with matters which one does not usually associate with life insurance medicine. These include the results of valvuloplasty for mitral stenosis (first presented in 1962 and now looking a little dated), the prognosis of chronic cor pulmonale, the pathogenesis and course of stroke, the prognosis of haemorrhagic diseases, and the aetiology of diabetes and its long-term prognosis.

With such a variety of content this book might reasonably be expected to have some appeal to physicians, epidemiologists, medical statisticians, and of course those concerned with life insurance methods. But few readers are likely to find so much of it useful that they would hasten to buy it. It is perhaps a book more for the library shelf than for one's own bookcase.

R. G. RECORD.

Sigerist, Medical Historian and Diarist

A Bibliography of the Writings of Henry E. Sigerist. Edited by Genevieve Miller. (Pp. 112+vi. $6.00.) Montreal: McGill University Press. 1966.
Henry E. Sigerist: Autobiographical Writings. Selected and translated by Nora Sigerist Beeson. (Pp. 247+xii. $5.75.) Montreal: McGill University Press. 1967.

Two important books dealing with the life and works of Henry Sigerist, the leading medical historian of his time, have been published by McGill University Press, Montreal. Each is complementary to the other, although the autobiography may have the wider appeal.

The bibliography, prefaced by a brief account of Sigerist's life-work by Professor Ackerknecht, of Zurich, consists of a list of books, papers, addresses, and reviews, 520 items in all, each dated, annotated, and indexed. Two outstanding entries are volumes I and II of the eight-volume *History of Medicine* which Sigerist had planned and begun only a few years before his death in 1957 at the age of 66, and which remained unfinished. Among his earlier books, *Socialized Medicine in the Soviet Union,* and *Civilization and Disease,* though subjected to much controversy, exercised a widespread influence.

For the general reader, the second of the two books under review may be of greater interest. Entitled *Autobiographical Writings,* it supplies a clear picture of the life and work of a remarkable man. In 1953, only four years before his death, Sigerist began to write his autobiography, which, unfortunately, goes no farther than his childhood in Paris and his schooldays in Zurich. From his notes and diaries, however, his daughter, Nora Sigerist Beeson, has been able to complete the picture in her father's own words dating from 1910, when, as a student in Zurich, he discovered that "medicine was the most fascinating of academic subjects." In 1919 he met Professor Karl Sudhoff, who had created an Institute for the History of Medicine, and in 1925, at the early age of 33, he succeeded Sudhoff in the chair of medical history, at that time regarded merely as "a delightful hobby for retired practitioners." Sigerist remained at Leipzig until 1931, when he was called to America to succeed W. H. Welch (the famous "Popsie" Welch) in the medical history chair at Baltimore. From that critical point in his career the autobiography is a series of extracts from the diaries which record his activities until 1947, when he retired from the chair and went to live in Switzerland, where he died ten years later. His Swiss home, "Casa Serena," Pura, was a remote retreat which became a Mecca for medical historians.

"To write a diary," Sigerist tells us, "is to stop each day, to think of what one wanted to do, and of what one did not do: the effect is very salutary." Little did he imagine that his diaries would one day appear in print, and that his comments, so helpful and so human, might even influence future generations. Is it a wild surmise, or only wishful thinking, to suggest that Sigerist may one day earn a place among the great diarists of literature? Certainly he achieved greatness as a scholar, and as a real friend to many, and his service to medicine was invaluable.

DOUGLAS GUTHRIE.

Books Received

Review is not precluded by notice here of books recently received.

Renal Transplantation. 2nd edition. By Roy Yorke Calne, M.A.(Cantab.), M.S.(Lond.), F.R.C.S.(Eng.). (Pp. 220+ix; illustrated. 63s.) London: Edward Arnold. 1967.

New Drugs. Evaluated by the A.M.A. Council on Drugs. 1967 edition. (Pp. 390+xiii. $3.50.) Chicago: American Medical Association. 1967.

Die Tollwut bei Mensch und Tier. By. Dr. Claus Eichwald and Dr. Horst Pitzschke. (Pp. 300; illustrated. £3 4s. 11d.) Jena: Gustav Fischer. 1967.

Klinische Chirurgie für die Praxis. Ergänzungs- und Registerband. Edited by Professor O. Diebold, Professor H. Junghanns, and Professor L. Zukschwerdt. (Pp. 300+ix; illustrated. DM. 74.) Stuttgart: Georg Thieme. 1967.

Die Pulmonale Hypertension bei Angeborenen Herzfehlern im Kindesalter. By K. Bühlmeyer. (Pp. 89; illustrated. sFr./DM. 22.) Basel and New York: S. Karger. 1967.

Morceaux Choisis sur les Rhumatismes Inflammatoires Chroniques de l'Enfant. By N. Bloch-Michel *et al.* (Pp. 260; illustrated. 40 F.) Paris: L'Expansion Scientifique Française. 1967.

Olduvai Gorge. Vol. 2. The Cranium and Maxillary Dentition of *Australopithecus (Zinjanthropus) boisei.* By P. V. Tobias. (Pp. 264 +xvi; illustrated. 90s.) London: Cambridge University Press. 1967.

The Haemolytic Anaemias. Congenital and Acquired. Part 3. Secondary or Symptomatic Haemolytic Anaemias. 2nd edition. By J. V. Dacie, M.D., Hon.M.D., F.R.C.P., F.R.S. (Pp. 719–991+vi; illustrated. 60s.) London: J. & A. Churchill. 1967.

Proceedings of the World Population Conference. 1965. Vol. 2. Fertility. Family Planning. Mortality. (Pp. 510+xiii. $7.50.) New York: United Nations Department of Economic and Social Affairs. 1967.

Lectures to Relatives of Former Patients. By Abraham A. Low, M.D. (Pp. 229. $5.00.) Boston, Mass.: Christopher Publishing House. 1967.

Synopsis of Pediatrics. 2nd edition. By James G. Hughes, B.A., M.D. (Pp. 1099+xvi; illustrated. 82s.) London: Henry Kimpton. 1967.

A Textbook of Sex Education. By Dr. Julia Dawkins. (Pp. 98+v; illustrated. 15s.) Oxford: Basil Blackwell. 1967.

Transactions of the Association of Life Insurance Medical Directors of America. Vol. 50. Edited by Samuel R. Moore, jun., M.D. (Pp. 362+x. No price given.) Boston, Mass.: Association of Life Insurance Medical Directors. 1967.

The Clerkenwell Riot. The Killing of Constable Culley. By Gavin Thurston. (Pp. 188+xv; illustrated. 28s.) London: George Allen & Unwin. 1967.

Invertebrate Nervous Systems. Their Significance for Mammalian Neurophysiology. Edited by C. A. G. Wiersma. (Pp. 370+x; illustrated. 72s.) London: University of Chicago Press. 1967.

The Origin of Life. By J. D. Bernal. (Pp. 345 +xvi; illustrated. 55s.) London: Weidenfeld & Nicolson. 1967.

Middle Articles

OUTSIDE EUROPE

Medicine in Burma Today

A. W. WOODRUFF,* M.D., PH.D., D.T.M.&H., F.R.C.P., F.R.C.P.ED

Brit. med. J., 1967, **3**, 551–554

Very great developments have taken place in Burma, and particularly in the medical services in Burma, over the past two decades, and a new administrative organization of these services was inaugurated on 1 January 1965. Little has been heard of these developments in Britain or elsewhere, yet they are remarkable and important. Remarkable in that they have been carried out without any considerable amount of external aid and in this way differ fundamentally from those which have taken place in Africa. Important in that very great emphasis has been given to taking medical services to the people in rural areas, an aim which has defeated the health administrators of many tropical countries. It is important, too, that these developments should be known; there are many lessons to be learned from them and there may be some opportunities for co-operation in furthering them. The opportunity recently arose to see something of these developments, and some of the changes that have occurred in the country during the past 20 years, when I was invited to Rangoon by the Burma Medical Association and to participate in its Annual Meeting.

First a word about why comparatively little is known of these developments outside of Burma. The short answer is, of course, that in recent years Burma has been relatively isolated; the passionate and understandable desire which the Burmese have for complete independence led them to leave the Commonwealth and, as a corollary to this, to make themselves ineligible for aid extended to Commonwealth countries. Likewise, in 1953 Burma terminated the arrangements which they then had for aid from the United States Government. The precipitating factor here was involved with the now almost forgotten Chinese Nationalist invasion of Burma at that time and the evidence that aid to these invaders was coming from American sources. There were various other reasons for the termination of the arrangements with the U.S.A., principal among which being an intense desire on the part of the Burmese people to avoid any help, no matter how desirable, if conditions were attached to it. This is mentioned as a matter of record; the purpose is to present some of the factors which enable us to understand the background to current developments in Burma and the reasons why these are proceeding with a minimum of outside aid. No doubt material developments could have taken place more rapidly had large-scale aid been accepted, but this desire for independence, so passionately cherished by the Burmese people, who prefer to develop along individual lines, is something which has won widespread respect. They, like everyone else, realize that South-east Asia is now and for some time has been in a highly inflammable state and they have no wish to become another Vietnam. Their country has in the last 20-odd years been torn by war several times, first in operations against the Japanese, then by civil war which continued in places until about 1960 and which was aggravated by the Chinese Nationalist invasion between 1950 and 1954, an invasion which came within 20 miles (32 km.) of the important town of Taunggyi in central Burma. A result is that only recently have they begun to see the end of a phase of national reconstruction.

Colour, Gaiety, and Hospitality

In reconstructing their country after all this trouble the Burmese people have a great desire to weave all that is best of their ancient culture into national development in its modern sense. This finds expression in the encouragement being given to traditional Burmese opera, of which there are schools in Rangoon and Mandalay. Burmese opera is certainly a fine art in the true sense of that term as meaning that skilful execution is aimed at as an objective in itself. It is not an art form which has been subjugated to propaganda purposes, and, in keeping with the Burmese national character, it is extremely colourful. Indeed, gaiety and a capacity for friendship and hospitality are outstanding characteristics of the Burmese, and colour is one of the most striking characteristics of the country.

This desire for colour is of course very obvious in the dress of the tribespeople from around the periphery of Burma. As we all know, there have been differences of opinion between these groups and the central government, and the present aim is to bring about their integration with the peoples of Burma proper. With this object a school for national groups has been established at Sagang, and here selected young persons are brought together for periods of a year and trained in local government, so that on returning to their homes they will be able to take a prominent part in running local affairs. I visited the Academy, and certainly they were an exceedingly happy group obviously getting on well together.

Thriving Teak Industry

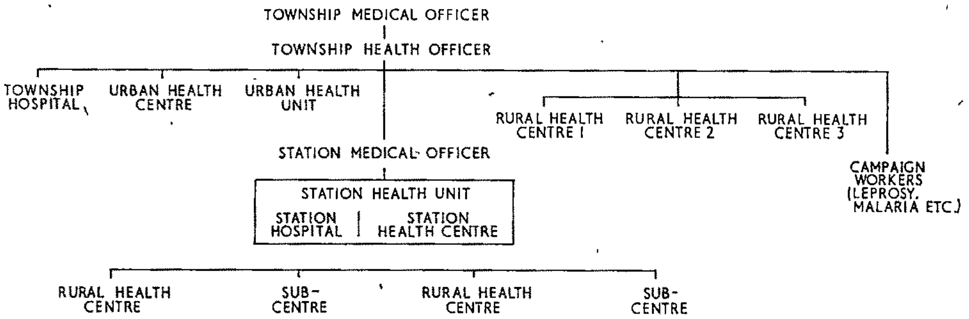
The Ava Bridge, near Sagang, partially destroyed in the last war, has been repaired, and some years ago was reopened. There was evidence near by that the teak industry is thriving, and there were many very large rafts of teak logs temporarily halted at Sagang on their way down the river. I was informed that exports of teak have surpassed their previous level and that a large demand for it has been created by the recently introduced improved processes for veneering cheap woods, such as pine, with teak.

Reconstruction of the Health Services

Regarding the magnitude of the task of reconstructing and developing medical services in Burma it must be remembered that, unlike India and the countries of Africa, building up after the last war had to begin from a medical service which had virtually collapsed during the Japanese regime. A major factor at that time had been the departure from Burma of large numbers of doctors and health auxiliaries on which the health service had mainly depended. To quote Tinker (1961), "Rangoon became a vast slum following the breakdown of the public services and the influx of thousands of refugees who erected basha huts in the main streets and in all open spaces. Everywhere malnutrition was widespread, malaria was rampant, not one vaccination was carried out after 1941, and there were several smallpox epidemics." Though the framework of the medical service was quickly re-established after the cessation of hostilities much that had been damaged could not be speedily restored; to take but one example, the vaccine depot at Meiktila had been razed to the ground, and, with the organization built around it, could not be readily replaced. Similar destruction elsewhere, together with the subsequent civil war, has meant that development in Burma has gone on slowly, with dependence on imported supplies to a much greater extent than in most other countries.

---

* Wellcome Professor of Clinical Tropical Medicine, London School of Hygiene and Tropical Medicine; Physician, Hospital for Tropical Diseases, London N.W.1.



Reorganized administration arrangements. (From *Burma Medical Journal.*)

The reorganized health services as inaugurated on 1 January 1965 are noteworthy in that they have been moulded with the aim of extending their frontiers to the rural workers and farmers, and a particularly important point is that preventive and social medicine is to be based at hospital centres. These preventive and social services will not form, as elsewhere, a separate organization divorced from clinical work. There is also to be complete unification of health services both of Burma proper and of the states, and the health services of the central government and the local administrative services have been merged into one.

Township Medical Officers

Burma has now a population of approximately 23 million and is served by 2,100 doctors—that is, one doctor for 11,000 inhabitants. A key person in the reorganized medical service is the township medical officer. He represents the Director of Health Services at the township level; he will have at least one additional medical officer under him even in the smallest township, and there can be as many as ten or more in the larger towns. The township medical officer, with the assistance of other medical officers and staff, will be responsible for all the functions of the health department in his district, both curative and preventive. In most cases he will be a doctor with general medical training, along with training in preventive medicine. The organization is as set out in the Chart, which is adapted from KoKo (1965).

Hlegu.—The population covered by the township medical officer will be variable, but one that I visited was at Hlegu, and is representative of the pattern. Here the town itself has some 10,000 people, and the district around it which the centre serves has approximately 60,000. The urban centres function mainly as general practitioner units. The station medical officer in this particular set-up was located at Phaunggyi, some 17 miles (27 km.) distant from the township of Hlegu. He was in charge of a new station health unit comprising a small hospital of 16 beds with an attached health centre. From such a station health unit there are normally to be run some four to six rural health centres staffed by health assistants, health visitors, or midwives. In other places rural health centres may not be run directly from a station health unit. Attached to an organization such as this there are the various campaign workers. The township of Hlegu was, for example, in the attack phase of the national malaria eradication programme. The kinds of diseases dealt with at this township hospital are shown in the Table. There are two main wards, a medical and a surgical, and a total of 50 beds. A small laboratory of the clinical sideroom type is equipped with a microscope and some simple reagents. In all the hospitals which I visited I was struck by the number of patients with amoebic dysentery and its hepatic complications, and this small hospital was no exception. The township of Hlegu is approximately 30 miles (48 km.) from Rangoon, and on the way to it one passes Taukkyan, one of the several British war cemeteries in Burma; this one, beautifully maintained, contains approximately 20,000 graves. On the stonework of the colonnade in the background are recorded the names of some 27,000 soldiers who died in the campaign in the last war in Burma or Assam but whose bodies could not be found or identified.

Admissions to Hlegu Township Hospital

	1965	Range 1961–5
Trauma	106	
Pneumonia	52	
Pulmonary tuberculosis	46	9–66
Intestinal helminths	39	39–723
Malaria	35	35–73
Beriberi	29	
Anaemia	28	
Snake-bite	26*	
Bacillary dysentery	21	1–131
Amoebic dysentery	17	3–132
Typhoid fever	13	2–13
Others	648	
Total	1,060	

* Including 3 who died.

Divisions

The country is at present divided into six divisions—Rangoon, Central, North-west, South-west, South-east, and Eastern. Later these will be subdivided to make nine. The divisions contain variable numbers of townships with their associated hospitals and organizations, and each division contains variable numbers of district hospitals. An example of one of these is the new General Hospital, Taunggyi, which has recently been completed and has 200 beds. Taunggyi is a town of 40,000, and is the capital of the Shan states, in which 2.2 million live. From most of central Burma malaria has now been eradicated, and it has disappeared from Taunggyi.

Co-operation between Military and Civil Medical Services

A great deal of co-operation takes place between the military and the civil medical services in Burma, and this is exemplified by the arrangements existing at Maymyo. This town of approximately 60,000 inhabitants has a civil hospital of 180 beds and the base military hospital of Northern Command, Burma, of 500 beds. Patients needing special treatment are transferred from the civil hospital to the military hospital. Here are five divisions—medicine, surgery, obstetrics, dentistry, and paediatrics—and eight specialists in charge of the main divisions plus sections of pathology, anaesthetics, and ophthalmology. Diseases of particular interest encountered here include, in addition to the dysenteries and some imported malaria, approximately 15 cases of mite typhus per month. When I was there towards the end of January they had had 30 cases in the previous two months. Here as at Taunggyi many liver abscesses are dealt with; there had been six in the six weeks preceding my visit to the hospital. They had also had six proved cases of typhoid in the previous year. A good deal of leprosy occurs; they had 60 cases in the hospital when I was there, and approximately 40–50 new cases are seen per year.

Workers' Hospital

There are various other hospitals below the teaching hospital level, and among these is the new Workers' Hospital in Rangoon. This has 200 beds, and is a very modern and well-equipped institution. It is outside the health services, being run by the Ministry of Labour, not the Ministry of Health, and is open to those who join a contributory scheme. It has five whole-time specialists—one each in medicine, general surgery, obstetrics, ophthalmic disease, and anaesthetics. There are 1,500 deliveries a year in the hospital, and it is of particular interest that about 100 patients suffering from liver abscesses are seen annually.

Teaching Hospitals

Mandalay

There are now medical schools at Mandalay and Mingaladon in addition to Rangoon proper. At Mandalay the school was opened in 1955 and now has three groups of graduates. The teaching hospital, until a new one is built, is the long-established Mandalay General Hospital. The accommodation is adequate, perhaps not more than adequate, and ancillary services are well established. Much of the preclinical accommodation is in a converted school. There are 50 graduates annually. A certain amount of new building is taking place; the preclinical buildings include some that are new and others that have been adapted from a school. The nurses have a very fine new building, and more building is to follow.

I was interested to learn that kwashiorkor is a common disorder in and around Mandalay. The scientific importance of its occurrence is increased by the fact that there is no malaria in the region now, and in the children with kwashiorkor helminthic infection is not a problem, so that the absence of these two infections—both of which in Africa are sometimes thought to precipitate an attack of kwashiorkor—suggests that that disease is more certainly the result of a pure nutritional deficiency in some and a deficiency with superadded bacterial or viral infection in others.

McRobert (1966) commented on the contrast between utilization of medical women in Britain and in Asia, and stated that "the education of medical women was one of the best things we did in Asia." In this connexion it is of interest to note that, whereas in Britain there is only one woman professor of general medicine among 27 medical schools, in Burma there is one from Mandalay among three medical schools, the one being Professor Daw Myint Myint Khin.

Leprosy.—A leprosy control project was started at Mandalay in 1958 and has become the base from which control throughout the country is very largely organized. There are approximately 140,000 patients with leprosy in Burma—that is, 6 per 1,000—and of these 25% have the lepromatous variety; when the project started there were 210,000. The World Health Organization is helping with this control project. Patients are treated in their homes, and admission to hospital or institution is reserved for those who are seriously ill. In each project area one doctor, two leprosy inspectors, and approximtely 30 paramedical personnel are employed. There are now 30 such areas. These paramedical personnel "dig out" the patients, visit them, and deliver the drugs personally and see that they are taken. The staff of 30 project areas are entirely Burmese with the exception of two members of W.H.O. personnel. In these project areas the survey is carried out in three parts. The first part is limited to established patients, whose treatment is organized and assured, and the second part comprises all schoolchildren in the project area and all known contacts; patients found in this way to have leprosy are rapidly brought under treatment. The third stage of the survey is then entered upon, and everyone in the project area is examined. It is found that even with the most assiduous industry in stages one and two, approximately 30% of those who have leprosy will be missed unless the third stage is carried out. The W.H.O. project leader, Dr. F. Noussitou, with whom I discussed this work, told me that because of the arduous nature of the duties and of the close co-operation required from the local population, comprehensive leprosy control and eradication of this kind has either failed or been only a partial success in every other country in which it has been tackled. However he, an Argentinian, was high in praise of both the quality of the Burmese staff with whom he had been provided and of the co-operation of the local people, the result of this combination being that the scheme was regarded by the World Health Organization as highly successful.

Many who have been to Mandalay will be pleased to know that the extensive war damage to the fort and to Pagoda Hill has now been completely repaired.

On the way from Mandalay to Rangoon by air there was an opportunity once again to see Mektilla, which at the end of the last war was extensively damaged but which has now been entirely reconstructed.

Medical Schools at Rangoon and Mingaladon

At Rangoon and near-by Mingaladon there are the remaining medical schools in Burma.

The Mingaladon School, named the Number 2 Medical Institute, Burma, was opened only in June 1963. The preclinical buildings are all new, are well equipped, and have a very good library. There is an intake of 50–60 students per year. The teaching hospital associated with the medical school is the much-expanded Defence Services General Hospital, Mingaladon.

Institute of Medicine No. 1 Rangoon and the Rangoon General Hospital

This hospital has been expanded from 750 to 1,400 beds since the end of the war, largely by converting the basements and parts of the somewhat spacious verandahs into wards. The eye, the ear, nose, and throat, the tuberculosis, and the children's sections have been moved out of the main hospital into special hospitals of their own, only some emergency work in these fields being done at the General Hospital. Many special units have been set up, including neurosurgery, thoracic surgery, urology, orthopaedics, hand surgery, plastic surgery, a leprosy reconstruction unit, a cancer unit, and a cardiological unit.

The Burmese medical qualifications have recently been accorded full recognition by our own General Medical Council.

The expansion of the hospital and preventive medical services has caused a very great increase in the demand for paramedical personnel, and this demand is being met by the construction of a fine new school for such personnel. It is located in the grounds of Rangoon General Hospital, so that the full facilities in the hospital will be available to the trainees.

Burma Medical Research Council and Institute

The Burma Medical Research Council was founded in October 1962 with the aim of improving the health of the people, of advancing medical and allied sciences through research, and of the co-ordination of work in medicine and of organizations concerned in medical research. The Burma Medical Research Institute is an executive arm of the Burma Medical Research Council and was opened in June 1963. The pattern on which the Council and the Institute have been founded and are run is based on that of the Medical Research Council here and its associated institute at Mill Hill. There are at present departments of bacteriology, experimental medicine, haematology, instrumentation, medical statistics, pharmacology, and physiology. The work on which they are at present engaged appears to have been well chosen, with the object of providing a baseline from which future studies can be extended. They are concerned with such subjects as prevalence of anaemia in Burma, the various blood groups in the country, the occurrence of haemoglobinopathies, biochemical norms in Burma, normal pulmonary capacity of Burmese, the pathology of liver disease in Burma, and the thiamine content of various strains of rice—important because there is still a great deal of beriberi in Burma.

School of Preventive and Tropical Medicine, Rangoon

Great efforts are being made to take curative and preventive medicine to the people, particularly those in the rural areas where 85% of Burma's population live. With the object of providing well-trained staff in sufficient numbers for carrying out this programme a School of Preventive and Tropical Medicine has been established and at present is being housed in No. 1 Medical Institute, Rangoon. Emphasis is of course to be entirely on diseases endemic in Burma ; the course will cover clinical and preventive aspects of these diseases and will occupy one academic year. The school was opened in the autumn of 1966 and 10 students were then to be admitted. The teaching departments comprise tropical medicine, hygiene and public health administration, epidemiology and statistics, and microbiology, with subsections for bacteriology, virology, parasitology, and serology. A comprehensive syllabus has been drawn up which should well equip those who are to go out into the districts as township medical officers with their teams and take part in the scheme of medical care outlined in the earlier part of this paper.

There are many doctors in Rangoon who are old students of schools in this country, and it is planned to continue to send as many as they have foreign exchange for or scholarships for, particularly to our more advanced diploma courses. One of the delights of going to Rangoon was to be greeted by 15 of my old D.T.M.&H. students, who arranged a very enjoyable reunion dinner.

Conclusion

Burma is an exciting place to be in ; the Burmese are working very hard with comparatively little and they are doing important things in a very workmanlike way. The recent recognition by the General Medical Council, London, of the Burmese medical degrees is further evidence of this. The Burmese are keen to have constructive criticism, and throughout my visit it was emphasized that they wanted that, not praise. Behind all this activity is their Prime Minister, General Ne Win, with his solid practical approach.

I came away with very great admiration for the approach to medical problems which is being followed in Burma, and I am sure that there are opportunities for co-operation between our two countries in this field. We can probably help them with selected personnel, and an epidemiologist for the new school of preventive and tropical medicine has already been seconded from the Department of Clinical Tropical Medicine, London School of Hygiene and Tropical Medicine. The fund of good will towards British people in Burma is immense. If their material resources could match their good will the Burmese would indeed be ideally placed.

There is much to be learnt from the way many things are being tackled in Burma and especially in the medical sphere, where dealing with large problems of disease is being imaginatively undertaken with limited resources. The Burmese have much to be congratulated upon. We for our part can help in various ways in this venture, and it is here, in increasing co-operation between the two countries, that this article may perhaps bear results.

REFERENCES

KoKo, U. (1965). *Burma med. J.*, **13**, 2.
McRobert, G. R. (1966). *Times*, 6 June.
Tinker, H. (1961). *Union of Burma*, 3rd ed., p. 214. London.

Approved Names

The second supplement to the November 1966 consolidated list of Approved Names is printed below. Communications relating to Approved Names should be addressed to the Secretary, British Pharmacopoeia Commission, General Medical Council, 44 Hallam Street, London W.1.

Approved Name	Other Names	Action and Use
Alprenolol	1-(2-Allylphenoxy)-3-isopropylaminopropan-2-ol Aptine is the hydrochloride	Beta adrenergic receptor blocking agent
Amfonelic Acid	7-Benzyl-1-ethyl-4-oxo-1,8-naphthyridine-3-carboxylic acid	Central nervous system stimulant
Aprotinin	Trasylol	A polypeptide proteinase inhibitor
Clorazepic Acid	7-Chloro-2,3-dihydro-2,2-dihydroxy-5-phenyl-1*H*-1,4-benzodiazepine-3-carboxylic acid AH 3232 is the dipotassium salt	Sedative
Diacetamate	4-Acetamidophenyl acetate	Analgesic
Droperidol	1-{1-[3-(4-Fluorobenzoyl)propyl]-1,2,3,6-tetrahydro-4-pyridyl}-benzimidazolone Droleptan	Neuroleptic
Felypressin	2-Phenylalanine-8-lysinevasopressin Octapressin	Vasoconstrictor
Gestronol	17-Hydroxy-19-norpregn-4-ene-3,20-dione Gestonorone (I.N.N.) SH 582 is the hexanoate	Progestational agent
Lidoflazine	*N*-{4-[4,4-Di-(4-fluorophenyl)butyl]-piperazin-1-ylacetyl}-2,6-xylidine	Cardiac stimulant
Mafenide	*α*-Aminotoluene-*p*-sulphonamide	Antibacterial agent
Meclofenamic Acid	*N*-(2,6-Dichloro-*m*-tolyl)anthranilic acid	Anti-inflammatory
Mepivacaine	1-Methyl-2-(2,6-xylylcarbamoyl)-piperidine Carbocaine	Local anaesthetic
Mithramycin	An antibiotic produced by *Streptomyces argillaceus* and *Streptomyces tanashiensis*	Antibiotic
Pancuronium Bromide	2*β*,16*β*-Dipiperidino-5*α*-androstane-3*α*,17*β*-diol diacetate dimethobromide	Neuromuscular blocking agent
Prazitone	5-Phenyl-5-(2-piperidyl)methylbarbituric acid AGN 511 is the hydrochloride	Antidepressant
Propyphenazone	4-Isopropylamino-2,3-dimethyl-1-phenyl-5-pyrazolone Present in Gevodin	Analgesic
Quinestrol	3-Cyclopentyloxy-19-nor-17*α*-pregna-1,3,5(10)-trien-20-yn-17-ol Estrovis	Oestrogen
Taloximine	4-(2-Dimethylaminoethoxy)-1,2-dihydro-1-hydroxyiminophthalazine	Respiratory stimulant

CONFERENCES AND MEETINGS

Otolaryngology Conference

[FROM A SPECIAL CORRESPONDENT]

The Second British Academic Conference in Otolaryngology took place in Oxford from 30 July to 4 August. It was attended by nearly 800 surgeons from 40 different countries.

The Summer Meeting of this Section of Laryngology of the Royal Society of Medicine was also held at the Conference, when the subjects discussed were the catarrhal child and facial paralysis. The President of the meeting, Mr. T. G. **Wilson** (Dublin), began by assuming that the term was meant to refer to inflammation of the mucosa of the upper respiratory passages. Predisposing factors to such infection included allergy, antibody deficiency, endocrine factors, heredity, environment, and perinatal infection. Mucoviscidosis, previously known as fibrocystic disease of the pancreas, was not a great rarity, occurring as it did in one in a thousand live births. Local factors were nasal and paranasal sinus infection and nasal obstruction caused by adenoids. Treatment consisted in providing and maintaining a clear airway, and this included the treatment of infected sinuses and the removal of adenoids.

Referring to the history of the word "catarrh," Dr. L. H. **Capel** (London) pointed out that Plato had deplored that the "Sons of Aesculapius" should have to invent terms like catarrh to describe a vague and faintly disreputable condition. It might be wrong to assume that the problem was entirely related to immunology and allergy, as possibly anatomical peculiarities in childhood might predispose to the condition. "Catarrhal" in this sense might be defined as that condition of the nasal airways in which an increase in secretion, or narrowing, was present. In Great Britain respiratory illness was the rule in early life, and if infections occurred early in life they tended to recur. Air pollution, social conditions, and exposure to infection in others were all epidemiological factors. The initial infection was usually viral in nature, and lowering of the outside temperature might favour its growth. Management should be directed to the treatment of infected sinuses, removal of obstructions such as adenoids, the reassurance of the parents, and the exercise of patience until puberty.

Intrauterine and Neonatal Factors

The third speaker, Dr. E. E. **Doyle** (Dublin), said that in considering intrauterine and neonatal factors infection of the liquor amnii might take place within 12 to 24 hours of the rupture of the membranes, but in fact children born after long labour showed no increased tendency to respiratory infection. Nevertheless, neonatal obstruction due to crusting was a common problem in Dublin, even to the extent of interference with suckling, though follow-up of these children showed no increased tendency to infection after the neonatal period. The allergic factor was much more common in Dublin in the lower income groups, and the problem was in general greater where overcrowding was present. Children living in these conditions often had chronically infected adenoids, tonsils, sinuses, and chronic bronchitis. It was remarkable to watch the weight gain and general physical improvement in these children when the adenoids and tonsils were removed and the sinusitis was cleared up. In older children and adolescents infection often appeared to be associated with an anatomical abnormality such as a deflected nasal septum, and vaccination against influenza in closed communities such as boarding schools served a useful purpose.

Facial Paralysis

Reviewing the causes of facial paralysis, Professor **Henry Miller** (Newcastle upon Tyne) pointed out that reassurance could be given to a patient who was believed to have had a stroke but who had weakness of the whole facial nerve; in fact the upper face escaped in supranuclear lesions, because the neurones of the facial nucleus controlling movement of the upper face received impulses from both cerebral hemispheres. Leprosy was the only cause of bilateral facial paralysis in which the upper face was more often affected than the lower. Dealing with Bell's palsy, Professor Miller emphasized that the history of an acute and non-progressive lesion, often preceded by local pain, was characteristic. A comprehensive review of world literature had yielded no single shred of scientifically valid evidence that surgical treatment exerted a favourable influence on the outcome of Bell's palsy.

Dr. **Deryck Taverner** (Leeds) emphasized that the management of Bell's palsy should be directed to accurate diagnosis, relief of pain, reassurance, accurate prognosis, and prevention of sequelae. In 10–15% of cases Wallerian degeneration occurred, with unsatisfactory recovery. The difficulty was in predicting in which cases this would occur, and he had found that anodal galvanic stimulation of the tongue, with assessment of the threshold at which a metallic taste was perceived, gave useful prognostic information in 95% of cases. Treatment with corticotrophin had been found to be so effective that he felt unable on ethical grounds to carry out further trials with untreated controls.

Surgical Approach

Professor L. B. W. **Jongkees** (Netherlands) dealt with the surgical approach to facial paralysis as a whole, pointing out its undoubted value in postoperative or post-traumatic paralysis, or paralysis associated with chronic middle-ear palsy. In particular, all cases of progressive facial paralysis should be seen by the otologist, unless there was another obvious cause. In Bell's palsy he believed that surgical decompression of the nerve should be carried out if denervation was complete, to confirm the diagnosis and to give a better chance for reinnervation to take place. He cited 200 patients in whom operation had been performed; only one patient had been dissatisfied, and then because of tinnitus.

Chemotherapy in Head and Neck Cancer

Professor D. F. N. **Harrison** (London) said that 200 patients with cancer of the head and neck had been treated under his care in the last five years. Most of them had already been treated by either surgery or some form of irradiation, or both, and the aim of chemotherapy at this stage was palliation. There had been little new in the development of chemotherapeutic agents during this time, but much had been learnt about what these agents could and could not do, and about how to avoid some of the undesirable toxic side-effects associated with their use. The powerful alkylating agent Epodyl (ethoglucid), which could be used only intra-arterially, had a life of some eight minutes; the aim must be to limit its action to a local arterial field. One of its cardinal properties was its ability almost invariably to relieve pain, by its destruction of peripheral nerve endings.

During the arterial infusion the bone marrow could be protected from damage by the cooling of the whole patient. This shunted blood away from the bone marrow and reduced the rate of metabolism in the marrow itself. Moreover, it might permit infusion into the internal carotid artery without causing cerebral damage.

Other speakers discussed other chemotherapeutic agents, including methotrexate, and the techniques of administration that might be employed. It was apparent that at present this form of treatment should be carried out only at centres big enough, and with sufficient equipment and trained personnel available, to be able to cope with the many problems and complications which may arise during treatment.

Correspondence

Letters to the Editor should not exceed 500 words.

Restrictions on Doctor in South Africa

SIR,—No doubt readers of the *B.M.J.* are aware of the recent "banning" orders served on Dr. R. Hoffenberg, a senior lecturer in the Department of Medicine, University of Cape Town. He is also a consultant at Groote Schuur Hospital, Cape Town, and a research worker of international standing.

Some of Dr. Hoffenberg's closer colleagues have discussed the more general aspects of the ban in the correspondence columns of *The Times*,[1] but we wish to refer here to the matter as it affects the medical profession. Dr. Hoffenberg's passport was confiscated in 1965, so that he was prevented from contributing to or learning from international conferences. Now his "banning" orders mean that he will not be allowed to teach students at the medical school or in the hospital; he will not be allowed to publish scientific material nor to attend any gathering whether academic or social.

We wish to remind the medical profession in this country that these punitive measures have been taken against Dr. Hoffenberg by the South African Government without any charge being brought against him, and he has no possibility of appeal. Dr. Hoffenberg's medical integrity is not in question, and we must therefore assume that he is being persecuted for his humanitarian work.

We trust that medical men in Britain will give all the support they can to professional bodies in South Africa should they decide to challenge the ban with the limited means available to them. Professor J. F. Brock, professor of medicine in the University of Cape Town, has already issued a statement in the strongest terms, which was published in the *Cape Times* of 2 August 1967. We have seen this statement and support Dr. Brock in his protest against the restriction of a valued member of the profession.—We are, etc.,

ADRIAN.
DUGALD BAIRD.
BRYAN N. BROOKE.
G. M. CARSTAIRS.
RICHARD DOLL.
DEBORAH DONIACH.
A. I. FRIEDMANN.
P. D'ARCY HART.
DENNIS KRIKLER.
J. E. LENNARD-JONES.
B. LEWIS.
EMANUEL MILLER.
J. S. MITCHELL.
L. H. OPIE.
T. R. E. PILKINGTON.
PLATT.
ARNOLD SORSBY.
JOHN WATERLOW.

London W.1.

REFERENCE

[1] *The Times*, August 9 and 12.

A Case for Cannabis?

SIR,—The marihuana psychosis reported by Dr. P. J. Dally (5 August, p. 367) is known in the literature as oneiric delirium or oneiric fantasy. I originally encountered it during my childhood in the Orange Free State, where our employees grew dagga (*Cannabis indica*) illegally and smoked the flowering tops. One of them was what contemporary marihuana smokers would call a "pot head," and was "stoned out of his mind" through smoking dagga constantly. I remember him as my first experience of a drug addict, by turns hilarious and feebly shaking, irrational, incapable of earning a living, ending his life as a grey shadow who emerged from his bundle of rags only when his wife offered him food or he needed more dagga. It is surprising to me that this condition, clearly described by various workers,[1-3] has never been mentioned in the numerous statements made by my colleagues in the popular press.[4,5]

During the past three years I have taken histories of the effects of cannabis on 40 people: some patients, and some habitués, either anxious to impress me as to its virtues or alarmed and shocked by their own physical and mental changes induced by the drug.

A pregnant girl of 16, who had taken small doses of amphetamine intermittently, smoked reefers from time to time. On one occasion she was offered black conga, a resin from North Africa, and smoked a quantity. She described herself as having felt as if she had been kicked by a horse, had terrifying nightmares, and was semiconscious the whole of the next day. She became violently antagonistic to the drug, and was taking nothing at all during psychotherapy.

Another boy left his public school at 16, and became in appearance and manner a typical junkie. He was afraid of other drugs than cannabis, but appeared to be a chronic schizophrenic during the whole period of three years' exposure to the drug. Following probation for drug possession he is in a steady job, and has lost his emaciated neglected appearance and abandoned his grandiose flights of fantasy. He does not appear to be still hallucinated.

A boy of 20 was given his first reefer outside a pub two years previously. While working as a painter and decorator he smoked a particularly strong reefer to ward off symptoms of influenza, and remained semiconscious for three days. During his exposure to the drug he behaved like a chronic mild schizophrenic, but came off the drug after being on probation and entered steady employment. Later, however, he deserted his pregnant wife to join the "Flower People."

Intermittent cannabis-smoking causes slight bronchitis, injection of the conjunctivae, and voracious appetite. Confusion, apathy, and bad temper last for two or three days, during which period barbiturates, alcohol, and phenothiazines produce quite atypical effects. The desire to work is lost, because the subject becomes sure that the job has already been mastered even if it was not really begun. Argument over this produces either a crushingly arrogant response or an extremely paranoid reaction. This change in personality trait is one on which cannabis-taking can be diagnosed in a school or a club; it is extremely striking, and takes up to two weeks to be reversed. More chronic subjects look ill and are emaciated in spite of their enormous appetites and thirst. Though they state that the drug can be easily given up, the psychic dependence appears to be similar to that of cocaine. Even a similar smell, let alone a whiff of the drug itself, excites a strong desire for a reefer. The "come down" lasts two to three weeks, and includes depression about losing the self-confidence and fantasy the drug induced.

In the early 1950s European doctors were warned by the Japanese that the amphetamine habit could produce psychosis, suicide, and major social problems.[6] Our literature has only recognized this psychiatric state recently. This is probably because the amount of habituation to this drug has only risen gradually, but also because the psychosis takes a few years to establish on the small doses of amphetamine which were normally used in Britain. Ten tablets of dexamphetamine-amytal mixture are now taken where one was taken five years ago; for this reason the psychosis develops more rapidly and is more obvious.

The original *Lancet* article "Pop Pot"[7] and the broadcast on "Today," which are quoted by pedlars to prove the harmlessness of marihuana, appeared in 1963. Dr. Dally's experiences and my own may indicate the beginning of a crop of cannabis psychotics which can increase the young population of our mental hospitals and slow down the estimated halving of this by the 1970s. Not unnaturally I become acutely apprehensive when I read authoritative articles in the popular press, signed by my colleagues, stating that this drug is less harmful than alcohol or tobacco. Until we, as doctors, can resolve our differences, we would be wise to confine our polemics to our professional journals.—I am, etc.,

London W.1. ELIZABETH TYLDEN.

REFERENCES

[1] Bouquet, J., *Bull. Narcot.*, 1951, 3, No. 1, 22.
[2] Chopra, I. C., and Chopra, R. N., ibid., 1957, 9, No. 1, 4.
[3] Cardeiro de Farias, R., ibid., 1955, 7, No. 2, 5.
[4] Stafford Clark, D., *The Times*, 11 April 1967.
[5] Andrews, G., and Vinkenoog, S. (editors), *The Book of Grass*, 1967. London.
[6] Nasaki, T., *Série de Rapports Techniques*, 1966, No. 10, W.H.O., Geneva.
[7] *Lancet*, 1963, 2, 989.

SIR,—I am reluctant to add to all the ill-informed comments on drugs, but I am at a loss to understand why the therapeutic value of a drug should be considered in relation to its social usage. I am sure that Dr. D. Stafford-Clark does not intend in his letter (12 August, p. 435) to imply that because a drug has some therapeutic value this in some way makes it possible to free it from restriction, but I have no doubt that the "pot" lobby will fall upon his statement and draw from it quite disastrous inferences.—I am, etc.,

DAVID WILD,
Deputy County Medical Officer of Health.
Chichester,
Sussex.

Dangers of the Woulfe Bottle

SIR,—I was interested to read the article by Dr. B. J. Freedman on the value of the Woulfe bottle for the humidification of oxygen (29 July, p. 277).

In the course of time the water in these bottles can, and often does, turn into a culture of *Pseudomonas aeruginosa*. Experiments with a slit-sampler show that organisms are carried over from the bottles in oxygen bubbled through the water.

It is important, therefore, that such bottles should be washed out and sterilized at frequent intervals. The risk of contamination would be greatly reduced if, in addition, the bottles could be kept empty and dry when not in use, and water put in only when a patient needed to be given oxygen for more than a short period.—I am, etc.,

W. M. EDGAR.

Department of Pathology,
Royal Infirmary,
Bradford, Yorks.

Friction is the Rub

SIR,—May I be permitted to voice a brief protest against the term "friction rub," which over the past few years has crept into the medical literature and has now achieved the distinction of appearing on the first page of the *British Medical Journal* in an otherwise most excellent leading article on "Chest Pain after Infarction" (5 August, p. 321). "Friction" and "rub" are each defined in terms of the other by all English dictionaries. Perhaps we shall soon be reading of murmur bruits and crepitation râles.—I am, etc.,

J. V. S. A. DAVIES.

Wolverhampton.

Investigating Hypertension

SIR,—There is certainly need for balance in the investigation of hypertension, and I write to support the author of your leading article (1 July, p. 4). We have had a particular interest in hypertension and its investigation for twenty years, and two clinics each week are run for the management of patients undergoing long-term treatment with potent drugs. Almost all are first admitted to hospital for assessment to ensure that such a heavy life sentence is really necessary. It must be exceedingly uncommon for any potentially remediable surgical condition not to be suggested by a good intravenous pyelogram and isotope renogram, and, if significant, further investigation would be indicated by failure to respond to medical treatment. I think there may be a tendency for those with a particular interest in the surgical treatment of renal hypertension not to persist with antihypertensive drugs in appropriate combination with or without salt restriction, because our experience has been that treatment, if relatively difficult, is usually satisfactory in such cases.

The detailed investigation of 1,000 cases by aortography is impressive (Wing-Commander P. W. Robertson, 29 July, p. 306), but presumably they were mainly undertaken in relatively young, otherwise well, males.

I am sure that such a programme is justified for pure research, particularly if there is a possibility that the conclusion will be reached that such elaborate investigations are not necessary in most cases, but from the practical point of view of ordinary investigation I think that aortography is rarely required. Undoubtedly, of course, the larger the number of such investigations the more frequently will anomalies be found, but it does not follow that surgical treatment is indicated. It would be of great interest to know how many patients in this series were actually treated surgically and followed for, say, at least two years.—I am, etc.,

R. W. D. TURNER.

Department of Medicine Annexe,
University of Edinburgh,
Edinburgh 8.

Diabetic Lipaemia

SIR,—The occurrence of diabetic lipaemia (milky plasma) was first described in the nineteenth century and remains a well-recognized but rare manifestation of uncontrolled diabetes mellitus.[1] Although prompt diagnosis and insulin treatment of diabetes mellitus have probably reduced the incidence of diabetic hyperlipaemia, reports of the condition still occur.[1 2] I wish to record a case of massive hyperlipaemia in a young diabetic who was thought to be reasonably well controlled with insulin therapy.

A 13-year-old boy was admitted to the Royal Devon and Exeter Hospital complaining of vomiting and severe abdominal pain for 24 hours. The boy was known to be a diabetic for three years before admission and was usually well controlled on 24 units lente insulin daily. On examination he had a tense abdomen but no masses were palpable. It was noted that he had a rapid respiratory rate and extreme difficulty in breathing. The white blood count was 30,000 cells/cu. mm., of which 83% were neutrophils. The blood sugar was 176 mg./100 ml., serum amylase was 160 Somogyi units/100 ml., serum sodium was 111 mEq/l., serum potassium was 3.1 mEq/l., serum chloride was 70 mEq/l., and bicarbonate 18 mEq/l. The serum was noted as being extremely milky in appearance. The urine contained glucose and a moderate amount of acetone.

Because of the uncertain diagnosis, laparotomy (Mr. C. Shaldon) was undertaken. At operation the stomach, jejunum, and bladder were dilated, but no cause was seen to account for these findings. A striking feature at laparotomy was the pink creamy consistency of the blood. After operation he was given 20 units soluble insulin three times daily and improved rapidly. Although the blood sugar was never apparently greater than 250 mg./100 ml., acetonuria persisted for a few days. After operation lipaemia retinalis was observed, but there were no microaneurysms or xanthomata. The plasma lipids were analysed on a preoperative specimen and on succeeding days. The results (Table) show a gross hyperlipaemia which gradually cleared. Since this time the boy has remained well and is receiving 36 units soluble insulin and 12 units protamine zinc insulin daily. Examination of the patient's parent's plasma has not shown any increase in the lipid content.

Day	Cholesterol (mg./100 ml.)	Total Serum Lipids (g./100 ml.)	Lipoprotein
0	1,350	14·9	Chylomicrons
3	508	3·4	Pre-β
5	540	2·4	β
6	490	1·76	β
9	—	1·14	—
19	—	1·56	—
3 months	186	0·9	β
6 ,,	113	0·6	—

Normal range—140–265 mg./100 ml. 0·34–0·9 g./100 ml.

The occurrence of massive hyperlipaemia in diabetes mellitus is described as a rare syndrome,[2] but was a more frequent observation in the era before insulin treatment of diabetes.[3] This case is unusual in that the boy had been well until 24 hours before admission, whereas other cases described have been preceded by a long period of illness.[1] It is probable that diabetic hyperlipaemia is an acquired but reversible form of fat-induced hyperlipaemia with subnormal post-heparin lipolytic activity and delayed removal of dietary fat.[1] The decreased activity of the enzyme appears to be secondary to hormone deficiency, which results in impaired synthesis of the enzyme in contrast to the inherited defect in enzyme synthesis seen in the familial disorder.

I should like to thank Dr. L. Haas and Mr. C. Shaldon, under whose care this patient was admitted, for permission to report this case.

—I am, etc.,

T. HARGREAVES.

Area Department of Pathology,
Exeter, Devon.

REFERENCES

[1] Bagade, J. D., Porte, D., jun., and Bierman, E. L., *New Engl. J. Med.*, 1967, **276**, 427.

[2] Mune, O., and Nørregaard, S., *Dan. med. Bull.*, 1966, **13**, 198.

[3] Joslin, E. P., Root, H. F., White, P., and Marble, A., *The Treatment of Diabetes Mellitus*, 10th ed., 1959. London.

Carcinogenic Properties of Ortho-dianisidine

SIR,—Dr. H. Lehmann's letter (19 August, p. 494) about the carcinogenic properties of ortho-tolidine (3:3′-dimethylbenzidine) and ortho-dianisidine (3:3′-dimethoxybenzidine) and his lament that in your leading article (22 July, p. 189) you do not give firm advice about whether these substances should be used or not in clinical routine practice raises an important question which at the moment cannot be answered in a simple and definite manner.

The Chester Beatty Research Institute has been asked from time to time to give guidance on this matter to individuals. The advice that has been given is as follows: While we believe that it is possible to handle these substances safely if adequate[1] precautions are taken, we think that suitable alternative methods should be sought, for sooner or later laboratory workers may become careless, and the dangerous substances must be manufactured, purified, and packed, possibly exposing other workers to a hazard.

Whether alternative techniques are satisfactory or not can often be assessed only in the framework of the duties of the laboratory concerned. However, the Association of Clinical Pathologists has already taken the initiative, and in a circular to its members[2] has asked biochemists who know of suitable alternative methods, particularly for techniques for the estimation of glucose by the glucose-oxidase method, to let the Association know. The leaflet gives a reference[3] to a bibliography of possibly useful tests for occult blood which are not based on carcinogens.

Some workers have informed me that they have changed to alternative techniques for glucose estimation—specific for glucose and not merely the estimation of reducing substances—which meet the needs of their particular laboratories.[4–6] Perhaps it would be helpful if details of their experiences with these methods were made available to biochemists, either through your columns or through the Association of Clinical Biochemists.

Similar problems have arisen in relation to the use of ortho-tolidine in tests for residual chlorine in water—in this case the Water Research Association has recommended an alternative test based on NN′diethylparaphenylene diamine, which is not believed to be carcinogenic—and in relation to the use of 1-naphthylamine in tests for nitrates in sewage effluents or in urine. Recently an alternative test for urinary nitrites has been proposed.[7] Here again it would be useful if the experience of those who have changed to alternative methods could be collated and brought to the notice of biochemists.

Since it is apparent that it will not be possible to abandon the use of all carcinogenic aromatic amines in medical biochemistry immediately, it would be wise in the meanwhile for the head of every laboratory where these substances are used to ensure that all his staff are aware of the possible dangers and of the necessary precautions, and to see that these precautions are in fact observed. —I am, etc.,

R. A. M. CASE.

Chester Beatty Research
Institute,
Institute of Cancer Research,
Royal Cancer Hospital,
London S.W.3.

REFERENCES

[1] Chester Beatty Research Institute and Harlow Industrial Health Service, *Precautions for Laboratory Workers who Handle Carcinogenic Aromatic Amines*, 1966. London.
[2] *Association of Clinical Biochemists*, 1967, News Sheet, No. 53, July, p. 2.
[3] Henry, R. J., *Clinical Chemistry Principles and Technics*, 1964. New York.
[4] Kelly, D. M., *Clin. Chem.*, 1965, **11**, 471.
[5] Brown, M. E., *Diabetes* 1961, **10**, 60.
[6] Bittner, D. L., and McCleary, M. L., *Amer. J. clin. Path.*, 1963, **40**, 423.
[7] McLean, J., and Henderson, A., *J. clin. Path.*, 1966, **19**, 632.

Transplacental Transmission of Herpes Simplex

SIR,—Gregg in 1941[1] and Swan and his associates[2] in 1943 first reported clinical observations on congenital anomalies in the offspring following maternal rubella. While Swan's observations were concerned chiefly with rubella, he postulated that other virus diseases in the mother might result in foetal maldevelopment.

Herpes simplex infection of the newborn may occur by transplacental transmission of the virus as well as by the more common mode of infection from active lesions in the birth canal.[3] Between 65% and 98% of adults will show neutralizing antibodies to the herpes simplex virus.[3] The incidence of herpetic lesion in the female genital tract is greater than generally recognized. Naib *et al.*[4] found that of approximately 40,000 indigent patients screened for cancer by routine "Pap" smear 62 (0.16%) had initial cytological evidence of a herpetic lesion. About one-third of these were pregnant. Because of these facts and because of the fact that herpes simplex virus in tissue culture causes a high percentage of chromosome aberrations,[5] it is plausible to suggest that herpes simplex cervicitis during early pregnancy may cause congenital malformations.

A 22-year-old primipara was admitted to the department of obstetrics and gynaecology at the General Hospital, Malmö, Sweden, on 23 June 1966 in labour. During the third month of pregnancy she was first seen in the outpatient service. At that time the labia majora were noticed to have several small ulcerations. The routine "Pap" smear showed initial cytological evidence of a herpetic lesion. The ulcerations healed spontaneously, and the pregnancy was uneventful until the 36th week of gestation, when the patient underwent a caesarean section because of toxaemia. The child was a phocomelus and died some hours after delivery because of respiratory distress. As far as we know the patient had not taken any medication during her pregnancy. From the age of 8 years she had been treated with insulin because of diabetes mellitus, which may give malformations, but as far as is known not of this kind.

The present congenital malformations and the maternal herpes simplex infection during early pregnancy may be coincidental. As no studies of a relationship appear to have been published, we hope that others may follow up cases with cytological evidence of herpetic lesions during early pregnancy, and report cases of foetal maldevelopment if any appear. —We are, etc.,

L. CEDERQVIST.
G. ELIASSON.
L. LINDELL.

Departments of Obstetrics
and Gynaecology, and Pathology
(Cytological Department),
General Hospital,
Malmö, Sweden.

REFERENCES

[1] Gregg, N. McAlister, *Trans. ophthal. Soc. Aust.*, 1941, **3**, 35.
[2] Swan, C., Tostevin, A. L., Moore, B., Mayo, H., Blach, G. H. B., *Med. J. Aust.*, 1943, **2**, 201.
[3] Mitchell, J. E., McCall, F. C., *Amer. J. Dis. Child.*, 1963, **106**, 207.
[4] Naib, Z. M., Nahmias, A. J., Josey, W. E., *Cancer (Philad.)*, 1966, **19**, 1026.
[5] Stich, H. F., Hsu, T. C., Rapp, F., *Virology*, 1964, **22**, 439.

Snakebite Poisoning

SIR,—Dr. H. A. Reid (5 August, p. 367) has drawn attention to a newspaper report of snakebite which occurred in a local man.

At the time some concern was caused by the presence of local pain and tenderness, and of dilated pupils and weakness apparently not caused by fear alone, following injury by an unusual snake. This was later identified as a European grass-snake. For the future we have learned from the incident that antivenom is kept in the zoo concerned.

Needless to say, the drama of the occasion was considerably less than was depicted in the press.—I am, etc.,

CHRISTOPHER GARDNER-THORPE.

City General Hospital,
Stoke-on-Trent.

Ehlers-Danlos Syndrome

SIR,—Ehlers–Danlos syndrome may have a wide variety of manifestations. It is often difficult to be sure of the diagnosis, particularly in mildly affected individuals, since the microscopic anatomy is in "a disputed state," and the basic defect is unknown.[1] Thus Mr. A. P. Barabas's suggested clinical subdivision of cases (3 June, p. 612) is most helpful in elucidating the probable heterogeneity of the syndrome, and particularly in pointing out the existence of an "arterial" type which may cause fatal haemorrhage in early adult life.

As Mr. Barabas is aware, intracranial arterial aneurysm has been reported as a complication,[2] and one of us recently described three cases of spontaneous carotid-cavernous fistula in Ehlers–Danlos syndrome.[3] Two of the patients are siblings, a sister and brother, and the sister has since died after suffering a succession of further arterial complications. A brief report of this case may therefore be of interest.

She was last seen in 1961, aged 37, with a spontaneous left carotid cavernous fistula associated with remarkable ectasia of the left internal carotid artery, and alarming haemorrhage occurred at the time of carotid arteriography. Carotid ligation was performed, and one month after operation she developed small aneurysms of the left radial artery and the left superficial temporal artery. The latter disappeared spontaneously. These episodes and further complications occurring up to 1964 have been reported.[3] Her previous history included lifelong easy bruising and a myocardial infarction at the age of 35.

In 1965 she still had an aneurysm of the left radial artery, which was later excised at another hospital. In April 1967 the patient complained of weakness, fatigue, and fever, and then developed severe right-sided headache and blurring of vision in the right eye. On admission to hospital she showed right proptosis and third-nerve palsy, suggesting a right internal carotid aneurysm. Angiography was deferred because of the previous experience and because she also had many features of a systemic disease resembling polyarteritis nodosa. These included fever, hypertension, chest pain, weakness and extreme tenderness of limb muscles, leucocytosis, normochromic anaemia, and a very high sedimentation rate. Skin and muscle biopsy proved inconclusive, showing only slight perivascular infiltration, but a disturbance in the pattern of elastic fibres, in some parts loose and in others arranged in compact masses with a tendency to form nodules, was noted, compatible with the diagnosis of Ehlers–Danlos syndrome (Dr. Mario Montes).

She was treated with corticosteroids, and subjective improvement and disappearance of fever followed; vision improved in the right eye, and the proptosis and right third-nerve lesion both regressed. However, chest pain recurred and electrocardiographic evidence of a further anterior myocardial infarction was seen. Subsequently, a further aneurysm appeared on the right radial artery, the mirror image of that earlier excised on the left. Soon after, she suffered sudden acute swelling in the left calf with agonizing throbbing pain. This was thought to represent rupture of another aneurysm, and at operation, reluctantly undertaken, a false aneurysm was found arising from the left posterior tibial artery. Some 10 days later another aneurysm appeared on the right anterior tibial artery. Finally the patient complained of acute abdominal pain and became unconscious. Blood was aspirated from the peritoneal cavity but there was no time to attempt operation before she died. Necropsy showed that she had ruptured an aneurysm of the splenic artery; other aneurysms were found on mesenteric arteries. Polycystic disease of the kidneys and liver was also found.

It seems worth emphasizing that this patient had thin and unusually smooth skin, but it was not redundant or hyperelastic, and her joints were not unusually lax. As noted previously,[3] her brother had a similar left-sided carotid-cavernous fistula at the age of 30, but we are not aware that he has ever had other arterial complications, although we have not yet had an opportunity to examine him. A full study of the family is in progress; there is no other positive evidence of Ehlers–Danlos syndrome, although there are instances of subarachnoid haemorrhage and of unexplained deaths.

This case, which will be presented in detail, supports Mr. Barabas's contention that there may exist an "arterial" type of syndrome. It provides a particularly florid example, with a similar illness occurring in milder form in a brother. Although usually regarded as an autosomal dominant trait,[1] the possibility of different modes of inheritance in a heterogeneous syndrome has always to be considered, and one might speculate that some cases of the "arterial" form might be transmitted as autosomal recessives. If this were so parents would not be expected to show the trait, and absence of family history could be compatible with this mode of inheritance, as in the case of Rubinstein and Cohen,[2] another of our own,[3] and number 27 of Barabas.

The features of systemic illness (fever, etc.) in our patient are not well explained and it may be noteworthy that they had occurred in milder form earlier in this patient's history. We wonder whether others have had similar experiences and whether more acute episodes of arterial damage may occur in the course of Ehlers–Danlos syndrome.—We are, etc.,

ROBIN M. BANNERMAN.
CARL J. GRAF.
JAMES F. UPSON.

Buffalo General Hospital,
Buffalo, New York, U.S.A.

REFERENCES

[1] McKusick, V. A., *Heritable Disorders of Connective Tissue*, 1966, 3rd ed., p. 179. C. V. Mosby, Saint Louis.
[2] Rubinstein, M. K., and Cohen, N. H., *Neurology (Minneap.)*, 1964, **14**, 125.
[3] Graf, C. J., *Arch. Neurol. (Chic.)*, 1965, **13**, 662.

Warning of Massive Pulmonary Embolism

SIR,—Dr. W. G. Smith (5 August, p. 370) rightly stresses the importance of early recognition and treatment of "warning" pulmonary embolus. This may not, however, be quite as usual as he suggests.

Coon and Coller[1] reported warning emboli in 25% of their cases of fatal pulmonary embolism, and Little, Lowenthal, and Mills[2] found that 7 of their 37 cases of fatal pulmonary embolism had evidence of warning embolus, an incidence of 19%.

A review of St. Thomas's Hospital records for the years 1959–64 shows a total of 76 cases of fatal pulmonary embolism. A definite warning embolus was recorded in 13 (17%) of these cases. In a further 16 cases symptoms of dyspnoea or chest pain were not considered sufficient for a definite diagnosis to be made, and in the remaining 47 cases sudden and profound collapse of the patient was apparently unheralded.

These figures suggest that massive fatal pulmonary embolism usually occurs without any warning. It is therefore all the more important to regard any symptom or sign of pulmonary embolus, however slight, as a potential "warning," and to treat it with the seriousness it deserves.—I am, etc.,

Middlesex Hospital,
London W.1.

DAVID NEGUS.

REFERENCES

[1] Coon, W. W., and Coller, F. A., *Surg. Gynec. Obstet.*, 1959, **109**, 259.
[2] Little, J. M., Loewenthal, J., and Mills, F. H., *Brit. J. Surg.*, 1966, **53**, 657.

Chemical Treatment of Skin Cancer

SIR,—Your leading article (15 July, p. 125) on this subject made good sense. On several occasions I have witnessed Dr. Frederick Mohs at work in his clinic, and have been deeply impressed by both the logic of his chemosurgical method of therapy and the care with which he carries it out. The success he achieves in cases of advanced skin cancer and cases of cancer which have recurred after previous radiotherapy or surgery is unequalled by that attainable by any other method.

Dr. G. M. King (19 August, p. 495) states that his results from treatment with 5% 5-fluorouracil (5-FU) ointment, though it is much too early to assess the long-term success rate, have been "quite impressive." This statement can carry little weight, firstly because it is unsupported by figures which can be interpreted by others, and secondly because it is easy to obtain "quite impressive" results in the treatment of skin cancer by a wide variety of methods. The results would certainly have to be far more impressive than those obtained by E. Klein and his colleagues[1] with 20% 5-FU to justify the widespread adoption of this method of treatment. The possible value of 5-FU in the treatment of solar or arsenical keratoses is in my view a matter for separate evaluation. —I am, etc.,

Chester Beatty Research Institute,
London S.W.3.

FRANÇIS J. C. ROE.

REFERENCE

[1] Klein, E., Stoll, H. L., Milgrom, H., Traenkle, H. L., Graham, S., and Helm, F., *J. invest. Derm.*, 1966, **47**, 22.

Hazard from Nylon

SIR,—I was interested to read of the case of ischaemia of the finger-tip of a small infant reported by Dr. G. G. Noott (5 August, p. 370). A similar case came under my care not long ago in which a loop of fibre inside the baby's glove had strangulated the finger-tip, resulting in gangrene of the part.

This is a hazard I had not come across before, and it seems obvious that mitts made of material would be much safer than knitted gloves or mittens on tiny babies.—I am, etc.,

Epsom District Hospital,
Epsom, Surrey.

E. N. CALLUM.

Treatment of Mendelson's Syndrome

SIR,—Dr. G. Taylor's letter (5 August, p. 368) outlines a very comprehensive regimen of treatment when aspiration of gastric contents has occurred, and states that "vomiting and regurgitation of stomach contents . . . should be regarded as preventable." However, apart from the excellent recognition that all women in labour must be suspected of having a full stomach, irrespective of their last oral intake of food or drink, and the advice on giving oral antacids before anaesthesia, he omits emphasis of the use of various techniques available at induction of anaesthesia for prevention of inhalation of gastric contents. Presumably these are taken for granted, but in such an important subject, where prevention is considerably superior to cure, any mention of prevention (points (1) and (2)) should stress the importance of a well-organized technique of induction, maintenance, and termination of anaesthesia.

Several methods are available for induction of anaesthesia: varying the position of the patient, general anaesthetic agents used,[1-3] use of cricoid pressure,[4] or use of regional analgesia.[5-8]

No method can guarantee 100% safety, and, although we are grateful for any new methods of treating Mendelson's syndrome when it has occurred, we should strive our utmost to reduce the incidence of this complication by taking all possible steps to avoid its occurrence.—I am, etc.,

General Hospital,
Southend-on-Sea.

M. J. WATT.

REFERENCES

[1] Inkster, J. S., *Brit. J. Anaesth.*, 1963, **35**, 160.
[2] Bourne, J. G., *Proc. roy. Soc. Med.*, 1954, **47**, 416.
[3] Wylie, D., ibid., 1955, **48**, 1089.
[4] Sellick, B. A., *Lancet*, 1961, **2**, 404.
[5] Lee, J. A., and Atkinson, R. S., *Synopsis of Anaesthesia*, 1964, 5th ed., p. 681. Bristol.
[6] Steel, G. C., *Proc. roy. Soc. Med.*, 1962, **55**, 933.
[7] Sadove, M. S., Levin, M. J., Rant-Sejdinaj, I., *Canad. Anaesth. Soc. J.*, 1961, **8**, 405.
[8] Thorne, T. C., *Proc. roy. Soc. Med.*, 1954, **47**, 301.

Stewart–Morel Syndrome

SIR,—A woman, 77 years old, was admitted to our unit complaining of headache, vertigo, exertional dyspnoea, and some joint pains. It was noted that she exhibited hirsutism, and she told us that it has been necessary for her to shave each day for about 20 years. She did not remember when she started menstruation, but her periods were regular and she had had the menopause at about the age of 45 years.

On examination there was pallor, slight pitting oedema of both ankles, and lipomatosis of both arms and thighs. Her blood pressure was 220/

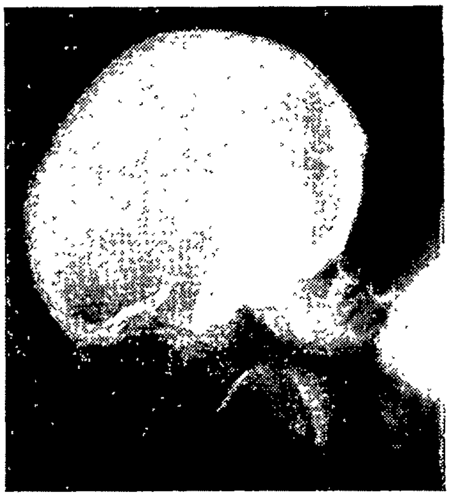


FIG. 1

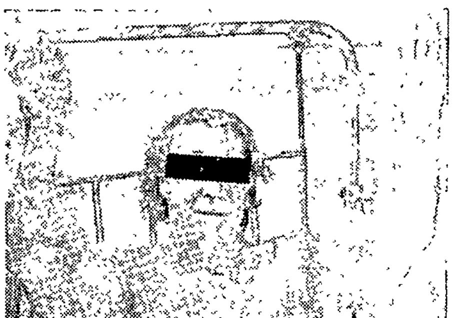


FIG. 2

110 mm. Hg. She was confused with paranoid trends and exhibited hallucinations at times. Depression had also been noted by her relatives before she was admitted to hospital.

Physical examination showed osteoarthritis of both knee joints and small joints of the hands, confirmed by *x*-ray. Intravenous pyelogram showed normal appearance of both kidneys. Her haemoglobin was 6 g./100 ml. and the blood picture was hypochromic and microcytic, which improved after iron therapy. Blood sugar, electrolytes, proteins, and cholesterol were normal. There was no glycosuria, and urinary 17-ketosteroid estimation was within normal limits. *X*-ray of the skull showed well-marked hyperostosis frontalis interna (Fig. 1). As seen in Figs. 2 and 3, obesity was mainly limited to the upper arms and thighs.

Association of hirsutism, obesity, and hyperostosis frontalis interna has been observed under the title of "Stewart–Morel Syndrome" or "Morgagni–Morel Syndrome." Morel reported 17 cases and Stewart reported a few cases.[1] Michaux described a case in 1959 presenting mental symptoms along with this syndrome.[2] Aubertin described a patient with arterial hypertension.[3] All say that the case is obscure. The newly formed bone is deposited in the inner aspect of the frontal bones with considerable thickening—resulting in atrophy of frontal lobes and pituitary dysfunction—and has almost always been recorded in women.

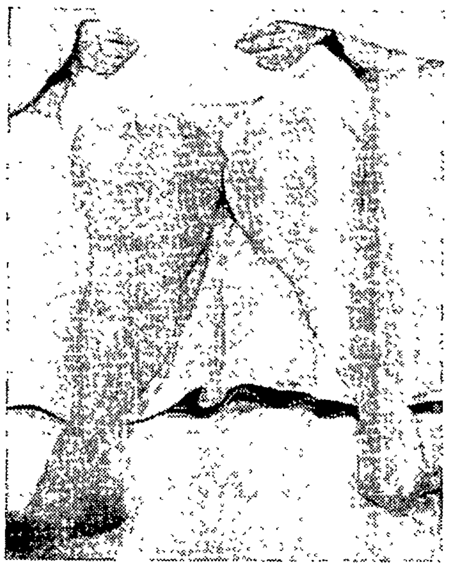


FIG. 3

Our patient presented all features of the syndrome—that is, hyperostosis frontalis interna, hirsutism, obesity, mental and nervous symptoms, and hypertension.—We are, etc.,

I. P. ROWLANDS.
B. C. DAS.

General Hospital,
Warrington, Lancs.

REFERENCES

[1] Weissenbach, R., *Bull. med. (Paris)*, 1953, 67, 125.
[2] Michaux, L., Buge, A., and Gautier, J-C., *Presse med.*, 1959, 67, 761.
[3] Aubertin Blanchot, P., Broussin, J., and Roy, A., *J. Méd. Bordeaux*, 1960, 137, 138. 301.

Hypogammaglobulinaemia in Adults

SIR,—Your special correspondent's account of my lecture on hypogammaglobulinaemia in adults (5 August, p. 362), given at the conference on disorders of protein metabolism at the Royal College of Physicians, London, contains some misquotations.

Hypogammaglobulinaemia in adults is of two types: primary, in which the deficiency of gammaglobulin is of unknown origin, and secondary, in which it is due to protein loss from the gut or kidneys or results from the effect of neoplasms upon immunoglobulin production. I did not say that the disease could be due to the toxic effects of drugs, and there is no evidence that hypogammaglobulinaemia can be caused in this way.

The eighteen patients whom I reported had all been diagnosed as having hypogammaglobulinaemia in adult life. The onset of the disease as judged by the history of recurrent infections was not, as stated in your report, always in adult life. In four of these adults the first onset of recurrent infections had occurred in childhood.—I am, etc.,

K. M. CITRON.

Brompton Hospital,
London S.W.3.

Cardiac Resuscitation

SIR,—As a lecturer and examiner in first aid for both Red Cross and St. John Ambulance Societies over the past nine years, I can substantiate Dr. J. D. Barrett's feelings (12 August, p. 437) that the indications for external cardiac compression are not understood by the majority of first-aiders who have only attended one or two courses. Often candidates state at examination that if the casualty does not respond by spontaneous breathing after the first four to six inflations of the lungs then external cardiac compression should be started. There is no thought of palpating the neck for pulsation, of observing the colour of the lips, or of noting the condition of the pupils. I feel that many casualties would be better with only basic first aid—that is, arrest of haemorrhage, ventilation of the lungs, and the treatment of cuts, burns, and fractures. I suggest that external cardiac compression should be taught to recognized "life-savers" who have passed at least two first-aid examinations and have shown aptitude in diagnosis, and not to those who have only just started.—I am, etc.,

W. E. HADDEN.

Public Health Office,
Swanage, Dorset.

Insulinotropic Action of Secretin

SIR,—Drs. D. R. Boyns, R. J. Jarrett, and H. Keen (10 June, p. 676) have confirmed the insulin releasing action of secretin in man but report evidence which they suggest throws doubt on the possible physiological role of this hormone in the regulation of insulin secretion. Some of our observations in studies related to this question and in studies of the effects of pancreozymin are at variance with theirs. In the earlier experiments of Boyns, Jarrett, and Keen with intraduodenal infusions of citric acid hypertonic solutions of glucose were delivered into the duodenum as a means of raising the blood glucose concentration.[1] With this procedure possible effects of the hypertonic solution on secretin release might obscure further effects of acidification of the mucosa. However, it is clear from the results of the three experiments reported in their recent paper that the infusion of 2.5 mEq of citric acid into the duodenum did not significantly modify the response to intravenous infusion of glucose.

We are in the course of a series of experiments in which hydrochloric acid is infused in the duodenum for a period of 20–40 minutes to a total dose of 30 mEq while glucose is given intravenously. This dose of acid does not exceed estimates of the normal acid secretion in response to a mixed meal.[2] In two out of three experiments distinctly higher levels of serum immunoreactive insulin were observed while the acid was infused into the duodenum; and in the third a difference in the same direction was recorded. Moreover, we have found that the intravenous infusion of synthetic human gastrin in six normal subjects modifies the response to intravenous glucose in the same manner as secretin, and it seems that this effect may be mediated by stimulation of acid secretion.

Our findings with a highly purified preparation of pancreozymin of verified exocrine activity differ from those of Boyns, Jarrett, and Keen. This preparation administered to eight subjects in doses of 25 to 50 μg. has consistently enhanced the rise in serum insulin associated with intravenous infusion of glucose and has accelerated glucose disposal. In fasting subjects little or no change in peripheral serum immunoreactive insulin is obtained when pancreozymin is administered intravenously, but a large transient rise in portal serum immunoreactive insulin has been observed. The same preparation of pancreozymin enhanced the change in serum insulin concentration associated with intravenous infusion of arginine in eight normal subjects. We believe that all preparations of secretin or pancreozymin must be tested for exocrine activity after use in experiments yielding negative results. Our findings will be presented at the forthcoming meeting of the International Diabetes Federation.

It is unlikely that duodenal infusion of isotonic glucose causes secretion of pancreozymin in man, and it has been shown by Dr. R. Preshaw at McGill[3] that such infusions do not produce exocrine effects of secretin in man. This procedure was used by McIntyre and his colleagues[4] to demonstrate enhanced insulin secretion in man during intestinal absorption of glucose. It appears, therefore, that an insulinotropic hormone other than secretin or pancreozymin is secreted when glucose is absorbed from the small intestine. However, the response to ingestion of protein together with carbohydrate suggests to us that stimulation of the endocrine pancreas is further potentiated to an extent not fully accounted for by the direct effect of circulating nutrients. The digestive secretagogues may be responsible for this potentiation.—We are, etc.,

J. DUPRÉ.
J. D. CURTIS.
J. C. BECK.

Fraser Laboratory for
Research in Diabetes,
Royal Victoria Hospital,
Montreal, Canada.

REFERENCES

[1] Boyns, D. R., Jarrett, R. J., and Keen, H., *Lancet*, 1966, 1, 409.
[2] Rune, S. J., *Clin. Sci.*, 1967, 32, 443.
[3] *Personal Communication.*
[4] McIntyre, N., Holdsworth, C. D., and Turner, D. S., *Lancet*, 1964, 2, 20.

Mortality of the Ambulance Ride

SIR,—The letter from Mr. C. H. Cullen and others (12 August, p. 438) inadvertently underlines the great importance of taking seriously injured patients to the proper centre even if it does mean a rather longer ambulance journey initially. Only in this way can the problem Mr. Cullen pinpoints be avoided. It is no use resuscitating a patient if he then has to travel to receive the necessary subsequent treatment. And, far from relating only to transfers between hospitals, this applies with great force within the hospital in the siting of *x*-ray departments and operating theatres in relation to the resuscitation room.

Those who have much experience of accident surgery know that in the critical phase, when a patient has just been resuscitated sufficiently for the anaesthetist to dare accept him for surgery, he must be transferred to the theatre *on tiptoe*. Trundling such a patient along a hundred yards of corridor will do the same as the ambulance journey did to Mr. Cullen's patient. A journey on a trolley stationary in a lift, however many floors are traversed, will affect him far less.

The place for resuscitation is the place which can supply the whole treatment. Staging patients for resuscitation en route can only increase the mortality.—I am, etc.,

Canterbury. F. G. St. Clair Strange.

Fulminating Ulcerative Colitis

Sir,—I must take issue with your correspondent Mr. T. A. Boxall (5 August, p. 368).

In the large majority of cases Professor Goligher and his team carried out a total proctocolectomy and not simply a subtotal colectomy (22 July, p. 193), although your leading article in that issue perhaps tended towards the less radical view.

Any surgeon who has had the experience of dealing with a rectal remnant which has continued to bleed severely, to perforate and to form abscesses and massive adhesions to bladder, urethra, and small intestine—requiring a second operation of great technical difficulty and severity—must surely hesitate to leave behind the rectum at the primary operation unless it can be clearly shown to be not more than slightly diseased.—I am, etc.,

Glasgow. D. M. Sinclair.

Casualty Department—or G.P. Service?

Sir,—Mr. R. S. Murley (22 July, p. 245) rightly criticizes your previous correspondents' (1 July, p. 46) defeatist attitude to the abuse of the hospital casualty service. This abuse is not only typical of the larger city centres but is becoming increasingly common in smaller hospitals serving a "well-registered" population since more and more general practitioners are adopting appointment systems. "I can't get an appointment at the surgery till Wednesday" is a familiar excuse to many a casualty officer on Monday mornings.

I would not agree, however, that the doctors' efforts to educate the public are "largely doomed to failure." Much can be done if the casualty staff are prepared to establish the department's reputation locally as a place where only genuine emergencies will receive attention. This entails close co-operation with the general practitioners, asking them to be firm with their patients who attend unnecessarily, making sure that local works first-aid personnel know this attitude, and so on.

Because casualty work is not recognized as a specialty in its own right, this venture may prove difficult. Support at management committee and medical staff committee levels is often lacking, and much of the out-of-hours work may be done by junior doctors from other departments who have no enthusiasm to help solve a problem which is not theirs to begin with. Only the creation of a proper career structure in this work will give casualty departments the type of staff they need to function to their best advantage and eliminate this abuse.—I am, etc.,

Stockton-on-Tees. J. H. Jennings.

Health of Students and Soldiers

Sir,—I would entirely agree with Colonel H. G. Skinner's comments on planning a health service (15 July, p. 178).

Some 15 years ago, when I was a postgraduate student at the London School of Hygiene and Tropical Medicine, I attended an elective course of lectures on what was to me a new subject—"Industrial Psychology." As the content of the course unfolded, it was interesting to note that we were covering the principles of man-management which had earlier been instilled into me as a very junior regimental medical officer by the more senior regimental officers of the battalion in which I was privileged to serve.—I am, etc.,

Eastern Command,
Hounslow, Middx. F. G. Neild.

Consultants' Views of G.P.

Sir,—Perhaps one should not take too seriously remarks made in the heat of debate, but some words ascribed to Dr. B. D. Morgan Williams (*Supplement*, 12 August, p. 115) call for comment.

He is reported as saying that "Teaching-hospital consultants saw only the worst side of general practice: they did not see the successes." I should like to record that in my own experience this is complete nonsense. Neither in private practice nor in outpatient clinics did I see only the worst side of general practice, and I cannot believe that my experience was unique. This kind of remark is to be deplored, and I feel someone ought to say so.—I am, etc.,

London, N.1. Cecil Flemming.

Radio Communication and the G.P.

Sir,—Referring to the letter from Dr. K. A. Harden, of Glasgow (5 August, p. 374), in this practice we do indeed have an arrangement whereby the hospital can hear our report radioed direct from the car.

This is done through a commercial organization—Air Call, of Hitchin—who on receipt of our message contacts the hospital by telephone, and by leaving the switch open in the control office allows the hospital doctor to hear our message. This saves many a letter in the wee small hours, and we can vouch for the great saving in time.—We are, etc.,

R. A. Briggs. D. G. Wray.
J. McN. Fullerton. E. V. Jones.

Houghton Regis,
Dunstable, Beds.

B.M.A. Department of Audio-visual Communication

Sir,—The pressure of urgent business at the Annual Representative Meeting at Bristol prevented me from presenting the report of the Film Committee and informing members about the future plans of the Association's new department of audio-visual communication. Briefly, for the immediate future, these are:

(1) To hold a three-day founding conference entitled "Educational Technology in Further Medical Education" at the University of Sussex on 3, 4, and 5 January 1968. (Full details will be published early this autumn.)

(2) To create an advisory service covering the content, availability, and suitability of audio-visual source material of all kinds and the advantages and disadvantages of recording and presentational apparatus in all media.

(3) To serve as a co-ordinating centre for individual effort in the whole field of audio-visual communication in medicine.

(4) To upgrade and recatalogue the present film library and to enlarge the library of audio tapes in order to increase its usefulness to doctors and others both at home and abroad. (Modern apparatus for the servicing of films returned by borrowers has now been installed.)

(5) To promote the making of clinical and health education films by bringing together medical men with ideas, film makers, and potential sponsors and to encourage the setting up of trust funds to sponsor specific projects.

Eventually it is hoped that a hallmarking system for medical films can be introduced which will enable a prospective user to identify titles whose professional and ethical standards are acceptable to the Association. The provision of training courses for medical teachers in the use of apparatus appropriate to the newer media of communication is also under consideration.

I am also happy to report that shooting has actually started on a film dealing with the problem of juvenile obesity that is being sponsored jointly with the British Life Assurance Trust. The newly appointed head of department, Mr. Charles Engel, will be taking up his duties in September.—I am, etc.,

T. A. Quilliam,
Chairman,
Film Committee of the B.M.A.

University College,
London W.C.1.

Points from Letters

Aversion Therapy of Homosexuals

Dr. C. E. Allen (Mold, Flintshire) writes: It is unfortunate that Dr. B. Kalcev (12 August, p. 436) claims that homosexuality is not a disease, because the dictionaries I have consulted suggest that a disease is merely an abnormal condition. The fact that it has a psychological basis does not make it any less a disease.

This is not to suggest that I feel that treatment should be forced on those who do not wish it. Since I have treated a very large number of homosexuals I know that anyone who tries to treat a patient who does not wish it is wasting his time. It should be appreciated that homosexuality leads to unhappiness. The homosexual is never able to fit comfortably into a society adjusted for heterosexuality. He is often unhappy during his youth because he feels different from others, and when old age comes is intolerably lonely. For these facts alone it is worth urging him to accept treatment, and, if he can respond, to be cured.

Obituary Notices

LEON GILLIS, M.B.E., M.CH.ORTH., F.R.C.S., F.R.C.S.ED., D.L.O.

Mr. L. Gillis, consultant orthopaedic surgeon in the Westminster Hospital Teaching Group at Queen Mary's Hospital, Roehampton, died at Birmingham, Alabama, U.S.A., on 9 August following an operation.

Leon Gillis was born in Johannesburg on 4 September 1908. He qualified in medicine at the University of Witwatersrand in 1935, and came to England in the following year. He took the M.Ch.Orth. at Liverpool in 1937, the Edinburgh Fellowship in 1942, and the English Fellowship in 1945; but before settling down to his chosen specialty he worked for a time in oto-laryngology, taking the D.L.O. (London) in 1940. He held a number of hospital appointments in and around Liverpool and later at the Borough General Hospital, Ipswich, before being appointed consultant orthopaedic surgeon at Queen Mary's, Roehampton, in 1943.

It was at Roehampton that his great work was done. Successive echelons of ex-Servicemen, both amputees and those suffering from the various sequelae of gunshot wounds of the extremities, owed their rehabilitation to his skill.

It was his special thesis that amputation and limb-fitting are parts of one operation, and he spoke and wrote endlessly to get this principle accepted throughout the country. Few had a wider knowledge than he of the problems of the amputee, and his two books on the subject—*Amputations*, published in 1945, and *Artificial Limbs* (1947)—became standard works. He had also an unrivalled knowledge of congenital limb deformities, including those due to thalidomide, and made special contributions to their management in the children's prosthetic unit at Roehampton. His opinion and advice on special problems in amputation and limb-fitting were sought by orthopaedic, vascular, and general surgeons all over England and from overseas. His achievements gained wide recognition, including appointment to the Arris and Gale lectureship in 1948, a Hunterian professorship in 1956, and the Joseph Henry Memorial lectureship in 1960. In 1947 he was honoured by the award of the M.B.E.

Leon extracted an unbelievable amount of working time out of every 24 hours. In addition to his work at Roehampton he was until 1961 consultant orthopaedic surgeon to the East Ham Memorial Hospital, Barking Hospital, and St. John's Hospital, Battersea. He was also consultant to the Ministry of Health's Limb-fitting Centre at Roehampton and surgical adviser to the Treasury. A long succession of registrars found him an erudite and stimulating teacher, and his biannual postgraduate courses were in great demand both from consultants and from candidates for the Fellowship. He wrote prolifically, contributing chapters to at least 10 major textbooks and publishing nearly 40 papers on a wide variety of subjects in medical and nursing journals. Somehow he found time, too, to serve on two hospital management committees and on the Orthopaedic Advisory Committee of the North-east Metropolitan Regional Hospital Board.

In his last years he was increasingly restricted by ill-health, but he fought most gallantly against it. His death followed an operation which he bravely and clear-sightedly accepted as a gamble that might not come off. He is survived by his wife and by two sisters.—A. G. R.

Colonel E. E. S. WHEATLEY C.B.E.(MIL.), D.F.C., T.D., M.R.C.S. L.R.C.P.

Colonel E. E. S. Wheatley, who died on 22 June at Kingston Hospital, combined several lives in one normal span and led a varied and exciting life as soldier and doctor.

Edward Eric Spencer Wheatley was born in India on 29 October 1898, the youngest son of Colonel Henry S. Wheatley and grandson of Major-General Wheatley, of the Bengal Cavalry. He was educated at Wellington College and the Royal Military Academy, Woolwich, whence he passed out second in his year, having also played rugby for the Military Academy. Commissioned in the Royal Artillery while still under the age of 18, he was almost immediately seconded to the new Royal Flying Corps. He served in France, Salonika, and North Russia and for his valour was awarded the D.F.C. He was shot down in Salonika while acting as observer, sustaining a severe injury to his right leg. This troubled him gravely for the next 30 years and left him with chronic osteomyelitis of the tibia. In 1946 he came back from Singapore and entered Millbank for an above-knee amputation.

Meantime, after the 1914–18 war, he rejoined his regiment, the Mountain Battery, Royal Artillery, in India. During his service there, in spite of the chronic osteomyelitis of his right leg, he boxed for the Army and acted for a period as A.D.C. to the Viceroy. On his return to England he transferred to the Army Pay Corps, qualifying as Paymaster, Aldershot Command.

In 1927, at the time of the "Geddes Axe," he decided to leave the Army and to study medicine. This he did at St. Thomas's Hospital, qualifying with the Conjoint diploma in 1932. He settled in Reading in general practice and did a good deal of surgery in addition. Joining the Territorial Army he raised No. 6 Motor Ambulance Column, which he took to France at the outbreak of the war in 1939. He later commanded No. 6 C.C.S. The next major move in this unusual life was Wheatley's mobilization of the 69th British General Hospital, which he commanded in the 1st Army landing in North Africa. After serving with the Central Mediterranean Forces until the end of the war he went to Singapore as A.D.M.S. Wheatley was decorated C.B.E. for his outstanding work and leadership in face of continual physical suffering. After the amputation of his leg he entered the Ministry of Pensions Artificial Limb Service, at Roehampton, in 1948. He continued to serve at Roehampton until 1963, when he retired.

A colleague writes: Kerry Wheatley was an outstanding soldier and doctor. We in the Limb Service who came to know and love him were gradually aware that his extraordinary ability for caring for the limbless derived from the various careers that had followed one another, logically, throughout his life. His knowledge of engineering learned at the Shop, his deep understanding of the life of the serving soldier and airman, his thirty years of suffering with a Great War wound, his leadership and command—these experiences trained him in a unique way for the unstinted service he lavished on his fellow amputees throughout the last fifteen years of his life. Thousands of those who have lost limbs as Servicemen or as civilians have reason to bless him for his knowledge and his practical sympathy. To see the tenderness with which he ministered to a maimed child was a benison given only to those who worked with him. He will not easily be forgotten at Roehampton.

J. CALDWELL, M.D.

Dr. J. Caldwell, a general practitioner in Paisley, died suddenly on 22 July while on holiday at Onich, near Fort William. He was 68.

James Caldwell was born in Paisley on 22 May 1899, and was educated at Paisley Grammar School and Glasgow Academy. During the first world war he served in France as a subaltern in the Argyll and Sutherland Highlanders. After demobilization he studied at Glasgow University, where he graduated M.B., Ch.B. in 1924 and proceeded M.D. in 1947. Following house appointments at the Royal Alexandra Infirmary, where he was senior medical resident, he visited the United States and spent some time at the Mayo Clinic. On his return he set up practice in his native town of Paisley, where he served the community as a general practitioner for 40 years. The care of the aged was a particular interest of his, and until three years ago he was active in the field of geriatrics. He was visiting physician to Glen-Coats Auxiliary Hospital from 1934 until 1962, when he was appointed to take charge of the new geriatric unit at Barshaw

Hospital. He was a representative at the Annual Meetings of the British Medical Association from 1930 to 1936, and again in 1938, and was chairman of the Renfrew and Bute Division from 1957 to 1959.

James Caldwell was a kindly, good-hearted man with a genuine interest in the well-being of his patients, many of whom regarded him as a personal friend as well as a beloved family doctor. Extremely fond of children, and with a boyish sense of fun, he made his visits memorable and welcome events to the younger members of the household, with whom he had endless patience. His clinical approach was always painstaking and scrupulously correct, and, although he kept well abreast of modern methods and treatment, he would on occasion take great delight in using, with effect, an old-fashioned remedy when more modern therapeutic agents had failed.

His pleasures were simple, and consisted mainly in his garden and conservatory, and the possession of a fine stamp collection. While devoted to his work, James Caldwell was also a very sociable man, and made a charming and interesting companion. He will be sadly missed by his many friends. He was a bachelor.—J. L. H.

G. R. CUBITT, T.D., M.B., B.CH., B.A.O., D.OBST.R.C.O.G., L.M.

Dr. G. R. Cubitt, a general practitioner in Sleaford, Lincolnshire, died on 24 July after a short illness. He was 54.

George Roland Cubitt was born in Waterville, Co. Kerry, on 16 October 1912, and was educated at the Farren Ferris College, after which he entered University College, Cork, graduating M.B., B.Ch., B.A.O. in 1938. He held resident posts in London before joining the R.A.M.C. in 1940. He served at home and in Europe during the second world war, and was deputy assistant director of medical services at the headquarters of the 30 Corps district, B.A.O.R., attaining the rank of major. On demobilization in 1945 he spent six months at the Rotunda Hospital, Dublin, and obtained the L.M. in 1946. He entered general practice in Sleaford the following year. It was largely due to his initiative that the Sleaford general practitioners joined together to form the Sleaford Medical Group, and designed their own health centre, which has proved an outstanding success in the district. In 1956 he took the diploma of the Royal College of Obstetricians and Gynaecologists from general practice. He was a devoted general practitioner, and also had many wide interests. He served as chairman of the Kesteven Division of the British Medical Association in 1954–5, and later was active in the affairs of the College of General Practitioners. He had been for many years a member of the Kesteven local medical committee. In addition, he was area commissioner of the St. John Ambulance Brigade, and a Rotarian, as well as a leading member of the Roman Catholic community. He never lost his interest in the Army, and was a keen Territorial. For his services he was awarded the Territorial Decoration. At the time of his death he was in command of 222 Field Dressing Station, R.A.M.C. (V.), with the rank of lieutenant-colonel.

Roland was an outstanding doctor, and one of the leading figures in medicine in the south of Lincolnshire, and his advice was sought by many, both in general practice and in the hospital and public health services. He had strong views of the duties of a general practitioner, and never spared himself. His pleasant personality made him very many friends, and he enjoyed their company. He was an ideal host, and many people will remember the happy evenings spent in his home. His death will leave a gap in the medical and public life of Sleaford, and also in a very wide area around.

Despite his many commitments, he enjoyed an ideally happy family life, and our sympathy is extended to his widow and three children.—A. A. H. and H. A. C.

G. R. MALKIN, M.R.C.S., L.R.C.P.

Dr. G. R. Malkin, formerly in general practice at Fownhope, Herefordshire, died at his home at Dawlish, Devon, on 6 August, after a long illness courageously and patiently borne. He was 67.

Godfrey Reginald Malkin was born in Staffordshire on 27 June 1900, and he received his medical education at St. Bartholomew's Hospital, London, where he qualified with the Conjoint diploma in 1930.

After various appointments he worked for a time in Worcestershire, and in 1939 he finally settled in general practice at Fownhope, Herefordshire, where he remained until his retirement in December 1965. He had in addition an extensive country practice which entailed a good deal of walking and rough travelling. Nevertheless, he found time to be honorary anaesthetist to the General Hospital, Hereford, until 1948, and during the second world war looked after the children at Brockhampton Court and an emergency hospital at Woolhope. After 1948 he found time to undertake the training of trainee assistants, and launched a whole series of young doctors on their life's work. Dr. Malkin was an extremely kind, patient, and capable physician, rightly beloved by his patients and neighbours. He had a deep interest in archaeology, entomology, and photography, and was a member of the Woolhope Club. For many years chairman of Fownhope Parish Council, he helped the village with its post-war building and reorganization. Interested in model-making, he had a wonderful workshop, and invented and made numerous models and gadgets which he used round his home.

We extend our heartfelt condolences and sympathy to his wife and family.—G. B. McM.

G. W. writes: With the death of Godfrey Malkin the profession in Herefordshire has lost a member of the type for which the county is noted—a first-class single-handed country doctor. He was an ideal man to act as a trainer, and seven of us passed through his capable hands. We are ever in his debt for the grounding he gave us in good general practice and the high example he himself set in his skill and humanity in dealing with all his patients, from landed gentry to gipsies. The esteem in which he was held was shown on his retirement, when, on a moving occasion in the village hall, he was presented with a large cheque and, something he prized much more, an inscribed list of the three hundred families who had contributed. Alas, his retirement, which he had planned to fill with his many interests, was ended after only two years by a painful illness borne with great courage. Having lived in his home for two years and known the happy family life he enjoyed so much, I know how much his loss will be felt by his wife and daughter.

S. W. MASLEN-JONES, M.S., F.R.C.S., F.R.C.O.G.

Mr. J. C. Newbold writes: Samuel Maslen-Jones (obituary, 5 August, p. 375) was a singular man, and lived a singular life in that he spent most of it serving a small special hospital. There are only a very few hospitals which deal with both obstetrics and gynaecology but nothing else, and the Women's Hospital, Wolverhampton, is such a hospital. Needless to say, this type of hospital cannot be matched for the training of specialists in obstetrics and gynaecology, and many men throughout the British Isles, and all over the world, can bear witness to this fact. With all the obstetrical and gynaecological abnormalities from a population of half a million under one roof a rare feast of clinical and teaching material is presented, and Maslen saw to it that each of his registrars and housemen left the hospital full of knowledge and very well trained. It was his custom to eat lunch with his residents, an even better place to teach than the bedside. There will be many reading this who owe Maslen a great personal debt, and I am sure they would wish me to express their gratitude to him.

As his colleague, it is not possible to speak of his character save in superlatives, which he would not have wished me to do. I can best illustrate the sort of man he was by the following stories from his life. When he first came to Wolverhampton the "Women's" was an individual hospital, and Maslen was responsible only to a lay committee. Within a few weeks he was "on the mat" because a patient had died—of which the committee disapproved. No radical surgery to extirpate cancer had ever been done before, and no risks had been taken. Maslen explained that it would be his policy to endeavour to cure women, whatever was wrong with them, and that, if the committee did not approve, they could have his resignation. He had no further trouble.

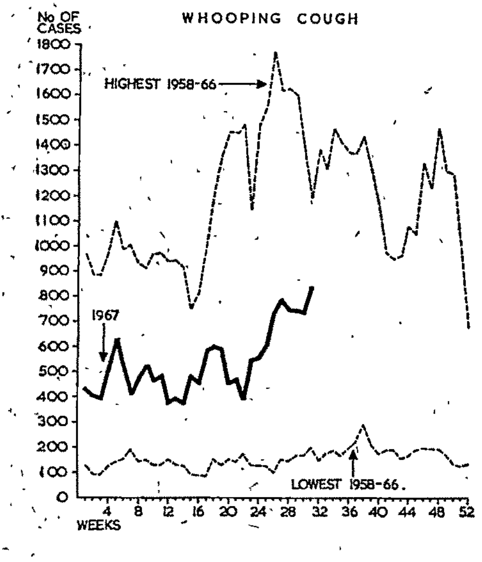
In conclusion, I must give an account of our first social meeting. Characteristically, this was an invitation to play golf. At one hole, which proceeded over the brow of a hill, the line was marked by a direction post. My ball was far and wide, but Maslen's, as usual, was absolutely straight and 50 yards short of the post. He asked me to walk ahead and remove the post. For a moment I suspected him of psychological warfare, but, being in no position to refuse, I walked on and took out the post. A well-struck iron soared exactly over the post-hole and would undoubtedly have hit the post had it remained in situ. And so he lived his life: straight, predictable, confident, skilful, unostentatious.

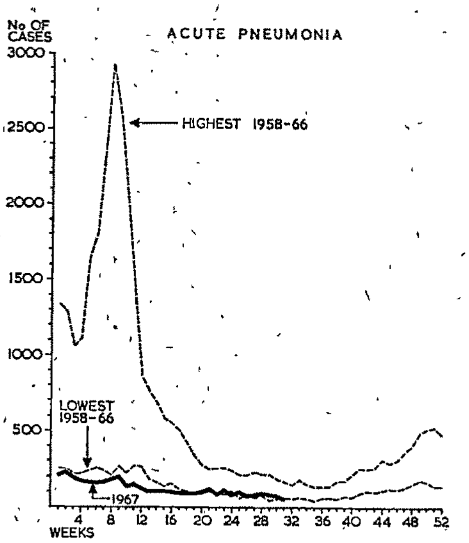
News and Notes

EPIDEMIOLOGY

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of whooping-cough and acute pneumonia in England and Wales. Figures for 1967 are compared with the highest and lowest figures for each week in the previous years shown





Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available.

	Week Ending 4 Aug.	11 Aug.
Dysentery		
Greater London	44	**44**
Redbridge	6	**13**
Lancashire	54	**54**
Manchester C.B. ...	2	**15**
Yorkshire East Riding ...	0	**12**
Haltemprice U.D. ...	0	**10**
Glasgow	21	**43**
Edinburgh	16	**21**
Food-poisoning		
Edinburgh	4	**39**
Glasgow	6	**23**
Measles		
Lancashire	358	**318**
Liverpool C.B. ...	96	**60**
Somersetshire	287	**152**
Bath C.B.	50	**54**
Warwickshire	196	**151**
Birmingham C.B. ...	55	**54**

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **5 August** (No. 31) and corresponding week 1966.

Figures of *cases* are for the countries shown and for Greater London. Figures of *deaths* and *births* are for the whole of England and Wales (London included), Greater London, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0		0	0	2	0	
Dysentery ..	243	44	61	3	3	390	72	65	1	
Encephalitis, acute ..	2	0		0		2	0		0	
Enteric fever: Typhoid ..	0	0	0	0	1	3	0	1	0	
Paratyphoid	5	0	0	0	0	1	0	0	0	
Food-poisoning	239	48	14	4		115	20	6	6	
Infective enteritis or diarrhoea under 2 years				19	51				16	
Measles* ..	4,220	291	17	65	56	8,796	978	59	42	
Meningococcal infection ..	6	1	5	1		11	1	2	1	
Ophthalmia neonatorum	5	1	0	0		14	1	0	0	
Pneumonia† ..	58	8	45	2	1	54	2	46	1	
Poliomyelitis, acute: Paralytic ..	0	0	0	} 0		1	1	0	} 0	
Non-paralytic	0	0	0			0	0	0		
Puerperal fever§	64	31	2	0		86	37	7	0	
Scarlet fever ..	168	22	17	15	3	220	26	11	2	
Tuberculosis: Respiratory ..	250	57	29	8		222	56	22	7	
Non-respiratory ...	51	12	6	2		49	13	11	3	
Whooping-cough	839	123	90	9	41	415	55	31	8	

DEATHS	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0		0	0	0	0		0	0	0
Dysentery ..	0	0		0		2	0		0	
Encephalitis, acute ..					0					0
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	5	2	0	0	0	6	1		1	0
Influenza ..	4	0	0	0	0	2	0	0	0	0
Measles ..	0		0	0	0	0		0	0	0
Meningococcal infection ..			0					0		
Pneumonia ..	483	75	10	10	3	510	79		8	7
Poliomyelitis, acute ..	0	0		0	0	0	0		0	0
Scarlet fever ..	0		0	0	0	0	0	0	0	0
Tuberculosis: Respiratory	} 31	5	0	1	1	} 29	4		0	1
Non-respiratory ..				0	0				0	1
Whooping-cough	1	0	0	0	0	0	0	0	0	0
Deaths 0–1 year	260	61	19	7	15	279	55	22	7	8
Deaths (excluding stillbirths)	8,642	1356	510	108	165	9,100	1478	517	99	163
LIVE BIRTHS	15,796	2558	859	261	545	17,165	2908	917	279	430
STILLBIRTHS	206	32	6			212	30			

* Measles not notifiable in Scotland, whence returns are approximate. † Includes primary and influenzal pneumonia. § Includes puerperal pyrexia.

MEDICAL NEWS

Technology in Medical Education

The place of educational technology in continuing medical education will be the theme of a founding conference for the new British Medical Association Department of Audio-visual Communications which is to be held from 3 to 5 January 1968 at the University of Sussex. The purpose of the conference is (*a*) to help medical teachers to become familiar with the contribution that educational technology can make; (*b*) to provide an opportunity for the exchange of views on the future development of the department; and (*c*) to introduce the head of the department, Mr. Charles Engel (see *B.M.J.*, 13 May, p. 453). A letter about the new department appears at p. 561.

Fire Hazards in Hyperbaric Treatment

A working party set up by the Western Regional Hospital Board (Scotland) concludes that the fire risks associated with hyperbaric treatment are sufficient to justify prompt action and continuing surveillance. In its report it makes a number of suggestions, including investigation of the risks in hospital wards where oxygen tents or oxygen incubators are used. The working party, which visited hyperbaric installations at Glasgow hospitals, does not consider that the hazards, if controlled in accordance with its recommendations, are grave enough to require curtailment of treatment in hyperbaric environments.

Benefits for Pneumoconiosis

New regulations affecting entitlement to benefits under the Industrial Injuries Act for pneumoconiosis came into operation on 16 August. They provide that the effects of emphysema or chronic bronchitis shall be treated as if they were the effects of pneumoconiosis in cases where disablement from pneumoconiosis or pneumoconiosis accompanied by tuberculosis would, if the person's physical condition were otherwise normal, be assessed at not less than 50%. The regulations apply to disablement benefit and industrial death benefit.

Providing Access for the Disabled

A new B.S.I. code of practice (C.P. 96) details general provisions that should be incorporated in new buildings for the convenience of the physically handicapped (see leader at p. 510). Copies of the code, *Access for the Disabled to Buildings, Part 1, General Recommendations,* can be obtained from B.S.I. Sales Office, 101–113 Pentonville Road, London N.1, price 10s. (plus 6d. postage to non-subscribers). Other parts of the code will cover specific building types.

Hospital Inpatients

Several new tables have been introduced into the Report on Hospital Inpatients Inquiry for 1963, Part 1, issued by the Ministry of Health and the General Register Office (H.M.S.O., £1 11s.). One of these shows the mean duration of stay in hospital for each diagnostic group by age, sex, and marital status; another, the patients treated in each hospital group according to their local authority area of residence. For the first time periods of preconvalescent care have been included in the duration of stay calculations. The report consists of detailed tables similar to those published in the corresponding volume for the preceding year.

R.C.S.I. Faculty of Radiology

The following officers have been elected: *dean,* Dr. O. Chance; *vice-dean,* Dr. W. J. MacHugh; *secretary,* Dr. D. Cantwell; *treasurer,* Dr. J. J. Magner.

Research on Air Pollution

A five-year programme of research on air pollution is to be undertaken at the Atomic Energy Research Establishment, Harwell, at an estimated cost of £535,000. It will aim at establishing the scientific facts required for an improved system of control. In an announcement last week the United Kingdom Atomic Energy Authority said the national cost of air pollution had been assessed at over £350m. a year, including costs of cleaning and damage to buildings. The chief pollutants had been smoke, dust, grit, and oxides of sulphur, but the greater use of oil fuels was increasing the amount of hydrocarbons, carbon monoxide, oxides of nitrogen, lead, and vanadium in the atmosphere. Harwell's main contribution is expected to be in analytical instruments and techniques, in studies of pollutant life cycles and reactions, and possibly in research on human inhalation. The work will be co-ordinated with other public research by Dr. Cecil Hall, director of the Warren Spring Laboratory of the Ministry of Technology.

Landscape Architecture for Hospitals

Practical advice to hospital planners and builders in making use of the natural resources of their sites is provided in a King's Fund report (*Landscape Architecture for New Hospitals,* 17s. 6d. post free). The author, Mr. J. Bodfan Gruffydd, was appointed by the fund in 1964 to advise on the layout and upkeep of hospital grounds (see *B.M.J.*, 1964, 25 July, p. 258). His report is wide-ranging and includes a section on design principles of therapeutic significance. There are 53 illustrations.

I.F.M.S.A. General Assembly

The sixteenth general assembly of the International Federation of Medical Student Associations was held from 1 to 12 August in Vienna. Delegates from nearly 30 countries were present. Among the British delegates were Mr. Cliff Allen, president of the British Medical Students' Association, and Mr. Michael Simpson, vice-president. The next general assembly will be held in Helsinki in 1968.

United Hospitals Choir

Since it was formed in 1951 the United Hospitals Choir has been giving regular concerts and recitals in London in aid of medical charities. Anyone may join who is connected with medical work. There is no audition. Rehearsals are held on Thursday from 7.30 to 9.45 p.m. at St. James's and St. Peter's School, Piccadilly. The autumn term starts on 28 September. There are vacancies in all voices. Further details can be obtained from the Honorary Secretary, Miss F. J. Allatt, 23 Guernsey Grove, London S.E.24 (telephone 674 6765).

Eli Lilly Fellowship (South Africa)

Medical practitioners registered in South Africa are invited to apply for the 1968 award of the Eli Lilly Medical Research Fellowship (South Africa). Details can be obtained from Dr. H. A. Shapiro, Chairman, Selection Committee, Eli Lilly Medical Research Fellowship (South Africa), P.O. Box 1010, Johannesburg, South Africa. The closing date for applications is 14 February 1968.

Clothing for the Disabled

Lack of communication within hospitals and between manufacturers and users is a main finding in a recent survey report on problems of clothing for the sick and disabled. The report recommends that an information centre should be established, also some form of regular publication, for the use of disabled persons in every environment and of relatives and professional staff. It also makes recommendations about the supply of suitable garments and their maintenance. Copies of the report can be obtained from the Disabled Living Activities Group, Central Council for the Disabled, 39 Victoria Street, London S.W.1, 10s. 6d. post free.

People in the News

▶ Dr. A. Isabel Scott has been appointed medical director to the National Drugs Advisory Board in Eire.

▶ Mr. A. G. Shaw, F.P.S., has been appointed secretary of the Association of the British Pharmaceutical Industry with effect from 1 November.

▶ Mr. James Loring has been appointed director of the Spastics Society.

News in Brief

The Minister of Health has agreed that the Liverpool Stanley Hospital, Liverpool 5, should continue to function for the time being. From 1970 there will be an annual review of the hospital facilities in that part of Liverpool, the final closure of the hospital being linked with the commissioning of the second phase of the new hospital at Fazakerley.

An exhibition of medical illustration, mainly anatomical and pathological, has been arranged at the Royal College of Physicians of London (11 St. Andrew's Place, London N.W.1). It is open from 10 a.m. to 5 p.m., Monday to Friday, until 1 December. View on application to Librarian.

Grants and Awards

The 1967 triennial Gower's Essay Prize on Epilepsy has been awarded to Dr. D. C. Taylor, Guy's Maudsley neurosurgical unit.

The British Empire Cancer Campaign for Research has announced grants to individual research workers amounting to £196,000. Nearly £25,000, the largest grant, will support a study of the basic mechanisms of cell differentiation that is being carried out by Dr. J. Paul, director of the cancer research department at the Royal Beatson Memorial Hospital, Glasgow. Dr. I. R. McWhinney receives a grant of £1,529 for an investigation into the presenting symptoms of cancer in general practice.

The Wellcome Trust is making a grant of £17,000 over two years in support of a study of sickle cell anaemia in Jamaica. The study will be conducted by the departments of medicine and haematology at the University of the West Indies.

The Royal Society announces that the Beringer Research Fellowship has been awarded to Dr. H. Festenstein, of the McIndoe Memorial Research Unit, to enable him to carry out research on histocompatibility—investigations of antigenic strength by cell cultural techniques in mice and the application of these techniques and that of serological typing to the selection of donors for renal transplantation in man—in the department of medicine and bacteriology, London Hospital Medical College.

Recent Publications

Hospital Services of Europe: report of the third European conference held in October 1966 by the International Hospital Federation in collaboration with the King's Fund. Copies can be obtained from the International Hospital Federation, 24 Nutford Place, London W.1, 10s. post free.

Commonwealth Collections of Microorganisms: *Directory of Collections and List of Species Maintained in Canada, 1967,* H.M.S.O., 9s. net.

Report on Safety, Health, Welfare, and Wages in Agriculture, 1 October 1965 to 30 September 1966, H.M.S.O., 2s. 3d. net.

A new British Council pamphlet *The Married Student: A Guide to Life in Britain* (price 6d.) is intended to help the overseas student to decide whether his wife (and children) should accompany him on his course of study. It supplements the handbook, *How to Live in Britain,* published for the British Council by Longmans, Green (price 1s.).

A Ministry of Housing and Local Government circular calls on local authorities to reduce air pollution caused by grit and dust discharged from boiler and furnace chimneys. It directs their attention to the report of a working party on grit and dust emissions (H.M.S.O., 3s.) and to a booklet, *Grit and Dust,* based on the report (H.M.S.O., 3s.).

Coming Events

British Society of Audiology.—Inaugural meeting, 8 September, 5 p.m., Royal Society of Medicine, 1 Wimpole Street, London W.1.

British Association of Manipulative Medicine.—Symposium by Mr. W. E. TUCKER on "Treatment of Athletic Injuries," Sunday, 24 September, 11 a.m., in London. Details from honorary secretary, 3 Arundel Terrace, Brighton 7, Sussex.

Royal College of General Practitioners (West of Scotland Faculty).—Residential course for new entrants to general practice, 25–29 September. Details from honorary secretary, West of Scotland Faculty, Royal College of General Practitioners, 9 Lynedoch Crescent, Glasgow C.3.

Association of Medical Record Officers.—Conference, "Computers and the Hospital Service," 5–6 October, Dental Hospital, Birmingham 4.

University of Salford Postgraduate Medical Institute.—Symposium, "Techniques of Behaviour Therapy," 21 October.

Societies and Lectures

For attending lectures marked ● a fee is charged or a ticket is required. Applications should be made first to the institution concerned.

Wednesday, 30 August

STOKE MANDEVILLE HOSPITAL.—(1) 12.15 p.m., Dr. W. Stokes: clinical cases. (2) 6 p.m., Dr. H. Frankel: case demonstration.

Friday, 1 September

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. R. Bignall: clinical demonstration.

Appointments

BIRMINGHAM REGIONAL HOSPITAL BOARD.—H. V. Morgan, M.B., F.R.C.P. (whole-time consultant physician with special experience in tropical medicine and communicable diseases to the East Birmingham group); S. P. B. Way, M.D., M.R.C.P. (whole-time or maximum part-time consultant pathologist to the Dudley and Stourbridge group); J. S. Mather, M.B., F.F.A. R.C.S. (part-time consultant anaesthetist to the United Birmingham Hospitals and the Birmingham (Selly Oak) group); G. B. Simon, M.B., D.P.M. (whole-time or maximum part-time consultant psychiatrist and medical director to the Mid-Worcestershire group).

HOME OFFICE.—I. A. Angus, M.B. (principal medical officer—regional medical officer, Prison Medical Service, N.W. region).

NATIONAL HEART HOSPITAL.—A. Gilston, M.B., F.F.A. R.C.S. (consultant anaesthetist); J. K. Ross, M.B., M.S., F.R.C.S. (consultant surgeon); M. J. L. Patterson, M.B., M.R.C.P. (consultant pathologist).

NATIONAL HOSPITALS FOR NERVOUS DISEASES, Queen Square, London W.C.—(Mrs.) Doreen A. Jewkes, M.B., F.F.A. R.C.S., D.A. (consultant anaesthetist to the National Hospital, Queen Square and Maida Vale Hospital).

NORTH-EAST METROPOLITAN REGIONAL HOSPITAL BOARD.—J. L. Reed, M.B., M.R.C.P., D.P.M. (consultant psychiatrist to Hackney and Queen Elizabeth group of hospitals and senior lecturer at St. Bartholomew's Hospital Medical College); J. A. Rumble, M.B., F.R.C.S., D.O. (consultant ophthalmic surgeon to Southend-on-Sea group of hospitals); Nina Shotts, M.R.C.S., F.D.S. R.C.S. (consultant dental surgeon to Tottenham and Enfield group of hospitals); A. N. Cammock, B.M., D.L.O. (consultant E.N.T. surgeon to Thames and Forest groups of hospitals); V. M. Tarkunde, M.B., F.F.R., D.M.R.E. (consultant radiologist to Romford group of hospitals).

Universities and Colleges

LONDON

The following have been reappointed or renominated as representatives of the University on the governing bodies indicated in parentheses: Dr. C. F. Harris and Professor J. G. Scadding (British Postgraduate Medical Federation); Sir E. Rowan Boland and Dr. J. Forest Smith (Guy's Hospital Medical School); Professor F. Goldby and Dr. C. E. Newman (King's College Hospital Medical School); Professor M. de B. Daly and Dr. M. I. A. Hunter (Royal Dental Hospital of London School of Dental Surgery); Dr. D. H. Brinton (St. George's Hospital Medical School); Professor R. S. F. Schilling (St. Thomas's Hospital Medical School); Dr. J. H. Humphrey, F.R.S. (University College Hospital Medical School).

The following have been recognized as teachers of the university in the subjects indicated in parentheses: *St. Mary's Hospital Medical School,* Dr. R. G. Bannister (medicine (neurology)). *St. Thomas's Hospital Medical School,* Dr. T. H. Foley, Dr. C. Rosendorff (medicine). *London Hospital Medical College,* Mr. A. W. Morrison (otolaryngology). *Guy's Hospital Medical School,* Mr. L. F. W. Salmon (otorhinolaryngology), Dr. H. M. Saxton (radiology), Dr. R. J. Vale (anaesthetics).

M.D.—G. G. Muir, N. McIntyre, B. B. Obeng.

M.PHIL.—*In the Faculty of Medicine:* Beatrice E. Bolger, Linette D. Iliff.

PH.D.—*In the Faculty of Medicine:* L. Black, R. P. Enever, Sally D. Everett, S. S. H. Nasser, H. C. B. Reed, Shirley H. Wray, M. M. Abou-El-Makarem, Valerie A. Cowie, T. K. Dasgupta, J. S. Greenspan, K. Nuki.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

At the meeting of council held on 28 July, with the president, Sir John Peel, in the chair, the following were admitted to Fellowship:

F. G. Grant (Northern Ireland), T. G. Robinson (United Kingdom).

The following were admitted to Membership:

K. B. Abdeen, R. B. Abdel-Shahid, K. Z. Abusief, M. L. Adiga, T. M. Andrew, R. Arora, D. O. Asekun, N. K. Baruah, A. S. Bataineh, N. Begum, S. M. Bekhit, A. Bhagwansingh, A. F. Buhagiar, G. D. Burns, D. Chanda, S. Chaterjee, A. M. Chrysaphinis, R. W. H. Clarke, R. V. Clements, T. B. Cochran, J. C. Creedon, D. G. Daniel, C. K. Das, J. Das, M. K. Datta, S. Datta, N. Debi, A. M. Dhoodhat, J. A. Doherty, N. J. Donnelly, T. G. Egan, M. N. El-Menoufi, H. A. R. El-Shallaly, M. V. A. Falla, J. Farmer, Joyce Fleming, J. G. Francis, T. A. Glanville, J. R. Grove, R. A. W. Guthrie, J. Herat, R. S. Hickling, M. Holsman, C. E. Horsfall, A. H. Talukder, Kathleen M. Hunt, R. J. A. Jackson, H. N. N. Jayasinghe, K. A. Johansen, Ivy S. John, F. S. Johnson, R. Karimi, J. I. Khalil, R. L. Khan, M. Khokhar, L. P. Knight, N. Koraishy, K. B. Kuah, S. B. Kuku, T. Kumarasamy, T. K. Kundu, B. Kuti, L. P. Lang, G. D. Lewis, C. Lwanga, G. MacKay, Flora McK. Maher, D. E. I. Mais, J. O. Martey, Mary Mathen, D. Maulik, M. Maung, J. W. W. Mears, S. Mitra, F. H. Morcos, S. Morcos, Gladys M. Morrison, A. K. Mukherjee, T. K. Mukherjee, P. J. Murphy, C. P. Murray, M. A. Mustafa, J. R. Newton, R. L. T. K. N. C. Hin, J. D. O. Noel, W. E. Nurse, Margaret H. Ogden, D. O. Olurin, T. O'Malley, J. J. O'Neill, P. S. Pai-Dhungat, S. S. Palnitkar, D. J. Pandya, E. Parry, M. Pawath, C. C. Petersen, K. K. Phyu, S. N. Prabhu, B. B. Pradhan, S. Puntambekar, Gillian Rahmaan, K. S. Raja, M. F. Reed, A. A. Reid, H. A. Richter, S. M. Shah, N. Shaikh, S. N. Sheikh, P. C. Shervington, T. K. Sidey, M. Sivasuriya, G. E. Smart, G. M. Smith, P. Som, S. V. Sood, S. P. Sookraj, B. A. Sorhaindo, Joanna South, M. Sriranganathan, H. Sternberg, A. D. Stewart, J. W. W. Studd, J. R. Sutherst, S. A. S. Syed, Pauline E. Tan, J. B. A. M. Thambu, J. Thomlinson, H. H. Topiwala, Gillian M. Turner, K. N. Varde, G. Wallace, Ann Ward, G. A. McH. Wyllie, K. K. Yeung, Shing-Kwan Yip.

At the meeting of council held on 29 July, with the president, Sir John Peel, in the chair, the following officers were elected: *president,* Sir John Peel; *vice-presidents,* Professor T. N. A. Jeffcoate and Professor J. A. Stallworthy; *honorary treasurer,* Mr. I. M. Jackson; *honorary secretary,* Mr. T. L. T. Lewis; *honorary librarian,* Mr. A. L. Gunn; *honorary museum curator,* Mr. R. M. Haines; *regional council honorary treasurers: Australia,* Mr. J. V. M. Coppleson; *Canada,* Mr. L. J. Quinn; *New Zealand,* Mr. K. D. Drayton; *South Africa,* Mr. H. McK. G. Agnew.

The following were admitted to Membership:

K. D. Chong, M. T. Dewar, D. T. Fatnani, L. R. Franklin, L. H. Goss, A. Himaya, P. J. Hirsch, S. Ramaswamy, J. C. Twomey, W. H. Utian, L. F. Van Druten.

Births

Anderson.—On 9 July 1967, in Johannesburg, South Africa, to Helen (formerly Harthoorn), M.B., B.S., D.Obst.R.C.O.G., and Ronnie Anderson, of Box 93, Serowe, Botswana, a brother for Laurence, James, and Jonathan—Andrew Richard Timothy.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON W.C.1. TELEPHONE: 01-387 4499. TELEGRAMS: *Aitiology, London W.C.1.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs.

ADVERTISEMENT AND SUBSCRIPTION ORDERS should be addressed to The Manager at B.M.A. House, London, or at 415 Bourke Street, Melbourne, Victoria, Australia.

MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the British Medical Association, B.M.A. House, London, or to the Scottish Secretary, B.M.A. Scottish Office, Drumsheugh Gardens, Edinburgh.

New Issues of Specialist Journals

Obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London W.C.1.

ABSTRACTS OF WORLD MEDICINE

The August issue (Volume 41, No. 8) is now available. Published monthly. Yearly subscription £6 6s. U.S.A. $18. Single number 12s. 6d.

BRITISH MEDICAL JOURNAL

LONDON SATURDAY 2 SEPTEMBER 1967

Pointers

Needs of Mentally Subnormal: Only about half of such patients seen in Birmingham required hospital care, and referring the remainder to the local authority would result in a better all-round service, according to Professor T. McKeown and Dr. I. Leck (p. 573). Leader on this page.

Heart Block: "Demand" pacemaker avoids competition between artificial pacemaking and returning normal sinus rhythm, and Dr. E. Sowton has found such a device to be clinically reliable (p. 576).

Phenylketonuria: Drs. J. B. P. Stephenson and M. S. McBean found that temporary phenylalanine hydroxylase deficiency is indistinguishable from phenylketonuria in early infancy, and therefore diagnosis should be re-examined lest treatment induce phenylalanine deficiency in a normal child (p. 579). They also report that mass screening by napkin-Phenistix test is not efficient for early detection (p. 582).

Treating Varicose Veins: Reliable method of detecting incompetent perforating veins by operative venography described by Mr. J. Townsend and colleagues (p. 583).

Myocardial Infarction in Pregnancy: Dr. E. Fletcher and colleagues describe five cases in elderly multigravidae (p. 586).

Hazards of Piped Air Supplies: Contamination by oil mist from compressors in the system detected by Drs. J. A. Bushman and P. A. Clark (p. 588).

Symptoms of Cerebral Metastases: These may be simulated by hypercalcaemia, and Dr. N. J. Strickland and colleagues report a case of bronchial carcinoma without bony or cerebral metastases presenting in this way (p. 590).

Oxygen Therapy: Dr. I. D. Green considers method used should depend on the patient's comfort, degree or risk of hypercapnia, and quality of supervision (p. 593).

Phagocytosis in Renal Failure: Dr. T. D. Brogan reports studies of phagocytosis by polymorphs in uraemic patients (p. 596).

Injection Complication: Subcutaneous atrophy after local corticosteroid injection suggests that deep injections of more dilute suspensions are preferable (p. 600).

Chlorate Poisoning: Successfully treated by peritoneal dialysis (p. 601).

Drug Addiction: Dr. T. H. Bewley writes on the drugs taken, the sources of supply, and the treatment of the addict (p. 603). Leader on S.T.P. (p. 570).

Diagnostic Virology: Inception of a comprehensive diagnostic service described by Dr. J. E. Banatvala and colleagues (p. 609).

Benefits of Automation: Use of computer to supply missing mortality data suggested by Mr. M. R. Hubbard and Dr. E. D. Acheson (p. 612).

Medical Registration: *Supplement*, p. 125.

Place of the Mentally Retarded

There is a continuum in the distribution of intelligence between highly gifted people at one end of the scale and idiots at the other. Thus no natural cleavage separates people who may be regarded as "mentally subnormal" from those of normal intelligence. Any division is arbitrary and a matter of convenience. An intelligence quotient of 70 on a properly standardized and administered test has achieved international recognition as a convenient boundary. This may result in 1.5% of a population such as ours being classed as "subnormal" by this criterion alone, or about 750,000 of a 50,000,000 population. Most of these people find their own niche in society and are an integral part of it. Clearly no special search should be made to "ascertain" this large number or to make special provision for them. There is not enough provision for those who are already known to hospitals and local authorities.

Social changes over the past half-century, together with a better understanding of the balance and distribution of human intellectual endowment, have led to a complete change of direction in the services for the mentally retarded. In 1909 the Eugenics Society was founded, and A. F. Tredgold,[1] writing in the first number of *Eugenics Review,* revived Morel's doctrine[2] of national degeneracy, which he described as "no myth but a very serious reality." Tredgold held that legislation concerning mental defectives was overdue, claiming that "the chief evil that we have to prevent is undoubtedly that of propagation." In 1913 the Mental Deficiency Act was passed, which restricted to the Board of Control the right of discharge of mentally deficient patients in institutions. However, N. Goodman and J. Tizard[3] found in 1962 that so far as imbeciles and idiots are concerned there is no evidence that their prevalence is increasing in Britain, possibly the reverse. Neither have surveys such as that carried out by the Scottish Council for Research in Education[4] supported the suggestion of a decline in national intelligence.

N. O'Connor and J. Tizard[5] showed ten years ago that with relatively little effort large numbers of institutionalized mental defectives could be placed in open employment in the general community. Official opinion now fully supports the view that so far as possible those of limited intelligence should be retained in the general community and placed in hospital or residential units only as a last resort. The report of the Royal Commission on the Law Relating to Mental Illness and Mental Deficiency[6] points out that the majority of the feebleminded are in the general community and that many are earning their living at simple occupations, and also that "There is increasing medical emphasis on forms of treatment and training and social services which can be given without bringing patients into hospital. . . ."

Though for over a decade the numbers of the mentally ill in hospital have fallen steadily, the numbers of the mentally retarded have tended to increase. They rose from 24,000 in 1929 to 56,000 in 1952, while in 1965 the number of subnormal and severely subnormal patients in

© *British Medical Journal,* 1967. All reproduction rights reserved.

psychiatric beds was 64,000.[7] The British Psychological Society appointed a working party, which looked at one aspect of this problem.[8] They showed that there seemed to have been little change in the proportion of more intelligent patients in hospital since the earlier work by O'Connor and Tizard.[5] For patients seen by psychologists in hospital (admittedly a selected sample) the average Wechsler I.Q. on admission was over 70, and, still more surprisingly, the average for the severely subnormal was 60. Their findings strongly suggest that if adequate resources in the way of psychiatric social workers, psychiatrists, employment officers, and others were deployed on rehabilitating the brighter patients then many more of them could be kept out or got out of hospital and into employment. Major obstacles at present are the difficulty of finding suitable lodgings and the dearth of open hostels.

This week in the *B.M.J.* Professor Thomas McKeown and Dr. Ian Leck review at page 573 some of the inadequacies of the hospital service in the light of the Ministry of Health Memorandum (65) 104 *Improving the Effectiveness of the Hospital Service for the Mentally Subnormal.* They have carried out a very useful survey of the mentally subnormal population in hospital at Birmingham, analysing it according to the needs of different groups of patients. The cost of the service is low—£9 per week compared with £15 for "chronic conditions," and £38 for acute children's illness, with beds for mental subnormality at the bottom of the price list. And the authors point out that the result is an inadequate rather than an economical service. In fact the investigation by the British Psychological Society points to a considerable reduction of numbers of inpatients which could be made almost immediately if the psychiatric team functioned as a vigorous rehabilitation unit and was suitably reinforced for this purpose.

McKeown and Leck suggest that responsibility for training should be transferred from the local health authority to the education authority and that a group of resident patients should be transferred to the local health authority. These ideas are logical but will be of no avail unless they are part of a larger and more radical overhaul of the system. If training centres are to go to the education authority they must be staffed by trained teachers specially qualified in the education of handicapped children, or at the very least the Scott Report[9] must be implemented in full and urgently. If patients now resident in hospital are to go to the local authority many new small residential units with adequate staff are required. This should be done not simply by passing the onus to the local health authority but by joint detailed planning and joint operation with the full support of the psychiatric team, including psychiatrist, psychologist, and social worker, so as to get the best use of the limited talent available, as described in the Brooklands experiment.[10]

Finally, both the Ministry circular and McKeown and Leck mention research, the lack of which has contributed powerfully to neglect of the problem of mental handicap. It would seem that thousands of pounds are readily spent on housing a patient for perhaps 40 or 50 years, while a few pounds per head of the institutional population cannot be found to advance studies on rehabilitation and causation.

---

[1] Tredgold, A. F., *Eugen. Rev.*, 1909, 1, 97.

[2] Morel, B. A., *Traité des dégénérescences physiques, intellectuelles et morales de l'espèce humaine.* 1857. Paris.

[3] Goodman, N., and Tizard, J., *Brit. med. J.*, 1962, 1, 216.

[4] Scottish Council for Research in Education, *The Trend of Scottish Intelligence.* 1949. London.

[5] O'Connor, N., and Tizard, J., *The Social Problem of Mental Deficiency.* 1956. London.

[6] Report of the Royal Commission on the Law Relating to Mental Illness and Mental Deficiency, p. 17, 1957. H.M.S.O.

[7] *Annual Report of the Chief Medical Officer for the Year for 1965.* Ministry of Health, 1966. London.

[8] Castell, J. H. F., Clarke, A. D. B., Mittler, P., and Woodward, W. M., *Bull. Brit. psychol. Soc.*, 1963, 16, 37.

[9] *The Training of Staff of Training Centres for the Mentally Subnormal, Ministry of Health*, 1962. H.M.S.O.

[10] Tizard, J., *Brit. med. J.*, 1960, 1, 1041

Training for Obstetrics and Gynaecology

Under the chairmanship of Professor C. H. G. Macafee a select committee of eminent gynaecologists has reported to the Council of the Royal College of Obstetricians and Gynaecologists on training for the practice of that specialty.[1] They have considered the teaching of obstetrics and gynaecology to undergraduates, the training and further education of general practitioner obstetricians, the training of specialists, research in obstetrics and gynaecology, the recruitment of specialists, and the staffing and organization both of teaching departments and of hospital departments of obstetrics and gynaecology. The select committee obtained its information from questionaries sent out to academic and part-time consultants, and the questions covered undergraduate education, preregistration students, the qualifications of specialist obstetricians and gynaecologists, staffing, research, and other matters. A questionary was also sent to final-year undergraduate medical students asking them to give their views on obstetrics and gynaecology and its teaching and why they would or would not choose this specialty as a career. With the information thus gained Professor Macafee visited several centres to gain first-hand knowledge of the problems of education, research, and recruitment.

The Committee have digested the information obtained for them and have produced an interesting picture of the state of obstetrics and gynaecology in Britain today. It might well be said that the facts and opinions on which the report is based are far from exhaustive, since only 55% of the undergraduate questionaries (nearly 1,000 replies) were returned, and from consultants there were 83 replies. But despite the relatively poor response rate the committee's views alone are worth having, for they confirm an uneasy feeling that all is not well with obstetrics and gynaecology. A similar rather gloomy view came from the United States in 1961.[2]

The report seems to be seeking a status for obstetrics and gynaecology within the field of medicine as a whole. The subject appears to be undervalued, and the document is a statement of faith in its future. It has been realized that a mechanistic view of reproduction and its disorders no longer meets the needs of today either in education or in practice, and something must be done about it if top-quality teachers and practitioners are to be attracted to the specialty. The report often refers to "our specialty," giving perhaps a hint of parochialism, exclusiveness, and separateness which may occasionally be seen to beset obstetricians and gynaecologists. Everyone will agree with the committee, however, that obstetrics and gynaecology is a subject deserving the attention of first-class minds, and it has useful recommendations that point the way to escape from narrow intellectual confines, it being necessary to "eradicate the old picture of obstetrics being a manipulative art and gynaecology a narrow branch of surgery."

---

[1] Royal College of Obstetricians and Gynaecologists, *The Training of Obstetricians and Gynaecologists in Britain, and Matters Related Thereto*, The Report of a Select Committee to the Council of the College, 1967. London.

[2] *The Recruitment of Talent for a Medical Specialty*, ed. Howard C. Taylor, jun., 1961. Saint Louis.

Students come to obstetrics and gynaecology full of enthusiasm, but this later fades, probably because of lack of intellectual stimulus and because of the demands of practice. There is little doubt that the aspirant to consultant status has a long, hard clinical grind involving much time resident in hospital and in relatively understaffed departments, necessitating long periods of separation from his family. Hospital authorities have been slow to recognize the importance of married quarters for many of their staff, but there would seem to be a special claim for resident obstetricians to be so catered for.

Most disturbing for the Royal College must be the conclusion that "obstetrics and gynaecology does not attract its full share of those who show outstanding ability as undergraduates." The reasons suggested for this are the heavy burden of clinical work with little time for study during training, long residence in hospital, slower promotion to consultant status than in other specialties, the limited scope of the subject, and poor research facilities.

If the report presents a true image of obstetrics and gynaecology, the senior members of the specialty must bear their full measure of responsibility for it. If they had had enthusiasm, dreamed dreams, and seen visions, the medical world would not have such a drab view of what obstetrics and gynaecology is. Undoubtedly the blinkers are being removed—and this report is a sign that they are. It is to be fervently hoped that its recommendations will be acted upon.

Antibodies in Schizophrenics

In recent years several groups of workers have found abnormalities in the proteins in the blood of schizophrenic patients,[1-5] while others have reported that the administration of serum from schizophrenics produces changes in behaviour of rats[6 7] and monkeys.[8] Attempts to duplicate these findings have sometimes been unsuccessful,[4 9 10] and it is still not clear how consistent these abnormalities are and how specific they are for schizophrenia.[11] Interest in the blood proteins of schizophrenics is largely the result of the work of R. G. Heath and his colleagues[12] in New Orleans. In 1958 they reported that "taraxein," a protein isolated from the serum of schizophrenics, would cause electroencephalographic and behavioural changes in monkeys and that it would reproduce many of the symptoms of schizophrenia in human volunteers.

If an abnormal protein is present in the blood of schizophrenics it may be an antibody. Searches for an antigenic abnormality in serum from schizophrenics have yielded both positive[13] and negative[14] results. Russian workers,[15] using a complement-fixation technique, found antibrain antibodies in a considerable proportion of schizophrenics and other psychotic patients, but their findings have not been confirmed by other workers using a more specific precipitin reaction.[16 17] P. R. J. Burch[18] has postulated an autoimmune origin of schizophrenia on theoretical grounds from a study of age- and sex-specific rates of first admission to hospital.

Recently Heath and his colleagues, continuing their work on taraxein, have reported results of a series of immunological investigations.[19-21] Brains were obtained at necropsy from both schizophrenic patients and controls. When brain sections were incubated with fluorescein-tagged antihuman gammaglobulin (F.T.A.-Hgg), fluorescence was observed in the nuclei of nerve cells in the septal region and in the basal caudate nucleus of schizophrenics' brains but not of control brains. When the sections were first incubated with serum from schizophrenics, F.T.A.-Hgg produced slight fluorescence in sections from the same areas of control brains, and intense fluorescence in sections of schizophrenic brains. Control sera had no such effect. When sections of schizophrenics' brain were pretreated with untagged antihuman gammaglobulin, the fluorescence produced by F.T.A.-Hgg was greatly reduced.

These results certainly suggested that antibody is attached to nerve cells in certain areas of the brains of schizophrenics and that the antibody is present in serum from schizophrenics.[19] Further experiments suggest that the antibody can combine with the nuclei of nerve cells in monkeys' brains.[20] Finally, antisera against specific areas (including the septal area) of both human and monkey brain were produced by the injection of homogenates into sheep. Fractions of the antisera were administered to monkeys and caused electroencephalographic changes (especially from the septal area) and behavioural changes which closely resembled those produced by taraxein.[21]

At first sight these results offer good evidence of an autoimmune mechanism in schizophrenia. However, few workers would accept the E.E.G. and behavioural changes in monkeys as equivalents of schizophrenia in man. The discovery of antibody in schizophrenics' brain and serum is of great interest, and this part of the experiment at least should be repeated in other laboratories. But a word of caution is needed before too many conclusions are drawn. The history of research into the causes of schizophrenia consists of a dishearteningly long series of promising leads which ultimately led nowhere. The taraxein theory, on which the whole of the present series of experiments was based, may go the same way. Indeed it does not command general assent. Furthermore, the fluorescent antibody technique can give rise to false positive results unless the greatest care is taken; unfortunately the authors do not give details of how they measured the fluorescence. Nor do they deal with the objection that there is no histological evidence of immunological damage in the brain of schizophrenics.[17] Finally, autoimmunity is a fashionable concept for explaining the origin of several other chronic, relapsing diseases as well as schizophrenia. It is salutary to recall that focal sepsis was once just as fashionable[22] and

[1] Fessel, W. J., *Arch. gen. Psychiat.*, 1962, **7**, 427.
[2] Kopeloff, L. M., and Fischel, E., ibid., 1963, **9**, 524.
[3] Sapira, J. D., ibid., 1964, **10**, 196.
[4] Gammack, D. B., and Hector, R. I., *Clin. Sci.*, 1965, **28**, 469.
[5] Noval, J. J., and Mao, T. S. S., *Fed. Proc.*, 1966, **25**, 560.
[6] Bergen, J. F., Pennell, R. B., Saravis, C. A., and Hoagland, H., in *Serological Fractions in Schizophrenia*, ed. R. G. Heath, 1963, p. 67. New York.
[7] Bishop, M. P., ibid., p. 77.
[8] Ferguson, D. C., and Fisher, A. E., *Science*, 1963, **139**, 1281.
[9] Lovegrove, T. D., and Nicholls, D. M., *J. nerv. ment. Dis.*, 1965, **141**, 195.
[10] Sanders, B. E., Small, S. M., Ayers, W. J., Oh, Y. H., and Axelrod, S., *Trans. N.Y. Acad. Sci.*, 1965, **28**, 22.
[11] Kety, S. S., *New Engl. J. Med.*, 1967, **276**, 325.
[12] Heath, R. G., Martens, S., Leach, B. E., Cohen, M., and Fiegley, C. A., *Amer. J. Psychiat.*, 1958, **114**, 917.
[13] Haddad, R. K., and Rabe, A., in *Serological Fractions in Schizophrenia*, ed. R. G. Heath, 1963, p. 151. New York.
[14] Faurbye, A., Lundberg, L., and Jensen, K. A., *Acta path. microbiol. scand.*, 1964, **61**, 633.
[15] Kuznetsova, N. I., and Semenov, S. F., *Zh. Nevropat. Psikhiat.*, 1961, **61**, 869.
[16] Fessel, W. J., *Arch. gen. Psychiat.*, 1963, **8**, 614.
[17] Rubin, R. T., *Brit. J. Psychiat.*, 1965, **111**, 1003.
[18] Burch, P. R. J., ibid., 1964, **110**, 818.
[19] Heath, R. G., and Krupp, I. M., *Arch. gen. Psychiat.*, 1967, **16**, 1.
[20] —— Krupp, I. M., Byers, L. W., and Liljekvist, J. I., ibid., 1967, **16**, 10.
[21] —— —— —— —— ibid., 1967, **16**, 24.
[22] Hunter, W., *Brit. med. J.*, 1927, **2**, 811.
[23] Cotton, H. A., *Amer. J. Psychiat.*, 1922, **79**, 157.

that it was offered, with much evidence, as a cause of schizophrenia.[23] During attempts to remove some of the less accessible foci, many patients died. At least the theory of autoimmunity is unlikely to lead to such therapeutic disasters.

Progress with Air Pollution

Since the winter of 1962 the National Survey on Air Pollution has been collecting data throughout the year on the concentration of smoke and sulphur dioxide in a representative sample of British towns. The data are processed by computer and are available to all interested workers through the Warren Spring Laboratory, Stevenage. In its 32nd Report,[1] covering a period of eight years since the establishment of the first smoke control areas, the Warren Spring Laboratory discusses the trends in the pattern of pollution as a consequence of the Clean Air Act of 1956[2] and of the changing fuel requirements of modern technology.

There has been a decrease in the consumption of coal with an increase in that of fuel oil, most of which has a high sulphur content. As a result the emission of smoke into the atmosphere has fallen while that of sulphur dioxide has risen. The decrease in smoke concentration in the ambient atmosphere was to be expected, but there has also been a welcome decrease in the sulphur dioxide concentration over the country as a whole, with a smaller decrease in London. This has been attributed to the care which is now being given to the location of new industrial sites and such factors as the height and design of industrial chimneys.[3] The level of pollution depends on the amount of material emitted and on the weather conditions determining how much pollution is blown away, so that the weather is a major factor in setting the pattern of pollution from year to year. Since the Warren Spring studies show considerable fluctuations from one year to the next any trend so far must be interpreted with caution.

While the Clean Air Act is helping to clear the air of smoke, the removal of sulphur dioxide from it presents a greater problem. The report points out the high cost of the process for removing sulphur dioxide at the Battersea and Bankside power stations and the lack of success in developing a more convenient system. At Battersea 20–30 tons of Thames water are used for every ton of coal burnt, and extension of the process is limited by the capacity of the river to take the effluent. The most practicable way at present of limiting pollution from sulphur dioxide is by sending it aloft by means of suitable chimneys and with a high speed of emission, so that the gas is diluted before coming down again.

Studies at Stevenage and Hornsea on the distribution and dispersion of pollution in streets carrying heavy motor traffic have shown that though pollution can be high it is also extremely local in character. The black smoke from diesel engines arouses public indignation, but petrol engines produce more carbon monoxide and higher concentrations of unburnt hydrocarbons, which are more likely to be injurious to health.[4] Devices for removing smoke from diesel exhausts are uneconomical. The solution lies in the correct maintenance and operation of the vehicle, and this should be controllable by adequate legislation. However, according to a report[6] issued by the National Society for Clean Air last week, if all manufacturers set their engines to the level permitted by a forthcoming British Standard, smoke on the road would increase. In the U.S.A. stringent regulations will apply to all 1968 petrol engines, limiting the discharge of carbon monoxide and hydrocarbons. Britain is free of the irritant photochemical smog produced by the action of strong sunlight on unburnt hydrocarbons which is so characteristic of Los Angeles,[7] but the dangerous effects of a build-up of carbon monoxide are equally applicable here, and this problem has not yet been given sufficient attention.

That air pollution worsens the plight of a patient with chronic lung disease is undoubted, and it is likely to contribute to the production of chronic bronchitis. But there is no proof yet that either smoke or sulphur dioxide in the concentrations encountered in polluted air are the substances causing the harm, though they may be. However, since the concentrations of other harmful substances are likely to vary in the same way as those of smoke and sulphur dioxide, these two are likely to remain at least useful indices of air pollution.

S.T.P.

By the standards of " pop " culture S.T.P. is an elderly drug ; it has been publicly discussed for nearly two months. On 16 June *International Times*, the fortnightly newspaper of the hippie movement, predicted its arrival in Great Britain,[1] by mid-July a tablet had been passed to the Home Office for analysis,[2] and by the end of July *International Times* had reported that the drug was in wider use in Britain[3] and warned that it could be dangerous.

The American Food and Drug Administration has identified S.T.P. as methyl dimethoxy methyl amphetamine,[4] a substance chemically related to both amphetamine and mescaline, but a good deal of doubt remains. *Time*,[5] which gives the credit for the distribution if not the synthesis of this latest hallucinogen to a San Francisco chemist, reports that the drug may be 5-methoxy-NN-dimethyltryptamine. This substance is related to the known hallucinogens bufotenine, dimethyltryptamine, and psilocybin, and also to a principle in reed canary grass which causes staggers in sheep.[6] It has also been suggested that S.T.P. is related to a group of hallucinogens, the piperidyl glycolates, studied in the 1950s by L. G. Abood and his collaborators[7] or to a chemical warfare agent called BZ.[5] These suggestions are based on the cholinergic effects of S.T.P. Alternatively, S.T.P. may well be related to a group of benzilic acid derivatives, of which the tranquillizer benactyzine, the hallucinatory anti-Parkinsonian compound benzhexol, the arousing drug pipradol, and the enzyme potentiator S.K.F. 525 are other examples. S.K.F. 525 proved to be so powerful and so non-specific a substance that it was useless for therapy: the reported dangerous potentiation of S.T.P. by the usual antagonists of lysergic acid diethylamide (L.S.D.)[2,3] suggest that it may be just such another substance.

---

[1] *The Investigation of Atmospheric Pollution 1958–1966*, 32nd report, 1967. H.M.S.O. London.
[2] *Clean Air Act*, 1956, Chapter 52, 1957. H.M.S.O. London.
[3] *Memorandum on Chimney Heights*. 1963. H.M.S.O. London.
[4] Reed, L. E., *Roy. Soc. Hlth. J.*, 1966, **86**, 227.
[5] Lawther, P. J., ibid.
[6] *Air Pollution from Road Vehicles*, National Society for Clean Air, 1967. London.
[7] Hamming, W. J., MacBeth, W. G., and Chass, R. L., *Arch. environm. Hlth.*, 1967, **14**, 137.

[1] *International Times*, 16 June, 1967.
[2] *The Times*, 8 August, 1967.
[3] *International Times*, 28 July, 1967.
[4] *F.D.A. Press Release Nos*. 67-78, 11 July, 1967.
[5] *Time*, International Edition, 7 July, 1967.
[6] Wilkinson, S., *J. chem. Soc.*, 1958, p. 2079.
[7] Abood, L. G., Ostfeld, A., and Biel, J. H., *Arch. int. Pharmacodyn.*, 1959, **120**, 186.

Not surprisingly, no controlled experiments have yet been done with S.T.P., but there seems little doubt that it is an active, dangerous, and powerful substance. A single dose (however much that may be) is said to give a 72-hour " trip,"[5] and the risk of suicide or psychotic breakdown seems likely to be correspondingly greater than with L.S.D.

Whatever its identity, the emergence of S.T.P. has raised several questions of interest. Whose is the responsibility to collect and sift information on drugs introduced in this way, to promote research, and to advise society on their control and appropriate uses ? Perhaps the L.S.D. and Cannabis Subcommittee of the Home Office's Standing Advisory Committee on Drug Dependence should extend its terms of reference to include drugs of this kind as they are developed. L.S.D. was not the first hallucinogen: S.T.P. is certainly not the last. New compounds may be developed with totally new actions for which the appropriate scientific descriptive language does not yet exist—a fact that may itself contribute to anxiety about such drugs. The definitive chemical identification of S.T.P. has probably been delayed as a result of deliberate obfuscation by those responsible for its synthesis and distribution—several different substances were apparently sold or given to the Federal Drugs Administration as S.T.P. by its informants.[4]

The iconoclasm of hippiedom and the ill-considered advocacy of people who should know better, including, unfortunately, a few members of the medical profession, are acting together to create an atmosphere in which firm action to control the spread of drug-taking is unpopular. Nevertheless, such action is needed. The statutory measures for the control of drugs need to be made more flexible, so that as soon as compounds such as S.T.P. enter circulation their unauthorized possession and distribution can be made an offence. Society has a responsibility to protect its members from drugs that can make them frankly insane or indeed kill them, as it has to stop the spread of communicable diseases.

Healing Processes in Wounds

Reactions to injury tend to be studied intensively in time of war and to be neglected in the subsequent peace. But fortunately for medicine the healing of wounds presents enough basic problems of deep interest to biologists to ensure that it remains a field of active research.[1] Though clinicians demand practical information about factors influencing healing, facts can come only from careful experimental work, and such experiments have already exposed some widely held fallacies.

The healing of a wound starts as an inflammatory reaction with infiltration by polymorphs and mononuclear phagocytes, and removal of debris by these cells. The reaction seems to be of importance to the subsequent healing. The ingrowth of new blood vessels, lymphatics, and nerves by budding from existing structures is relatively well established[2] and has fairly recently been confirmed by electron-microscopy.[3] A practical point is that new blood vessels are abnormally permeable to particulate matter,[4] including bacteria, and this may possibly facilitate infection of the wound from the blood stream.

The commonly held view of the origin of fibroblasts is that they migrate from the borders of the wound after division of existing fibroblasts. Alternatively it has been suggested that fibroblasts may be derived from haematogenous mononuclear cells.[5] However, all spindle-shaped cells in granulation tissue are not fibroblasts. The fibroblast can be identified with certainty only by electron-microscopy. It is then seen to have a large nucleus and nucleolus, extensive rough-surfaced endoplasmic reticulum, dense cytoplasmic bodies, peripheral cytoplasmic vesicles, dispersed Golgi network, numerous large mitochondria, and aggregates of fine filaments at the periphery of the cell.[6] The possibility that blood cells turn into fibroblasts may perhaps be proved only by use of blood cells labelled with a stable marker in conjunction with electron-microscopy.

Experimental studies show that collagen is synthesized by hydroxylation of proline and then biosynthesis of the protein in the endoplasmic reticulum of the fibroblasts. From here the protein passes into the extracellular space, where it acquires the characteristic banding (700 Å) of collagen. The mitochondria are not significantly involved in this process but the Golgi complex and peripheral vesicles are, especially if the collagen is destined to enter into a complex with polysaccharide. The clinical relevance of these observations is apparent from study of scorbutic animals, vitamin-C deficiency being one cause of defective healing of wounds. In scurvy wounds are normal except for the absence of collagen fibrils. Electron-microscopy shows the fibroblasts have an abnormal endoplasmic reticulum, with plenty of ribosomes but lack of regular orientation. Filamentous extracellular material (presumably fibrillar protein) is present, but this lacks the regular banding of collagen. It is not yet clear whether failure of wound healing in vitamin-C deficiency is due to changes in the properties or the structure of fibroblastic ribosomes and endoplastic reticulum or whether these are secondary to a failure to hydroxylate proline.[7]

In addition to the synthesis of collagen, contraction of the wound area is a vital part of healing. It is now realized that this phenomenon is not due to contraction of collagen fibres or to loss of extracellular or intracellular water. Nor is it due to ingrowth of epithelium from the wound margins. The contraction is in fact a complex and poorly understood process, yet it is of great importance in living tissues. It seems to be due to tensions within the granulation tissue filling the wound, orientated towards lines of stress, and associated with removal of cells and extracellular material, including collagen.[8-10] Likewise the cessation of wound contraction is also of clinical importance. M. Abercrombie[10] believes that it may occur when the advancing edges of the

[1] *Wound Healing*, Proceedings of a Workshop, ed. S. M. Levenson, J. M. Stein, and N. Grossblatt, 1966. Washington, D.C.

[2] Florey, H., and Jennings, M. A., in *General Pathology*, ed. H. Florey, 1962, 3rd ed., p. 449. London.

[3] Cliff, W. J., *Phil. Trans. B*, 1963, **246**, 305.

[4] Schoefl, G. I., *Ann. N.Y. Acad. Sci.*, 1964, **116**, 789.

[5] Gillman, T., and Wright, L. J., *Nature (Lond.)*, 1966, **209**, 263.

[6] Ross, R., and Benditt, E. P., *J. Cell. Biol.*, 1965, **27**, 83.

[7] —— in *Wound Healing*, ed. S. M. Levenson, J. M. Stein, and N. Grossblatt, 1966. Washington, D.C.

[8] Abercrombie, M., James, D. W., and Newcombe, J. F., *J. Anat. (Lond.)*, 1960, **94**, 170.

[9] Billingham, R. E., and Russell, P. S., *Ann. Surg.*, 1956, **144**, 961.

[10] Abercrombie, M., in *Wound Healing*, ed. S. M. Levenson, J. M. Stein, and N. Grossblatt, 1966. Washington, D.C.

[11] Johnson, F. R., in *Wound Healing*, ed. S. M. Levenson, J. M. Stein, and N. Grossblatt, 1966. Washington, D.C.

[12] Weiss, P., and Kavanau, J. L., *J. gen. Physiol.*, 1957, **41**, 1.

[13] Grillo, H. C., in *Wound Healing*, ed. S. M. Levenson, J. M. Stein, and N. Grossblatt, 1966. Washington, D.C.

[14] Pories, W. J., Henzel, J. H., Rob, C. G., Strain, W. H., *Lancet*, 1967, **1**, 121.

[15] Raekallio, J. *Exp. molec. Path.*, 1965, **4**, 303.

skin approach within a certain distance of each other. Most collagen is laid down after contraction ceases, possibly because it is only then that the contents of the wound are under tension.

Another feature of the healing of wounds is epithelization. A covering of epithelium often grows in advance of the contraction process and without hindering it. The classical view that mitotic activity in epithelium is confined to the edges of a wound is true only of skin and some other sites. Nevertheless, it is best to consider epithelial proliferation and epithelial migration as separate phenomena of healing.[11] Current views tend to regard the destruction of the normal cell architecture of a tissue (" negative feedback ") rather than local hormones as leading to cell proliferation in healing.[12] It is now known also that denervation has no effect on healing provided the wound is protected from trauma.[13]

Despite advances in knowledge obtained by research workers recently surgeons are in practice sometimes baffled by the unpredictability of the healing process. Of special note, therefore, is a report by a surgical team of dramatic acceleration of healing of open wounds in patients given zinc sulphate 2 mg. three times daily by mouth.[14] The results suggest that the process affected was wound contraction, and they indicate a state of zinc deficiency in a group of healthy, well-fed, young American males. It is possible that trauma, burns, or other stress may greatly increase the short-term need for zinc and that this deficiency cannot be made good by a normal diet. The action of zinc would presumably lie in providing a prosthetic group for enzymes required for wound healing. Certainly activation of enzymes occurs in wounds,[15] and some of the enzymes are of the type to require metallic prosthetic groups. The results obtained with zinc sulphate offer a straw at which surgeons may be prepared to grasp, especially as no ill effects were reported.

Diet and Alcohol in Gout

A low-purine diet has been used in the treatment of gout for many years, because reduction in purine metabolism will lower the synthesis of urate. A high-purine diet may cause the level of uric acid in the serum to rise. For example, F. G. W. Marson,[1] in a study of eight patients (seven of whom were hyperuricaemic), showed that a change from a low- to a high-purine diet raised the serum uric acid by an average of 1.3 mg./100 ml. In a patient who is already mildly hyperuricaemic such a rise might be sufficient to produce clinical gout.

It is remarkable, however, that the effect of fasting on the level of uric acid in the serum is equally striking. That it may produce hyperuricaemia, with a reduction in the urinary excretion of urate, has been known at least since 1909.[2] The hyperuricaemia appears to be due to increased levels in the serum of β-hydroxy-butyric acid and acetoacetic acid, with a resulting ketosis. This has the effect of interfering with the renal excretion of uric acid and lowers the ratio of urate clearance to creatinine clearance.[3-5] Fasting in one recent study[6] caused an average rise, above the base-line achieved on a low-purine diet, in the serum level of uric acid of 1.1 mg./100 ml. after 24 hours in five gouty patients and an average rise of 2.0 mg./100 ml. after 48 hours in a further eight patients. In practice potent uricosuric drugs and xanthine-oxidase inhibitors have a profound effect in lowering the serum level of uric acid in gouty patients, and in ordinary circumstances a low-purine diet gives only a marginal benefit, if any at all.

The association between alcohol and gout is traditional. In fact patients will sometimes deny a family history of gout for fear that the doctor will interpret this as evidence of alcoholism. Nevertheless, there is some truth in the belief that taking alcohol may provoke an attack. The serum uric acid is indeed higher when a patient is acutely intoxicated than when sober.[7] This is apparently associated with lactate, which inhibits renal excretion of urate,[8, 9] and is increased in the blood in alcoholic intoxication. The administration of lactate to patients will cause hyperuricaemia.[7, 10] F. P. Alepa and his colleagues[11] and S. Jakovcic and L. B. Sorensen[12] have both recently demonstrated a raised serum lactate level together with hypoglycaemia and ketonaemia in association with hyperuricaemia in patients with glycogen storage disease. In these cases the hyperuricaemia is due to a reduced renal clearance of urate and also to increased biosynthesis of purine.

It is possible that many true alcoholics combine a high intake of alcohol with lack of food, so that the combined effect of these two factors, each capable of producing hyperuricaemia, may be more profound. M. J. Maclachlan and G. P. Rodnan[6] have confirmed that small amounts of alcohol cause only a slight rise in serum uric acid, but when the alcohol was taken during a short period of fasting the rise in the serum uric acid was greater than that which followed fasting alone.

Thus a high-purine diet, fasting, and alcohol intake are associated with acute attacks of gout. Furthermore, it is known that sudden changes in the serum level of uric acid may provoke an acute attack of arthritis whether the serum uric acid is rising or falling. It is a common experience that acute gout may be precipitated by treatment either with uricosuric drugs, such as probenecid,[13] or with allopurinol,[14] both of which lower the level of serum uric acid in different ways. Maclachlan and Rodnan's study[6] again showed that rapid fluctuations in serum uric acid, usually exceeding 1 mg./100 ml., were associated with acute attacks of gout, 13 out of 19 attacks occurring in relation to a rapidly falling serum level of uric acid and six with a rising level.

Since we can now exercise metabolic control of gout readily by correction of hyperuricaemia with potent drugs, the use of a low-purine diet has become of little advantage to the patient. Moreover, since the acute attacks of gout may be precipitated by rapid fluctuations in serum levels of uric acid the patient should avoid alcoholic excesses, maintain an adequate food intake, and be on a constant regimen of drug therapy.

[1] Marson, F. G. W., *Quart. J. Med.*, 1953, **22**, 331.
[2] Cathcart, E. P., *J. Physiol. (Lond.)*, 1909, **39**, 311.
[3] Scott, J. T., McCallum, F. M., and Holloway, V. P., *Clin. Sci.*, 1964, **27**, 209.
[4] Lecocq, F. R., and McPhaul, J. J., jun., *Metabolism*, 1965, **14**, 186.
[5] Goldfinger, S. Klinenberg, J. R., and Seegmiller, J. E., *New Engl. J. Med.*, 1965, **272**, 351.
[6] Maclachlan, M. J., and Rodnan, G. P., *Amer. J. Med.*, 1967, **42**, 38.
[7] Lieber, C. S., Jones, D. P., Losowsky, M. S., and Davidson, C. S., *J. clin. Invest.*, 1962, **41**, 1863.
[8] Gibson, H. V., and Doisy, E. A. A., *J. biol. Chem.*, 1923, **55**, 605.
[9] Michael, S. T., *Amer. J. Physiol.*, 1944, **141**, 71.
[10] Yü, T. F., Sirota, J. H., Berger, L., Halpern, M., and Gutman, A. B., *Proc. Soc. exp. Biol. (N.Y.)*, 1957, **96**, 809.
[11] Alepa, F. P., Howell, R. R., Klinenberg, J. R., and Seegmiller, J. E., *Amer. J. Med.*, 1967, **42**, 58.
[12] Jakovcic, S., and Sorensen, L. B., *Arthr. and Rheum.*, 1967, 10, 129.
[13] Mason, R. M., *Ann. rheum. Dis.*, 1954, **13**, 120.
[14] Rundles, R. W., Metz, E. N., and Silberman, H. R., *Ann. intern. Med.*, 1966, **64**, 229

Papers and Originals

Institutional Care of the Mentally Subnormal*

THOMAS McKEOWN,† M.D., PH.D., D.PHIL., F.R.C.P.; IAN LECK,‡ M.B., PH.D.

Brit. med. J., 1967, 3, 573–576

The trend of progressive opinion concerning the hospital care of the mentally subnormal is well expressed in a Ministry of Health Memorandum [(65)104] on *Improving the Effectiveness of the Hospital Service for the Mentally Subnormal.* It states: "In the absence of complicating conditions, such as severe physical disability or disturbed behaviour, the severely subnormal patient who has been adequately investigated and treated ought not to be primarily the responsibility of the hospital services for long-term care. Ultimately, when facilities outside hospitals are fully developed, continued hospital care will be necessary only for patients who require special or continuous nursing and for those who, because of unstable behaviour, need the kind of supervision and control provided by a hospital." Our object in this paper is to estimate the proportion of patients now in hospital who, according to these criteria, require hospital care and to consider the future organization of institutional care of the mentally subnormal in the light of the findings.

In 1965 an investigation was made of the needs of all (1,652) Birmingham patients (874 male and 778 female) in 13 hospitals for the subnormal in the Birmingham area. Each patient's requirements were assessed by a hospital doctor and nurse in charge of the ward. A previous report (Leck, Gordon, and McKeown, 1967) showed that in most respects Birmingham patients were similar to the subnormal in all hospitals in England and Wales. The exceptions were the lower proportion of young patients in Birmingham hospitals (accommodation for them in the area is deficient) and the higher proportion classified as "severely subnormal."

Classification of Patients According to their Needs

The earlier paper gave details of patients' requirements for medical care, nursing care, training, and occupation, and the results were brought together in an attempt to present a picture of the essential needs of the whole hospital population. As a basis for the present discussion the observations are summarized in Table I. The types of care are here arranged in order of decreasing complexity—from "investigation or active hospital treatment" to "sheltered environment"—and each patient is uniquely classified according to the most complex type of care he required.

TABLE I.—*Classification of Patients According to Type of Care Required*

Care Required	No.	%
Investigation or active hospital treatment	7	0·4
Mental and basic nursing	366	22·2
Mental nursing	286	17·3
Basic nursing	212	12·8
Checking and counselling	302	18·3
Sheltered environment	479	29·0
Total	1,652	100

Medical Treatment

Only seven of the 1,652 patients were thought to need medical investigation or treatment of a kind which would have made it necessary for them to be in hospital. This is much lower than the estimate (10%) made by Pilkington (1966) and confirmed by him in a recent survey (personal communication) of the proportion of his patients who required "detailed specialist, day-to-day diagnosis, care, and treatment." There are probably two main reasons for the difference.

Firstly, there is considerable regional variation in the pattern of care of the mentally subnormal. Birmingham is a relatively compact area in which paediatric and child psychiatric centres do a considerable amount of investigation which might elsewhere be done in hospitals for the subnormal. The mental hospitals are reasonably convenient and deal with more high-grade subnormal psychopaths than in some other regions. The pattern of care is also affected by the shortage (already referred to) of hospital accommodation for children.

But the estimate of the proportion of patients needing hospital investigation and treatment is also influenced by the judgement of the medical staffs on the scope for active measures. At the present time there are considerable differences of opinion and practice concerning the application of special methods. In some hospitals biochemical and structural abnormalities are investigated and a few centres are equipped for chromosome examination. Special units have been established for autistic children, for deaf subnormal children, for adolescents, for psychopaths, for psychotic children. In the United States, in the field of mental retardation, research is given high priority, and a large number of research units have been established in hospitals. Collectively these developments comprise the growing edge of the field of mental subnormality, but they have not yet greatly influenced the work of the average hospital, where active investigation and treatment are still restricted to a very small proportion of patients.

A further 794 of the 1,652 patients were considered to require treatment (mainly tranquillizers, anticonvulsants, sedatives) which would not have made it necessary for them to be in hospital. The remaining 851 patients were said to need no medical treatment.

Nursing Care

In relation to the organization of hospital care of the subnormal the most important features of the classification in Table I are the subdivision of the various types of nursing and the distinction between nursing and other forms of personal

---

* This investigation was supported by a grant from the Nuffield Provincial Hospitals Trust.

† Professor of Social Medicine, University of Birmingham.

‡ Wates Foundation Senior Lecturer in Community Medicine, University College Hospital Medical School, London W.C.1.

care. About half the patients (871) were thought to need nursing: the seven who required investigation or hospital treatment (which would include skilled nursing) and 864 in need of mental nursing and/or basic nursing. Mental nursing is taken to comprise the care and supervision of potentially difficult patients. Basic nursing includes personal services, such as washing, dressing, feeding, lifting, attention to bladder and bowel of the incontinent, which require only a limited degree of nursing skill and experience.

Checking and Counselling

The other 781 patients, about half of the total population, needed only "checking and counselling" or a sheltered environment without personal service. The distinction between mental nursing and checking and counselling is important. The latter are interpreted as advice about activities such as dressing, washing, and time-keeping; the patients concerned have to be reminded about these things, but apart from such advice they need no other personal service. It seems essential to distinguish this kind of care, which can be provided by untrained staff, from skilled, basic, and mental nursing for which training is required.

Relation of Hospitals to Other Services

According to the recommendation quoted in the opening paragraph (that hospital care should be restricted to those "who require special or continuous nursing and . . . who, because of unstable behaviour, need the kind of supervision and control provided by a hospital") the evidence presented in Table I suggests that about half the patients now in hospital should not be there. This is the proportion of patients who need no medical or nursing care, and who require, in addition to training and occupation, only a sheltered environment with, in some cases, the simple personal attention described as checking and counselling. The central question concerning the future organization of institutional care of the subnormal is whether the two groups of patients—those who need medical and nursing care and those who do not—should be in the same institution and under the same administrative authority.

Before attempting to answer this question we should remind ourselves of the present difficulties of mental subnormality hospitals, which are perhaps the most formidable confronting any branch of the hospital service. The most serious problem is their inability to attract staff, particularly skilled staff. A recent estimate of nursing strength in the Birmingham Region showed that the number of trained nurses in posts was about two-thirds of the establishment and the number of student and pupil nurses was only one-third. These deficiencies had to be compensated so far as possible by an increase in the number of enrolled and other assistant nurses, which was much above the establishment.

The difficulties of medical staffing are well known. A recent survey of consultant psychiatric establishments in mental subnormality hospital groups of 1,000 or more beds in England and Scotland (Heaton-Ward, 1967) showed that the number of beds per full-time consultant equivalent ranged from 260 to 1,185. The national average (628) was far above the figure (300) recommended by the Mental Deficiency Section of the Royal Medico-Psychological Association in 1960. The high consultant bed ratios for established posts are due largely to the lack of applicants for consultant appointments: some hospital boards see little point in creating posts which there is little prospect of filling. Similar difficulties are encountered in attracting other professional workers such as psychologists and physiotherapists.

But the deficiencies of the hospitals are not only in respect of medical and nursing care. The Birmingham investigation included an assessment of the occupation required by each patient, and Table II shows the proportions engaged in the occupations recommended for them. Of the 1,242 patients regarded as suitable for some type of activity, only about half (630) were in the occupation recommended, and 101 had no occupation of any kind. These results indicate that in many hospitals for the subnormal opportunities for education, training, and employment are very deficient.

TABLE II.—*Proportion of Patients in Recommended Occupation*

Occupation	No. of Patients Recommended	Patients in Recommended Occupation	
		No.	%
Training { Elementary	112	70	62·5
Training { Scholastic	8	3	37·5
Domestic work on wards	80	52	65·0
Therapeutic occupation or vocational rehabilitation	755	323	42·8
Work in hospital service departments	159	100	62·9
Work outside hospital	128	82	64·1
Total	1,242	630	50·7

The figures quoted here give some idea, though an inadequate one, of the difficulties of mental subnormality hospitals. They are unlikely to be resolved by minor modifications in practice, and require nothing less than a radical reorientation of hospital work in relation to other medical and social services.

The key to this reorientation, we suggest, lies in separating patients who need medical and nursing care from those who do not. Under present conditions the requirements of neither group can be well met: the medical care of the first is prejudiced by inflation of their numbers with patients without medical needs; and the educational and welfare services for the second group are quite inadequate because they are provided in a hospital environment and by the wrong authority. These difficulties could be removed by restricting the hospital responsibility to what is essentially the medical task, and by assigning to educational and welfare authorities patients who need training, employment, and a home.

Fig. 1 shows diagrammatically the present organization of services for the subnormal; the figures apply to the Birmingham population at the beginning of 1965. At that time there were under the health authority 116 children and 20 adults waiting for admission to hospital, and under the education authority 29 children needing admission to E.S.N. residential schools. Places were required for a further 133 children in E.S.N. day schools.

Fig. 2 shows the arrangements which would result from the proposed redistribution of responsibilities. The patients in

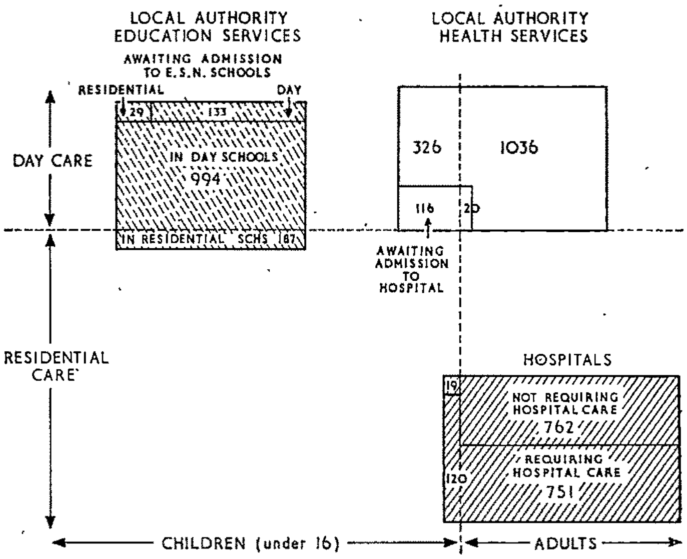


FIG. 1.—Diagram showing existing responsibilities for the subnormal. Birmingham, 1965.

hospital who need no medical or nursing care would be transferred for residential care to health or welfare departments (762 adults) or to the education department (19 children). In return the hospitals would receive the 116 children and 20 adults for whom admission was needed. E.S.N. residential and day schools are shown expanded to accommodate the children on their waiting-lists. Finally the remaining 326 children under the health authority in 1965 would be transferred to the education authority.

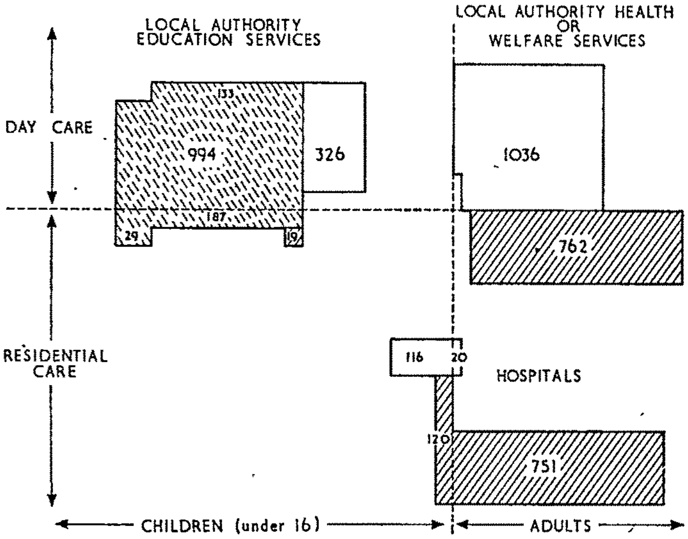


FIG. 2.—Diagram showing a proposed redistribution of responsibilities for the subnormal.

The last is possibly a controversial suggestion which is perhaps not essential to the present proposals. Such children have had advantages from being under the health department, and there is undoubtedly some risk that because of their relatively low potential for education they might be less well cared for under an education authority. Certainly the small number of children who can be kept at home in spite of substantial medical and nursing needs are best under the health department. But for most subnormal children living at home the main requirement is for education and training services, and we share the view expressed in a recent publication of the British Psychological Society (1966) that these services should be the responsibility of local education authorities. In Birmingham administration of the junior training centres has already been delegated by the health department to the education authority.

Hospital Care

We have seen that restriction of responsibility to patients "who require special or continuous nursing and . . . who, because of unstable behaviour, need the kind of supervision and control provided by a hospital" would reduce the hospital population of the subnormal to about half its present size. The way would then be open for reappraisal of the organization of hospital services, and particularly for consideration of the relation between subnormality hospitals and others.

As in the case of the mentally ill and chronic sick, it has been assumed hitherto that the subnormal should be segregated. This segregation results from historical circumstances and has had serious disadvantages which may be summarized as follows:

Heterogeneity of Patients.—Like other types of hospital patients, the mentally subnormal vary greatly in their medical, nursing, and social needs. Indeed they are the most heterogeneous of all hospital patients, since approximately half do not require medical and nursing services and should not be regarded as a medical responsibility.

Staffing Difficulties.—We have already referred to the formidable difficulty of providing staff, particularly professional staff. Again, as in the experience of mental and chronic hospitals, nurses and doctors cannot be attracted in sufficient numbers to institutions isolated from the main stream of professional interest. The problems which result from this isolation have been discussed fully and critically by Pilkington (1966). He refers not only to the effect of isolation on recruitment but also to its influence on the attitude of existing staff.

Excessive Hospital Size.—Though a good case can be made for large hospitals which receive all types of patients, they have serious disadvantages when their work is confined to a single class such as the mentally subnormal. Yet because of staffing and other difficulties in isolated institutions, concentration of patients is almost inevitable, and mental subnormality hospitals may have 1,000 or even 2,000 beds. The problem is aggravated by a number of administrative anomalies—for example, the linking of salary scales to bed numbers—which discourages discharge of patients and reduction of hospital size (Pilkington, 1966).

Lack of Research in Mental Subnormality.—In recent years there has been some increase in interest in the field of mental subnormality, but the pace of investigation is still very slow in relation to the size and variety of the problems. The remoteness of the hospitals from research centres, and particularly from teaching hospitals, undoubtedly contributes powerfully to this neglect. Indeed it seems unlikely that mental subnormality can receive the attention that is needed so long as the vast majority of hospital patients are in institutions rarely visited by research workers.

Costliness of an Adequate Service.—It could hardly be said that investment in the care of the mentally subnormal has been excessive, but the low cost has resulted from an inadequate rather than an economical service. If the level of care were raised to the standard now taken for granted in acute hospitals the cost in the existing segregated hospitals would undoubtedly be very considerable; for it would be necessary to reproduce laboratory and treatment services which already exist in other hospitals, but which cannot be used by the mentally subnormal so long as they are isolated.

These undesirable consequences of isolation point clearly to the need to unite mental subnormality and other types of hospitals. So long as the patients include large numbers who require no medical or nursing care, and so long as other hospitals—mental, chronic, and acute—are dispersed, this proposal is unrealistic. But if responsibility is restricted to patients needing medical and nursing care, and if major centres are designed for all other types of hospital work within a balanced hospital community (McKeown, 1958), it will be desirable to include provision for the mentally subnormal. In this way, and probably only in this way, will it be possible to raise the standard of their care to an acceptable level.

At least two objections will be raised to this proposal. It will be said that it would be unnecessarily expensive to care at a common hospital centre for patients whose medical and nursing needs are mainly basic nursing and psychiatric supervision. In reply we would say that while provision for the mentally subnormal, as for chronic and psychiatric patients, would be costly in the expensive wards of the traditional acute hospital, there is no reason why it should be so in appropriately designed facilities within a balanced hospital. Moreover, cost is not the only consideration, since history has shown that a satisfactory service cannot be provided in isolated institutions.

The other likely objection is that the number of beds required for the mentally subnormal is too large to be acceptable at a common site such as a district general hospital would offer. Some people are doubtful about the advisability of including all psychiatric patients, on the grounds that 175–350 beds (according to the optimism of the estimate) per 100,000 of population would create an imbalance between psychiatry and other services. The proposal to add a further 80 beds per 100,000 (the number suggested by our results) is certain to be resisted for the same reason.

These objections are rooted in a traditional view of hospital work in which the centre of interest is the patient with acute physical illness, and other types of patients—the majority—take a secondary place. The number of beds required for psychiatric and mentally subnormal patients is large because they comprise a considerable part of the total hospital population; and with the continued decline of acute illness their contribution, together with that of the aged sick, will be even larger. Medical research has not yet been very successful in unravelling the nature of these problems, and many patients still require prolonged care. But this is not a reason for accepting an inferior standard of care, and given well-designed services there are no financial or other grounds for not admitting all types of patients, including the mentally subnormal, at the same hospital centre in approximately the proportions in which they are found in the general population.

Summary

Investigation of the medical, nursing, and social needs of all Birmingham patients (1,652) in hospitals for the subnormal showed that only about half needed the kind of care—mainly basic nursing and psychiatric supervision—which made it necessary for them to be in hospital. The other half of the patients required training and occupation—both inadequately provided in hospital—in a sheltered environment with, in some cases, simple personal attention described as checking and counselling.

In accord with the recommendations of HM(65)104, it is suggested that hospital responsibility should be restricted to patients needing medical and nursing care and that the remainder should be transferred to local health, welfare, and education authorities. The reduction in the number of mentally subnormal patients in hospital would make it possible to care for them with all other hospital patients at a common centre. Only in this way will it be possible to focus research interest on the problems of the subnormal and to raise the standard of their care to an acceptable level.

For collaboration in the assessment of patients' needs we are indebted to the medical superintendents (Drs. R. A. Browne, A. P. Buchan, T. Crowley, A. S. Patterson, and R. J. Stanley) and staffs of the mental subnormality hospitals in the Birmingham Region. Dr. Stanley also provided valuable advice about the organization of the inquiry and the interpretation of its results. The data were collected and analysed with the help of Dr. W. L. Gordon, Miss Ida Giles, and Mrs. Betty Mann. National statistics relating to patients in mental subnormality hospitals were made available by Miss E. M. Brooke, of the Ministry of Health. Finally we should like to express our indebtedness to Dr. T. L. Pilkington for giving us the results of his investigation and for his helpful comments on our own.

REFERENCES

British Psychological Society (1966). *Children in Hospitals for the Subnormal.* London.
Heaton-Ward, W. A. (1967). *Brit. med. J.*, 1, 234.
Leck, I., Gordon, W. L., and McKeown, T. (1967). *Brit. J. prev. soc. Med.*, 21, 115.
McKeown, T. (1958). *Lancet*, 1, 701.
Pilkington, T. L. (1966). In *Report of the Annual Conference of the National Association for Mental Health*, p. 50. London.

Clinical Application of Demand Pacemakers

EDGAR SOWTON,* M.D., M.R.C.P.

Brit. med. J., 1967, 3, 576–578

Treatment of patients with chronic complete heart block by artificial pacemakers reduces the one-year mortality from approximately 40% to approximately 17% (Sowton, 1967), and with modern techniques and apparatus the morbidity is now low. Parsonnet, Gilbert, and Zucker (1966) reported that after the first few months have been successfully negotiated there is a high probability that one or two uneventful years of stable pacing will follow, and Chardack, Gage, Federico, Schimert, and Greatbatch (1966) claim a better than 90% chance that any individual patient will experience uninterrupted pacing for at least 18 months.

One problem found with patients treated by fixed-rate pacemakers is that sinus rhythm may return, so that competition occurs between natural and artificial pacemakers. This leads to an irregular ventricular rate, palpitations, variations in systemic pressure which occasionally cause symptoms, and the possibility of dangerous arrhythmias provoked by pacemaker stimuli falling in the vulnerable period of the cardiac cycle (Sowton, 1965). These risks are especially important when short-term pacing is carried out in patients with temporary heart block following cardiac infarction (Harris and Bluestone, 1966), because the threshold for arrhythmias is considerably lower than normal and the chances of sinus rhythm returning are considerably higher.

Competition can be avoided by the use of a pacemaker which automatically detects any spontaneous activity and cannot deliver a stimulus until a preset interval has elapsed: such pacemakers are referred to as "demand," "standby," "ventricular-inhibited," or "R-top" units. A pacemaker capable of functioning in this way was described as early as 1956 (Leatham, Cook, and Davies, 1956), and several other external demand units have been described more recently (Nicks, Stening, and Hulme, 1962; Zacouto, 1963; Lemberg, Castellanos, and Berkovits, 1965). Completely implanted demand pacemakers have also been produced, but experience is still limited. Chardack *et al.* (1966) have reported successful results in animal experiments with a Medtronic unit and have implanted similar units in patients (personal communication, 1967). Experience in animals with American Optical miniaturized demand units has been reported by Goetz, Dormandy, and Berkovits (1966), and these units have been used externally in patients; a very few of these pacemakers have also been completely implanted (Berkovits, personal communication, 1967). Most experience under clinical conditions with fully implanted units in patients has probably been gained with the Cordis Ventricor II Standby pacemaker, and Parsonnet, Zucker, Gilbert, and Myers (1966) have reported successful results for periods of over a year. In the present paper some of the clinical experience at the National Heart Hospital and Institute of Cardiology with various types of demand pacemakers is described.

Material and Methods.—The patients were all treated at the National Heart Hospital, initially as inpatients and subsequently followed in the pacemaker clinic. All had had complete heart

---

* Institute of Cardiology and National Heart Hospital, London W.1.

block at some period and all those treated with long-term pacing had a history of Stokes–Adams attacks. The results are best considered in two groups.

Short-term Demand Pacing

Six patients were paced in this way for periods of up to 21 days because of acute block following cardiac infarction, and 15 patients were paced for periods of up to 16 days as a preliminary measure before long-term pacing. Temporary external units have been mainly of two types. Most patients were treated with the commercially available version of the pacemaker designed by Davies (Leatham *et al.*, 1956) in which the E.C.G. input is obtained from ordinary limb leads. More recently a pacemaker designed and built at the Institute of Cardiology has been employed (Norman and Obeyesekera, 1967; Sowton and Norman, 1967). A few patients were also paced with American Optical monitor pacemakers, Model 10750, which incorporate a demand pacemaker.

A large number of measurements of the R wave detected from different transvenous electrodes in the right ventricle have now been made and indicate the amplitude ranges from 2 millivolts to above 30 millivolts under different conditions: even higher values may be found with intramural leads. Since the amplitudes recorded from transvenous electrodes were usually more than 5 millivolts, it is apparent that demand pacemakers should be inhibited by an input signal of about 1.0 millivolts, and this level has proved satisfactory in practice. The rate of rise of the R wave is also important and maximum sensitivity of this pacemaker is achieved at a frequency of 30 cycles/sec.

In all patients competition was completely avoided with each of the three types of external pacemaker. Stable pacing was achieved with each of the three units and there was no detected incidence of failure to pace when the preset time interval following an R wave was exceeded.

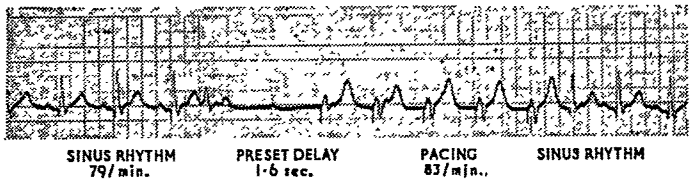


Fig. 1.—On-demand pacing. E.C.G. from a patient with intermittent heart block. After 1.6 seconds asystole pacing automatically starts but the pacemaker is again inhibited by the return of sinus rhythm.

With the Davies pacemaker the interval following an R wave before pacing begins can be adjusted within wide limits, and this interval is independent of the stimulation rate; Fig. 1 illustrates a typical E.C.G. obtained from a patient being paced with this apparatus. There are several features of this pacemaker which are not in keeping with modern techniques, notably the use of a relay in the circuit and the need for skin-contact electrodes to detect the E.C.G., but in our experience it has proved reliable and has been in clinical use until recently.

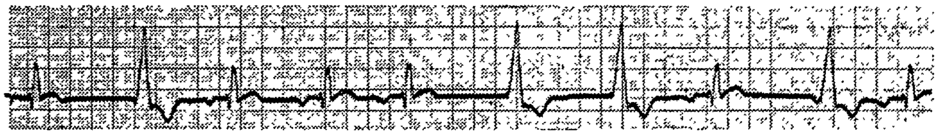


Fig. 3—E.C.G. obtained with Institute of Cardiology demand pacemaker. The pacing stimuli are provided as necessary to prevent the heart rate falling below 60 beats per minute.

The American Optical demand pacemaker also suffered from the disadvantage that skin-contact E.C.G. electrodes are used to detect spontaneous cardiac activity; movement of the patient may produce artifacts which inhibit the pacemaker, and there is the possibility that displacement of one E.C.G. pick-up electrode resulting in loss of the input signal allows the pacemaker to stimulate and produce competition. Apart from this disadvantage, however, the pacemaker functions satisfactorily.

The Institute of Cardiology demand pacemaker also has a control which adjusts the interval following a spontaneous R wave before pacing impulse is delivered; in this pacemaker this interval is not independent of the pacing rate, so that a simple control determines the minimum ventricular rate below which the pacemaker stimulates. The pacemaker itself (Fig. 2) detects spontaneous cardiac activity via the right ventricular transvenous electrode, which is also used for stimulating, and so avoids the complexity associated with E.C.G. limb leads. The pacemaker has proved extremely simple in use; all that is necessary is for the rate control to be set to the minimum acceptable ventricular rate. If the spontaneous rate is above this level the pacemaker is completely inhibited, but if the spontaneous rate falls below the minimum then the pacemaker provides such stimuli as are necessary to maintain the rate at this minimum level. A typical E.C.G. recorded with this pacemaker is shown in Fig. 3.

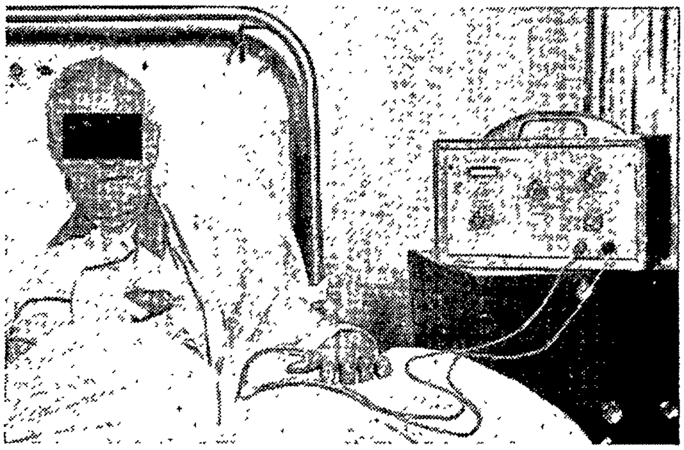

[redacted]

Fig. 2.—Institute of Cardiology demand pacemaker in use. Spontaneous cardiac activity is monitored via the same electrode used for pacing.

Long-term Demand Pacing

Seven patients have been treated with fully implanted demand pacemakers for periods of up to 10 months. Two types of implantable demand pacemakers have been used, in each case detecting the spontaneous R wave and stimulating the heart through a right ventricular transvenous electrode. In five cases the pacemaker was a Cordis Ventricor II and in two cases a Medtronic demand pacemaker. Two prototype miniaturized demand pacemakers produced in the medical physics department of the University of Groningen, Holland, were also used in six patients for periods of up to 10 days; these were attached to transvenous electrodes but were carried externally.

Both types of implanted pacemakers have performed satisfactorily and competition has been avoided in all patients. The time interval which must elapse before a stimulus is produced is such that the minimum ventricular rate is 70/min. with the Ventricor II and the Groningen University pacemakers and 60/min. with the Medtronic. Spontaneous sinus rates in these patients occasionally fell below these levels, particularly during sleep, so that paced activity occurred from time to time apart from development of transient heart block. In no case did this result in competition or unpleasant symptoms, though the patients were able to recognize that a particular ventricular beat was paced rather than spontaneous; they were presumably able to make the distinction because of the longer diastolic pause before the first paced beat and also because the paced beat was not preceded by a suitably placed atrial contraction and consequently resulted in a smaller stroke volume and a reduced systolic blood pressure.

During periods of normal sinus rhythm an implanted demand pacemaker is inhibited and normal E.C.G. records therefore give no indication of its presence. The Groningen University model contains a magnetically operated switch which bypasses the demand facility, so that the unit temporarily operates as a conventional fixed-rate pacemaker; application of an external magnet over the pacemaker during E.C.G. recording thus enables a check to be made that the pacemaker is functional. A similar switch is incorporated in some of the American Optical pacemakers used by Goetz *et al.* (1966), but the Cordis and Medtronic units used in these patients do not have this feature. The function of these pacemakers can be checked by manœuvres which slow the heart below the inhibiting rate so that the pacemaker begins to stimulate. Carotid sinus massage was usually adequate in the cases described here, but occassionally a slow injection of 2–10 mg. of Tensilon (edrophonium chloride) was needed; this produced transient slowing and allowed the pacemaker to function for two or three beats. The ideal dose of edrophonium is that which does not quite slow the heart beneath the inhibiting rate for the pacemaker, so that carotid sinus massage can be used in addition to produce an R–R interval which will cause the pacemaker to stimulate.

Discussion

Competition can occur only when significant non-paced cardiac activity is present in a patient with a fixed-rate pacemaker. The major risk of competition is that a pacemaker stimulus falling during the vulnerable period may provoke fatal ventricular fibrillation, and this is most likely to occur when the cardiac threshold for ventricular fibrillation is unduly low. This situation arises when the patient has been given cardiotoxic drugs or has some condition such as acute myocarditis or recent ischaemic damage. The dangers of pacemaker-induced ventricular fibrillation are particularly great after cardiac infarction and in the immediate postoperative phase after the surgical implantation of a pacemaker with attachment of electrodes to the myocardium (Sowton, 1965).

About 25% of all patients with complete heart block who are considered for long-term artificial pacing return to sinus rhythm, at least for short periods, and, as probably 12,500 patients in Britain have chronic complete heart block, there are about 3,000 patients with intermittent block. About two-thirds of these patients may be expected to suffer from Stokes–Adams attacks, and this suggests that artificial pacing is at present indicated for some 8,000 patients in the British Isles, of whom 2,000 should be treated with demand pacemakers. Unfortunately there is no known way to distinguish patients who may return to sinus rhythm once pacing has started, and so there is a case for treating all patients in need of long-term pacing with demand pacemakers as soon as it has been demonstrated that these units are at least as reliable as the simpler fixed-rate type. It should be noted that both atrial-triggered and ventricular-triggered pacemakers also function as demand pacemakers when necessary, but these units are outside the scope of the present paper.

Demand pacemakers are more complicated than simple fixed-rate units, but the implanted types used in the present study are based on the well-proved circuits of the standard Cordis and Medtronic pacemakers. Much of the manufacturing technique and accumulated experience obtained with standard pacemakers has been incorporated in the production of these demand units, in addition to the similarities of much of the circuitry. Since each of the basic pacemakers concerned has a good reputation for reliability, a lifetime of two years for the implantable demand units does not seem unrealistic; however, until actual experience with a large number of units under clinical conditions over this period of time has been obtained, reliability figures must remain hypothetical. Early versions of implantable demand pacemakers have proved unduly sensitive to interference from external electrical fields and several changes in design have been recently introduced to overcome this problem. In none of the cases described here have the patients noted any symptoms related to external interference with pacemaker function, but until wider experience is available it seems wise for implanted demand pacemakers to be used only at hospitals which possess the necessary electronic and medical experience to carry out frequent follow-up checks on the patients. The external demand units currently available have proved very reliable, and it is recommended that they be used in preference to fixed-rate pacemakers in all patients when the threshold for ventricular fibrillation is low.

Summary and Conclusions

Demand pacemakers which do not stimulate during spontaneous cardiac activity are theoretically indicated for all patients treated with short-term pacing and for many patients needing long-term pacing.

A demand pacemaker for short-term pacing has been developed and shown to be clinically reliable. The stimulating electrode is also used as an intracardiac E.C.G. lead to monitor spontaneous activity.

Twenty-one patients have been treated for periods of up to 21 days with external demand pacemakers connected to transvenous right ventricular electrodes.

Seven patients have been treated with fully implanted demand pacemakers for periods of up to 10 months. If these units prove to be reliable over longer periods demand pacemakers should be used for most patients at present treated with conventional fixed-rate units.

REFERENCES

Chardack, W. M., Gage, A. A. Federico, A. J., Schimert, G., and Greatbatch, W. (1966). *Progr. cardiovasc. Dis.*, **9**, 105.
Goetz, R. H., Dormandy, J. A., and Berkovits, B. (1966). *Lancet*, **2**, 599.
Harris, A., and Bluestone, R. (1966). *Brit. Heart J.*, **28**, 631.
Leatham, A., Cook, P., and Davies, J. G. (1956). *Lancet*, **2**, 1185.
Lemberg, L., Castellanos, A., jun., and Berkovits, B. V. (1965). *J. Amer. med. Ass.*, **191**, 12.
Nicks, R., Stening, G. F. H., and Hulme, E. C. (1962). *Med. J. Aust.*, **2**, 857.
Norman, J., and Obeyesekera, P. (1967). Unpublished.
Parsonnet, V., Gilbert, L., and Zucker, I. R. (1966). *Ann. thorac. Surg.*, **2**, 561.
—— Zucker, I. R., Gilbert, L., and Myers, G. H. (1966). *J. Amer. med. Ass.*, **196**, 784.
Sowton, E. (1965). *Brit. Heart J.*, **27**, 311.
—— (1967). *Mod. Conc. cardiovasc. Dis.*, **36**, 31.
—— and Norman, J. (1967). *Wld med. Electron.* In press.
Zacouto, F. (1963). *Arch. Mal. Cœur.*, **56**, 1296.

Diagnosis of Phenylketonuria (Phenylalanine Hydroxylase Deficiency, Temporary and Permanent)*

J. B. P. STEPHENSON,† M.A., B.M., M.R.C.P., D.C.H.; M. S. McBEAN,‡ M.B., B.S.

Brit. med. J., 1967, 3, 579–581

It is becoming evident that the diagnosis of classical phenylketonuria cannot always be made with certainty before it is judged necessary to prescribe a low-phenylalanine diet (Schneider and Garrard, 1966; Berry and Wright, 1967). If the diagnosis remains uncertain the results of dietary treatment cannot be properly assessed, and there remains the unwelcome possibility that harm may be done by depriving normal children of phenylalanine (Bessman, 1966). This paper reports a striking case of temporary phenylalanine hydroxylase deficiency as an illustration of the problems involved. Later we sought evidence of persisting phenylalanine hydroxylase deficiency in a group of children who have received low-phenylalanine diet. The results of treatment of these children are described elsewhere (McBean and Stephenson, 1967).

Methods

Serum phenylalanine (and tyrosine) was estimated by the snake venom L-amino-acid oxidase method of La Du and Michael (1960) or as modified by Henry (1964), except where indicated in the text. Blood phenylalanine was estimated by the Guthrie test (Guthrie and Susi, 1963). Urine phenylpyruvic acid: standard qualitative ferric chloride and Phenistix tests (Woolf, 1963) graded 1+ to 3+ (slight to strong). Urine orthohydroxyphenylacetic acid: one-dimensional paper chromatography.

Psychometric tests: Griffiths quotients (G.Q.) and Stanford Binet Form L-M intelligence quotients were measured by psychologists of the department of child psychiatry.

Phenylalanine Hydroxylase Deficiency of Early Infancy (Temporary "Phenylketonuria"): Case Report

The patient, date of birth 2 June 1966, was the second male child of unrelated parents. He was delivered by elective caesarean section at term because of previous obstetrical difficulties. Birth weight 3.04 kg. He was fed on National Dried Milk from 3 June and was slightly jaundiced during his first week. Hyperphenylalaninaemia was demonstrated by routine Guthrie test at the age of 5 days.

Investigations.—7 June—Guthrie test: blood phenylalanine 12 mg./100 ml. Urine: tyrosyluria. 20 June—Guthrie test: blood phenylalanine 50 mg./100 ml. 27 June—Urine: orthohydroxyphenylacetic acid present; no tyrosyluria. 30 June—Guthrie test: blood phenylalanine 40 mg./100 ml. 5 July—Urine: $FeCl_3$ 3+; Phenistix 2+. Serum phenylalanine 32.6 mg./100 ml. Serum tyrosine 3.0 mg./100 ml.

On 5 July, when he was clinically normal and weighed 3.4 kg., he was started on low phenylalanine diet (Minafen, cow's milk, Ketovite syrup, and blackcurrant syrup). His progress is summarized in Table I.

After the first month of treatment the serum phenylalanine did not rise above 2 mg./100 ml., but he maintained a steady weight gain. During the second month of treatment he suffered a series of convulsions (not hypoglycaemic) and developed hypochromic anaemia with normal serum iron. Despite progressive increase in phenylalanine intake up to 116 mg./kg./day his serum phenylalanine did not rise to 3 mg./100 ml. The diagnosis of phenylketonuria was therefore questioned, and normal milk diet was offered after four months of restricted phenylalanine. Nonfasting serum phenylalanine levels rose only slightly above normal, but orthohydroxyphenylacetic acid was detected in the urine at this time. During the following three months no phenylpyruvic acid was detected in the urine.

TABLE I.—*Progress of Temporary "Phenylketonuric" on Low-phenylalanine Diet*

Age in months	Month of Diet	Phenylalanine Intake/Day mg.	Phenylalanine Intake/Day mg./kg.	Serum Phenylalanine (mg./100 ml.)	Fe Cl_3	OHPAA*	G.Q.†	Clinical Impression
1		1,000	300	32·6	+	+		Normal
2	1	280	64	0·0–2·8				
3	2	350	60	0·5–1·0				Convulsions. Anaemia
4	3	470	70–78	0·0–2·0				
5	4	470–870	64–116	1·8–2·0				
6		1,500	200	3·1–4·0		+	62	
7		Unrestricted diet		0·8 (fasting)			72	Plump. Sociable. Probably retarded

* Orthohydroxyphenylacetic acid.
† Griffiths quotient.

On 20 January 1967 an oral phenylalanine tolerance test was carried out, with 100 mg. of L-phenylalanine per kg. body weight, administered by gavage (Table II). Serum estimations were made in duplicate.

TABLE II.—*Phenylalanine Tolerance Test on Patient Aged* 33 *Weeks.* L-*phenylalanine* 100 *mg./kg. by Gavage at Zero Time*

Time	Serum Phenylalanine mg./100 ml.)	Serum Tyrosine (mg./100 ml.)	Urine OHPAA
Fasting	0·8	1·1	None
1 hour	3·4	1·2	
2 hours	3·6	2·5	
3 "	2·3	1·8	Very faint trace
4 "	2·1	1·4	

Comment

The fasting serum phenylalanine was unequivocally normal and the rise in serum tyrosine after phenylalanine loading confirmed the presence of phenylalanine hydroxylase activity. The diagnosis of classical phenylketonuria was therefore excluded.

At the time of writing the child was 8 months old, well nourished, and socially responsive, but the clinical impression of a degree of psychomotor retardation was supported by psychometric tests (Table I).

The child's parents have normal serum phenylalanine levels, but their genotype has not yet been established.

Reassessment of Presumptive Phenylketonurics

The recognition of temporary "phenylketonuria" prompted a review of the diagnosis of other presumptive phenylketonurics.

---

* From the University Department of Child Health and the Royal Hospital for Sick Children, Glasgow.
† Registrar in Medical Paediatrics, Royal Hospital for Sick Children, Glasgow C.4.
‡ Research Assistant, Royal Hospital for Sick Children, Glasgow C.4.

In this report we include only those children who have received low-phenylalanine diet and have been studied until after their first birthday (McBean and Stephenson, 1967). Because of this minimum follow-up period cases detected by mass neonatal screening by the Guthrie test are not included, nor are infants who have removed to other districts. Table III shows the clinical features of those infants detected in the first three months of life.

TABLE III.—*Infants Detected in First Three Months: Clinical Features*

Case No.	Sib. with PKU	Clinical Features Before Treatment					I.Q. <80 After 1 Year (lowest)
		Vomiting	Eczema	Retardation	Convulsions	Others	
1	Yes						
2	„						+(73)
3	„					"Looks like sib with PKU" (mother)	
4*		+				Pyloric stenosis	+(73)
5†			+	+			+(79)
6*						Anorexia. Screaming. Thrush. Pyuria	
7†			+		+		
8†				+			

* Presented with symptoms.
† Detected by napkin-Phenistix screening test.
PKU ≙ Phenylketouria.

Partington (1961) has stressed the frequency of early symptoms in phenylketonuria (vomiting, feeding problems, colic, ? pyloric stenosis, irritability, eczema and other rashes, suspected retardation, and, later, seizures). It is evident that none are specific, but it may be that such symptoms will be found to be more frequent in true phenylketonurics. Certainly in two of these patients the symptoms were valuable in bringing the child to hospital at an early age. Routine urine testing then revealed the diagnosis. Case 4 was detected in this way in January 1961, after pyloromyotomy (for marked hypertrophic pyloric stenosis). The other infants were detected either because an older sibling was known to have classical phenylketonuria or through routine napkin-Phenistix testing by the local health authorities (Stephenson and McBean, 1967).

Table IV gives some of the biochemical findings. The degree of positivity of the Phenistix reaction on fresh urine is recorded in preference to the ferric chloride reaction because it is more easily defined. In all cases the unacidified urine also gave a typical green colour with aqueous ferric chloride (Woolf, 1963).

TABLE IV.—*Infants Detected in First Three Months: Biochemical Features*

Case No.	Age at Test (days)	Biochemical Features Before Treatment		Highest Serum Phenylalanine After One Year (mg./100 ml.)
		Urine Phenistix	Serum Phenylalanine (mg./100 ml.)	
1	11	+ + +	30·0*	25·2
2	20	+ + +	65·0	50§
3	26	+ + +	57·4	20·0
4	47	$FeCl_3$ 3+	37·1†	34·0
5	59	+ + +	69·0	22·6
6	82	+ + +	30·0*‡	23·0
7	77	+ + +	70·2	66·2
8	82	+ + +	60·6	> 20§

* Chromatographic method (Berry, 1957).
† Five days after pyloromyotomy.
‡ Four days after diet started.
§ Guthrie inhibition assay.

It is evident that all these children, including those who were asymptomatic, have a persisting tendency to hyperphenylalaninaemia. In three (Cases 1, 6, and 7) dietary control has been excellent since early infancy, but at ages 3½, 4½, and 2 years, respectively, hyperphenylalaninaemia was induced by feeding a normal phenylalanine diet for a few days. (Complan was substituted for Cymogran for this test. The use of ordinary foodstuffs for such a trial is contraindicated in case the phenylketonuric child loses his taste for the low-phenylalanine diet.) In the remaining five cases[1] the high serum phenylalanine levels resulted from dietary indiscretions (excess phenylalanine intake).

The older patients (Cases 11–33), detected at age 6 months to 10 years, all gave evidence of permanent enzyme defect. In Cases 11–30 this was demonstrated by hyperphenylalaninaemia over the age of 1 year. Three earlier cases (Nos. 31–33), with severe mental retardation, did not have serum phenylalanine estimations, but two of them had typical phenylketonuric siblings, and the urine of the third contained phenylpyruvic acid, which disappeared during low-phenylalanine diet. In all cases the urine gave a typical positive reaction with ferric chloride, and the initial I.Q. was always below 80. Table V shows the distribution of serum phenylalanine levels, which tend to be lower than in the young infants.

TABLE V.—*Distribution of Serum Phenylalanine Levels in Phenylketonurics Diagnosed Age 6 Months to 10 Years (Cases 11–33)*

Serum Phenylalanine	No. of Children
Under 20 mg./100 ml.	1*
20— „	5
30— „	9
40— „	2
50— „	3
Not known	3

* 18 mg./100 ml. at age 10½ years.

No attempt was made to assess the likely genotype of these children by testing their parents, but the course in all cases suggests the diagnosis of homozygous phenylketonuria.

Discussion

When infant screening was introduced it was assumed that the new-found phenylketonurics would be differentiated from the remainder of the population as sharply as was the case in older children and adults. There is now increasing concern about the validity of this assumption (Bessman, 1966; Schneider and Garrard, 1966; Perry *et al.*, 1967; Berry and Wright, 1967). In the first place, it may be that the biochemical abnormalities of heterozygotes for the usual gene of phenylketonuria overlap with those found in (homozygous) phenylketonurics, making definitive diagnosis in the asymptomatic neonate impossible (Schneider and Garrard, 1966). Secondly, and perhaps more important, there might be delayed maturation of the enzyme phenylalanine hydroxylase even in infants of normal genotype. We have presented evidence to show that the infant whose case is described above had just this disorder. Until treatment was started in the fifth week of life he had the biochemical syndrome of severe phenylalanine hydroxylase deficiency (serum phenylalanine over 30 mg./100 ml., with urine phenylpyruvic acid and orthohydroxyphenylacetic acid), but by the age of 5 months his phenylalanine tolerance was normal. Indeed, the results of his fasting serum estimations (Perry *et al.*, 1967) and tolerance test (Hsia *et al.*, 1956) suggest that he is unlikely even to be heterozygous for the usual gene of phenylketonuria, irrespective of the probable genotype of his parents.

We may speculate briefly on the probable sequence of events in this case. Originally he had tyrosyluria, and could be classed as the type 2 phenylalaninaemia of Berry and Wright (1967), with presumptive deficiency of both phenylalanine hydroxylase and parahydroxyphenylpyruvic oxidase systems. The two enzyme systems then matured at different rates, parahydroxyphenylpyruvic oxidase rising to normal some weeks before phenylalanine hydroxylase. In our reassessment of presumptive phenylketonurics we have found no further cases of temporary enzyme deficiency, but the report of the Cincinnati conference on the treatment of phenylketonuria (Berry and Wright, 1967) suggests that milder examples may not be rare.

---

[1] Cases 9 and 10 are not described: follow-up details are not available.

A probable instance was reported by Moncrieff and Wilkinson (1961), though at the time of diagnosis the method for serum phenylalanine was not yet entirely satisfactory.

The effect of a low-phenylalanine diet on our case of temporary phenylalanine hydroxylase deficiency is of particular importance. Despite a normal gain in weight throughout treatment, and a phenylalanine intake never below 60 mg./kg./day, serum phenylalanine levels remained persistently low. There is only limited information on the phenylalanine requirements of normal infants, but Snyderman *et al.* (1955) suggest that less than 90 mg./kg./day might be unsafe. This figure was derived in part from observations on the weight gain of infants on differing phenylalanine intakes. However, it may be possible, as in the case described above, for normal weight gain to occur despite phenylalanine deficiency. If so, the optimum phenylalanine intake for a normal child may be much higher than 90 mg./kg./day. The particular concern is that harm might be done to the developing brain by phenylalanine deprivation (Bessman, 1966). There is suggestive evidence that general undernutrition during infancy will inhibit subsequent intellectual development (Stoch and Smythe, 1963), and isolated phenylalanine deficiency might do likewise. This is supported by the delayed psychomotor development in our case and in those reported by Rouse (1966) and Moncrieff and Wilkinson (1961). A fall in developmental quotient may also be seen in phenylalanine-deficient phenylketonuric infants (Brimblecombe *et al.,* 1961, and personal observations). In both the normal and phenylketonuric infants there is a tendency for the developmental quotient to rise after the phenylalanine deficiency is corrected, but the possibility remains that some damage may have been done.

In this somewhat disturbing situation, with no satisfactory criteria for making the diagnosis of phenylketonuria in early infancy, and with the danger of harming normal children by phenylalanine deprivation, some would advocate that the low-phenylalanine diet should not be given (Bessman, 1966). We would strongly oppose this, for the undoubted benefits of treating true phenylketonurics from early infancy would be lost (McBean and Stephenson, 1967). Well-controlled dietary treatment might indeed prevent brain damage even in temporary "phenylketonurics" if transient hyperphenylalaninaemia (and its biochemical consequences) is harmful. Rather one should concentrate on avoiding phenylalanine deficiency, using the strict criteria of Umbarger *et al.* (1965), whose well-controlled patients have a serum phenylalanine of 3 mg./100 ml. or more, no urine orthohydroxylphenylacetic acid, and urine phenylalanine 25–150 μg./ml.

Perhaps initial tyrosyluria may be a common accompaniment of temporary phenylalanine hydroxylase deficiency, as in our case, and may serve as a warning. If during treatment a serum phenylalanine concentration of 3 mg./100 ml. is difficult to sustain, or frequent changes in phenylalanine intake are found to be unnecessary (Umbarger *et al.,* 1965), or one of the parents can be shown not to be heterozygous (Hsia *et al.,* 1956 ; Perry *et al.,* 1967 ; Woolf *et al.,* 1967), then the diagnosis of phenylketonuria must be reconsidered. At the present time we would recommend a diagnostic trial of normal milk intake for young infants, and a substitution of Complan for Cymogran in older children, for a maximum of 10 days, with biochemical monitoring. In conclusion, we emphasize that the diagnostic difficulties and the consequences of error are so great that all suspected cases of phenylketonuria should be referred to special centres.

Summary

Temporary phenylalanine hydroxylase deficiency is described in a child thought to be genetically normal on the basis of his later response to phenylalanine loading. The condition is indistinguishable from phenylketonuria in early infancy, and might remain unrecognized during low-phenylalanine diet. Because it is possible that mental subnormality may result from clinically mild phenylalanine deficiency in such infants, the diagnosis of phenylketonuria should be re-examined when a serum phenylalanine concentration of 3 mg./100 ml. is difficult to sustain or where the genotype of one of the parents is in doubt.

Thirty-one children who had received low-phenylalanine diet were reassessed. Evidence of phenylalanine hydroxylase deficiency persisting beyond the first birthday was obtained in all.

We thank Professor J. H. Hutchison and Dr. R. A. Shanks for advice and criticism ; Dr. L. I. Woolf for orthohydroxyphenylacetic acid estimations ; and Dr. J. S. Stevenson for making available the results of Guthrie tests. Psychological testing was carried out by Mrs. Peggy Emerson and Miss Valerie Labrum.

REFERENCES

Berry, H. K. (1957). *Proc. Soc. exp. Biol. (N.Y.),* **95**, 71.

—— and Wright, S. (1967). *J. Pediat.,* **70**, 142.

Bessman, S. P. (1966). Ibid., **69**, 334.

Brimblecome, F. S. W., Blainey, J. D., Stoneman, M. E. R., and Wood, B. S. B. (1961). *Brit. med. J.,* **2**, 793.

Guthrie, R., and Susi, A. (1963). *Pediatrics,* **32**, 338.

Henry, R. J. (1964). *Clinical Chemistry : Principles and Techniques,* p. 309. New York.

Hsia, D. Y-Y., Driscoll, K. W., Troll, W., and Knox, W. E. (1956). *Nature (Lond.),* **178**, 1239.

La Du, B. N., and Michael, P. J. (1960). *J. Lab. clin. Med.,* **55**, 491.

McBean, M. S., and Stephenson, J. B. P. (1967). *Arch. Dis. Childh.* In press.

Moncrieff, A., and Wilkinson, R. H. (1961). *Brit. med. J.,* **1**, 763.

Partington, M. W. (1961). *Pediatrics,* **27**, 465.

Perry, T. L., Tischler, B., Hansen, S., and MacDougall, L. (1967). *Clin. chim. Acta,* **15**, 47.

Rouse, B. M. (1966) *J. Pediat.,* **69**, 246.

Schneider, A. J., and Garrard, S. D. (1966). *J. Pediat.,* **68**, 704.

Snyderman, S. E., Pratt, E. L., Cheung, M. W., Norton, P., and Holt, L. E., jun. (1955). *J. Nutr.,* **56**, 253.

Stephenson, J. B. P., and McBean, M. S. (1967). *Brit. med. J.,* **3**, 582.

Stoch, M. B., and Smythe, P. M. (1963). *Arch. Dis. Child.,* **38**, 546.

Umbarger, B., Berry, H. K., and Sutherland, B. S. (1965). *J. Amer. med. Ass.,* **193**, 784.

Woolf, L. I. (1963). In *Phenylketonuria,* edited by F. L. Lyman, p. 257. Springfield, Illinois.

—— Cranston, W. I., and Goodwin, B. L. (1967). *Nature (Lond.),* **213**, 882.

Phenylketonuria: A Reassessment of Mass Infant Screening by Napkin Test[*]

J. B. P. STEPHENSON,[†] M.A., B.M., M.R.C.P., D.C.H.; M. S. McBEAN,[‡] M.B., B.S.

Brit. med. J., 1967, **3**, 582

Most local health authorities in Great Britain have used the Phenistix test on wet napkins or diapers (napkin-Phenistix test) to screen all young infants for phenylketonuria (Centerwall *et al.*, 1963). This test is a sensitive and reliable method of detecting phenylpyruvic aciduria (Gibbs and Woolf, 1959; Woolf, 1963), which is an early sign of true phenylketonuria (Allen *et al.*, 1964; Berry and Wright, 1967). Some practical difficulties have been emphasized by Hudson and Ireland (1959), but information is lacking on the effectiveness of the napkin test in mass detection programmes. In the Birmingham screening survey (Boyd, 1961) one case was found out of 18,981 tested, which was thought to be adequate, assuming a regional incidence of one in 20,000 births. In Edinburgh a similar incidence was predicted, but the one expected case was missed (Farquhar *et al.*, 1962).

Present Study

With the assistance of the seven local health authorities involved we have investigated 15 true phenylketonurics (Stephenson and McBean, 1967) who were born when screening programmes were in operation, between 1960 and 1965. Siblings of previously known phenylketonurics have been excluded from the study. The dates and results of napkin tests were determined from the Child Welfare record cards. The details are given in Table I.

TABLE I.—*Phenylketonurics Born into Napkin-Phenistix Screening Programmes*

Phenistix Result		No. of Patients
Positive	Under 3 months old	4 (youngest aged 53 days)
	Over 3 months old	2 (1 aged 9 months; I.Q. 47)
Negative		6 (2 tested under 3 weeks only: 1 in hospital aged 6 weeks)
Not tested		3 (1 ?negative aged 42 days: no record made. 1 only at home aged 5–11 weeks)
Total		15

TABLE II.—*Results of 16 Napkin-Phenistix Tests on 12 Phenylketonurics, Related to Age of Testing*

Age (weeks)	No. of Tests	Results	
		Positive	Negative
1–3	6	–	6
5–10	4	1	3
>10	6	5	1

It is apparent from Table II that all napkin-Phenistix tests in the first three weeks of life were negative, but much more serious is the fact that even in the age group 5–10 weeks only one of four tests was positive.

When the four patients with negative napkin-Phenistix tests over the age of 5 weeks were finally diagnosed they were all obviously affected, and in each case the urine reacted strongly with ferric chloride. Table III shows the serum phenylalanine levels and I.Q. at the time of diagnosis.

TABLE III.—*Missed Phenylketonurics: Finding on Diagnosis*

Age at Negative Napkin Test	Age at Diagnosis (months)	Serum Phenylalanine (mg./100 ml.)*	I.Q.
5 weeks 2 days	9	26	43 (Cattell)
7 „ 1 day	3	70	51 (Griffiths)
9 „ 3 days	25	42	46 „
6 months	24	51	50 „

* La Du and Michael (1960).

Conclusions

This investigation shows that the napkin-Phenistix test in a mass screening programme is not an efficient tool for the early detection of classical phenylketonuria. Even the detection rate of 27% under the age of 3 months is probably optimistic, because cases missed towards the end of the period—for example, 1965—may not yet be obviously retarded, and most of the children at risk have not entered school.

A great deal of enthusiasm, hard work, and organizational skill have gone into the execution of these mass screening programmes, but the time has come for such energies to be directed towards more efficient methods of detection.

This study would have been impossible without the co-operation of the medical officers of the Health Departments of Airdrie, Clackmannan, Clydebank, Falkirk, Glasgow, Motherwell, Paisley, Ealing, and Londonderry. We thank Professor J. H. Hutchison and Dr. R. A. Shanks for encouragement and criticism.

REFERENCES

Allen, R. J., Heffelfinger, J. C., Masutti, M. D., and Tsau, M. U. (1964). *Pediatrics*, **33**, 512.
Berry, H. K., and Wright, S. (1967). *J. Pediat.*, **70**, 142.
Boyd, M. M. M. (1961). *Brit. med. J.*, **1**, 771.
Centerwall, W. R., Berry, H. K., and Woolf, L. I. (1963). In *Phenylketonuria*, edited by F. L. Lyman, p. 117. Springfield, Illinois.
Farquhar, J. W, Kansas, E. T., and Tait, H. P. (1962). *Lancet*, **2**, 498.
Gibbs, N. K., and Woolf, L. I. (1959). *Brit. med. J.*, **2**, 532.
Hudson, F. P., and Ireland, J. (1959). Ibid., **2**, 885.
La Du, B. N., and Michael, P. J. (1960). *J. Lab. clin. Med.*, **55**, 491.
Shephenson, J. B. P., and McBean, M. S. (1967). *Brit. med. J.*, **3**, 579.
Woolf, L. I. (1963). In *Phenylketonuria*, edited by F. L. Lyman, p. 251. Springfield, Illinois.

---

[*] From the University Department of Child Health and the Royal Hospital for Sick Children, Glasgow.

[†] Registrar in Medical Paediatrics, Royal Hospital for Sick Children, Glasgow C.4

[‡] Research Assistant, Royal Hospital for Sick Children, Glasgow C.4.

Detection of Incompetent Perforating Veins by Venography at Operation

JULIAN TOWNSEND,* M.B., B.CHIR., F.R.C.S. ; HUGH JONES,† M.S., F.R.C.S.
J. EDMUND WILLIAMS,‡ B.SC., M.R.C.P.ED., F.F.R.

Brit. med. J., 1967, 3, 583–585

All types of varicose veins can be treated successfully by a radical stripping operation in which the whole system of diseased veins and related perforating veins is removed (Myers, 1957 ; Arenander, 1960 ; Sherman, 1964). Simple procedures such as high ligation, with or without stripping of the main saphenous trunk, though widely practised, are much less successful, even in the early and uncomplicated case. Great saphenous incompetence is usually obvious, and can be convincingly demonstrated by the Brodie–Trendelenburg test. Femoro-saphenous reflux fills the superficial veins with blood at a low pressure only (Cockett, 1956).

Incompetent perforating veins, however, are easy to overlook, and their presence cannot be excluded with certainty by any clinical test. They are present in 90% of cases (Sherman, 1949), and are especially important as a cause of varices which persist or recur after operation (Mathiesen, 1953 ; Lofgren, Myers and Webb, 1956 ; and many others), and as the cause of ulcers. Cockett and Jones (1953) showed that the venous drainage of the lower part of the leg is through short perforating veins to the deep vessels, and only indirectly through the saphenous systems. Thus in this area any superficial venous disease is likely to stem from the perforating vessels, and it is here in the "gaiter-area" that the high intermittent pressures in the deep veins can be transmitted to the surface through incompetent perforating veins, leading to ulceration (Arnoldi, 1966). "Varicose ulceration" due solely to incompetence of superficial veins does not occur, for incompetent perforating veins can be found in association with every venous ulcer (Sarjeant, 1964 ; Arnoldi, 1966 ; Haeger, 1966). It is true that saphenous incompetence may be a contributory cause of ulceration and that ulcers may be healed by removal of the saphenous vein, but the effect is unpredictable and healing often only temporary (Moore, 1957 ; Haeger, personal communication, 1966).

It is sometimes thought that stripping out the saphenous trunk destroys the perforating veins, but Sherman (1949) has shown that about one-half of all perforating veins, and most of the incompetent ones, are not directly connected with the saphenous trunks. Radical stripping operations, though repeatedly shown to be very effective, are not practised by the majority of surgeons, who perhaps feel that the time and trouble required and the trauma to the patient are not justified even by a reasonably certain cure. Another prevalent view, that varicosis is a progressive condition essentially unsuited to radical cure, has some basis in fact, but is founded more on a practice of inadequate diagnosis followed by inadequate surgery.

Preoperative diagnosis of incompetent perforating veins is difficult. Various clinical signs are described but none is reliable. Surgeons experienced in venous disease commonly find at operation incompetent perforating veins which they have not detected previously. The lesser operations which are commonly practised often leave incompetent perforating veins intact, with the attendant risk of persistent or recurrent varices and ulcers. If it were possible to locate incompetent perforating veins accurately and confidently it is probable that they would be ligated more frequently and with greater economy than is now usual, and with improved results. For this reason some methods of venography have been examined and the findings assessed by surgical exploration. A technique of venography has been evolved which with practice is easy to perform, easy to interpret, and reliable.

It is widely held that there is no place for routine venography in the treatment of varicose veins. This is not our experience. Accurate diagnosis leads to precise surgery, and may obviate the need for a formal operation, such as that of Cockett and Jones (1953), in which an incision half the length of the tibia is sometimes made in order to ligate a single incompetent perforating vein, or even without finding one at all (Dodd and Cockett, 1956).

The results of venography were compared with a number of common physical signs, the most useful of which was found to be palpation of fascial defects. We agree with many other writers that the fascial defect lies not in the deep fascia, where a hole is rarely palpable, but in the superficial fascia, where a varix lies at the superficial end of an incompetent perforating vein. All fascial defects and all incompetent perforating veins shown by venography were exposed at operation, and the competence of any perforating vein was tested by the bleed-back test of Turner Warwick (1931).

Method

Before operation the position of the dilated veins was marked on the skin. The leg was then palpated, and all fascial defects were marked, and then labelled with a lead shot secured by adhesive plaster.

The anaesthetized patient was placed on a radiolucent table top, with a 5-degree foot-down tilt. Under aseptic conditions a sternal-puncture needle was inserted horizontally deep into the lower end of the tibia in the position shown in Fig. 1. Injection of a little isotonic saline and the withdrawal of a stream of blood into the syringe confirmed that the needle was correctly placed. Difficulty in making the injection was due to the needle being either too low or not far enough in. With the leg in the anatomical position the *x*-ray tube and film were placed to take an anteroposterior view, with the ankle joint just included at the lower end.

The veins were drained by raising the leg to 30 degrees for 30 seconds. Omission of this step led to excessive dilution of the opaque medium. The leg was lowered and 20 ml. of warm 45% Hypaque (sodium diatrizoate) was injected in 30 seconds. As soon as injection was completed the foot was replaced in the anatomical position and the film exposed. A second film was placed to include the femoral condyles and exposed immediately after gently flexing the foot up and down. The leg was again raised to ensure that no medium remained stagnant in the veins, and any possible risk of thrombosis was avoided.

Interpretation

Incompetence is almost certain when a perforating vein is seen with localized filling of veins at its superficial end, for then

---

* Senior Surgical Registrar.
† Consultant Surgeon.
‡ Consultant Radiologist.
Varicose Vein Clinic, Cardiff Royal Infirmary.

flow must have been outward (Fig. 2, a, b, and c). When several incompetent perforating veins are present there may be dense filling of some superficial veins, and it is then impossible to say whether a given perforator has filled from within or without. An abnormal perforator is enlarged and may be irregular or tortuous superficially ; there may be localized dilatation of the deep or superficial veins at either end of it. A localized superficial varix is a strong indication of the presence of an incompetent perforating vein (Fig. 3, b).

Any medial perforator which fills from within is incompetent, but lateral muscular perforators, which are often large and double, may fill from within yet be competent unless there is also definite filling of overlying superficial veins (Fig. 2, c and d).

When an incompetent perforating vein has been recognized on the *x*-ray film it is not always easy to find the corresponding site on the leg, but by reference to the lead markers it is possible to gauge the level with great accuracy. This information, in conjunction with the skin-markings of varices and fascial defects, is interpreted with reference to the anatomy of the perforating veins, good accounts of which have been given by Sherman (1949) and Sarjeant (1964), and usually allows accurate location of the site of incompetence.

When the radiographic information is considered on its own it is likely to be less valuable than when combined with clinical signs. For this reason it is advised that the surgeon should co-operate in the interpretation of the venograms, especially as he has the opportunity to examine the veins at operation, and so correlate the clinical and radiographic signs with the actual state of the veins.

Anteroposterior views only were used, and proved adequate, firstly because nearly all the clinically important perforating veins lie in the tibial and peroneal groups, which show best in this projection, and secondly because the incompetent posterior muscular perforating veins are easy to recognize clinically.

The method of intraosseous venography does not invariably show the deep veins, and reliable information on these can only be obtained by other techniques.

Results

So far 31 patients have been treated and 46 legs operated on. It is believed that few incompetent perforating veins remained undiscovered, because during the course of the operations many perforating veins were seen by chance at sites other than those under investigation, and all these additional perforating veins appeared normal. Those tested by the method of Turner Warwick (1931) were competent.

The clinical, venographic, and operative findings are shown in the Table.

Results of Exploration at All Sites Where Incompetent Perforating Veins (I.P.V.) Were Diagnosed by Clinical Signs and by Venography

Preoperative Diagnosis		Findings on Exploration		
Diagnostic Procedure Leading to Exploration	No. of Sites	Diagnosis Confirmed (I.P.V. Found)	Diagnosis not Confirmed (No I.P.V. Found)	I.P.V. Found Elsewhere
Clinical signs	112	72	40	32
Venography	109	96	13	8
Total (clinical signs, venography, or both)	156	104	52	Nil

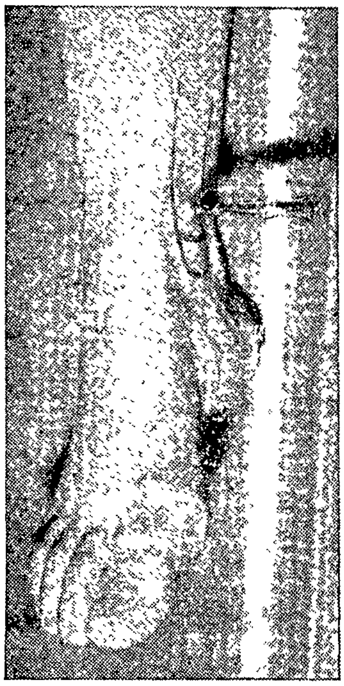


FIG. 1.—The needle is inserted just above the base of the medial malleolus and pushed well in. (A Salah needle, gauge 15 or 12, was used for most of these venograms, but several other types were used.)

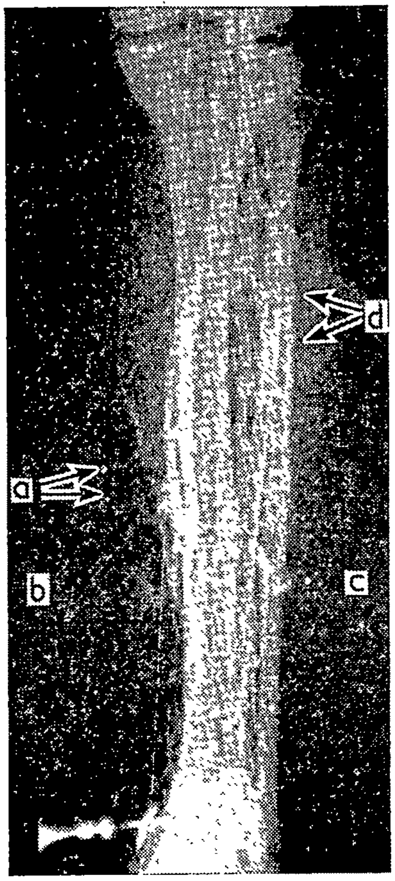


FIG. 2.—a, b, and c, Incompetent perforating veins with filling of overlying superficial veins. d, Paired peroneal muscular veins filling from the deep veins. Note the paired deep calf veins (normal) and paired popliteal veins (variation).

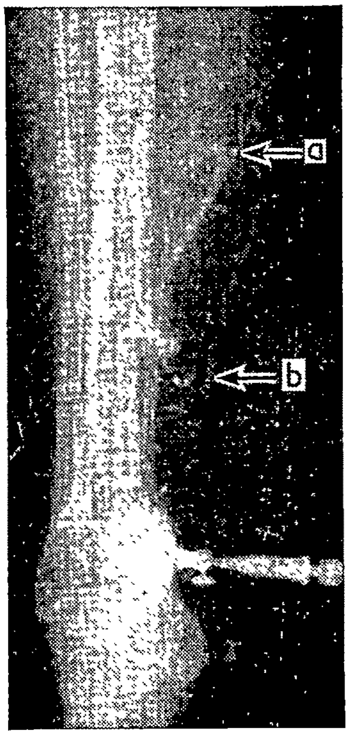


FIG. 3.—a, Fascial defect (with lead marker) seen to be due to superficial varix only. b, Incompetent perforating vein with overlying superficial varix. Note the distance between the fascial defect and the perforating vein.

A total of 104 incompetent perforating veins were found at operation. Clinical signs had detected 72 (69%) of these and missed 32 (31%). A further 40 explorations were made on clinical grounds without any incompetent perforating vein being found. Venograms had detected 96 (92%) of the 104 incompetent perforating veins, but had failed to detect the remaining eight. Another 13 sites were explored because of venographic signs, but no incompetent perforating veins were found.

The distribution of all the incompetent perforating veins found is shown in Fig. 4 and corresponds well with that found by Sherman (1949) in nearly a thousand radical operations.

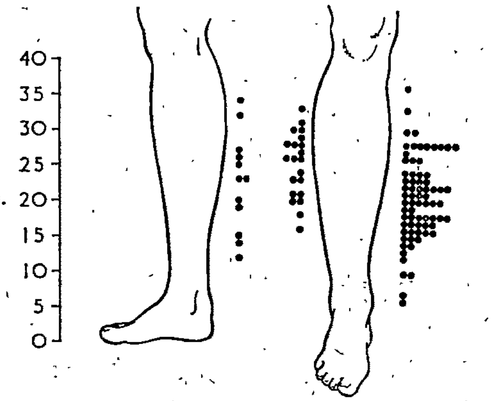


FIG. 4.—Distribution of incompetent perforating veins in 46 legs with varices. The medial group are those lying behind the tibia, the lateral group are closely related to the fibula. The remainder were posterior muscular perforating veins; all of these were detected clinically, but three were not detected by venography. There were no incompetent anterior perforating veins in this group of patients.

Discussion

Intraosseous venograms are easy to interpret because of the lack of superficial venous filling (Fig. 5). We have found the calcaneum a little less satisfactory in this respect than the malleoli. We have also used the lateral malleolus, as recommended by Cockett (1953), but have found that demonstration of the important perforating veins medial to the lower third of the tibia was not always reliable. Injection into the lower tibia has proved better: it is a little more difficult to insert the needle, but satisfactory injection can always be made and films of diagnostic value obtained.

The method described is simple to perform and requires few extra facilities. The whole examination should add less than 10 minutes to the operating-time for bilateral varices. There have been no complications. The precise information obtained is of value in two ways: firstly, the operation can be more comprehensive than when reliance is placed on clinical tests alone, and, secondly, the operation can be planned to minimize the number and extent of the incisions. The technique and interpretation are likely to give difficulty if venography is used only as an occasional procedure to investigate the complex problem, but they become simple with practice.

Even in "primary" long saphenous varices an incompetent perforating vein is often present and may be surprisingly large. Such a vein can easily be ligated through a small incision over it. A variety of cases have been treated, ranging from simple "primary" varices to post-thrombotic ulcers. Venography proved helpful in 36 of the 46 legs and in all types of case. Despite the fact that excision of varices was not practised, very few postoperative injections have been required.

Summary

Incompetent perforating veins are usually present with varicose veins. They are responsible for most of the complications and for some recurrences. They should be obliterated.

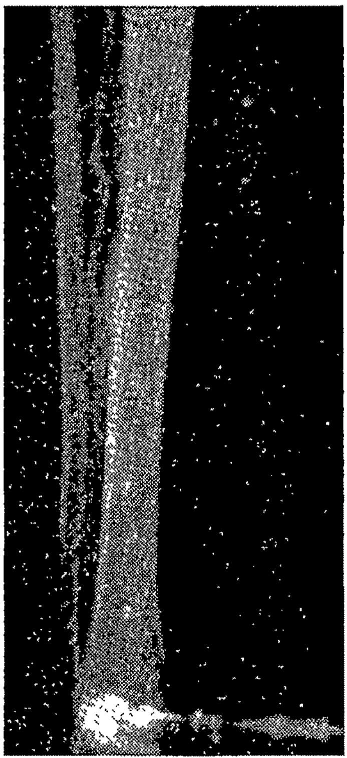


FIG. 5.—No incompetent perforating veins present. The dye passes from the bone marrow to the deep veins, but none escapes into the superficial veins.

A method of operative venography is described which has proved reliable in the detection of incompetent perforating veins and much superior to clinical examination alone.

The information obtained made possible a more comprehensive and more precise operation in three out of every four legs treated.

We thank the radiographers of Cardiff Royal Infirmary and Llandough Hospital for their willing assistance, and Miss Kathleen Davies for patient secretarial help.

Requests for reprints should be addressed to Mr. J. Townsend, c/o the Secretary, Varicose Vein Clinic, Royal Infirmary, Cardiff.

REFERENCES

Arenander, E. (1960). *Acta chir. scand.*, Suppl. No. 260.
Arnoldi, C. C. (1966). Ibid., 132, 628.
Cockett, F. B. (1953). *Brit. J. Radiol.*, 26, 339.
—— (1956). *Brit. med. J.*, 2, 1399.
—— and Jones, D. E. E. (1953). *Lancet*, 1, 17.
Dodd, H., and Cockett, F. B. (1956). *The Pathology and Surgery of the Veins of the Lower Limb*, p. 358. London.
Haeger, K. (1966). *Venous and Lymphatic Disorders of the Leg*, p. 86. Copenhagen.
Lofgren, K. A., Myers, T. T., and Webb, W. D. (1956). *Surg. Gynec. Obstet.*, 102, 729.
Mathiesen, F. R. (1953). *Acta chir. scand.*, 105, 376.
Moore, J. M. (1957). *Scot. med. J.*, 2, 319.
Myers, T. T. (1957). *J. Amer. med. Ass.*, 163, 87.
Sarjeant, T. R. (1964). *Surg. Clin. N. Amer.*, 44, 1383.
Sherman, R. S. (1949). *Ann. Surg.*, 130, 218.
—— (1964). *Surg. Clin. N. Amer.*, 44, 1369.
Warwick, W. T. (1931). *The Rational Treatment of Varicose Veins and Varicocele*, p. 60. London

Acute Myocardial Infarction in Pregnancy

E. FLETCHER,* M.D., F.R.C.P.; E. W. KNOX,* M.D., M.R.C.P.I.
P. MORTON,* M.D., M.R.C.P.ED.

Brit. med. J., 1967, 3, 586–588

Obstructive coronary artery disease is the rarest form of primary organic heart disease encountered during pregnancy. Myocardial infarction occurring during pregnancy was confirmed for the first time at necropsy by Katz (1921). The first case of recurrent myocardial infarction during pregnancy and labour, with electrocardiographic evidence, was published in 1935 by Reis and Frankenthal. Since then a few further case reports have been published by various authors. Bedford (1964) was able to collect only four cases in the British literature, to which he added one of his own. In a recent review Watson *et al.* (1960) collected 23 authentic cases of myocardial infarction during pregnancy or labour. To this number may be added the case of Magner (1961), that of Bedford referred to above, and the five cases described in this paper, a total of 30 in the world literature.

This paper presents the clinical and electrocardiographic data of five women who sustained major episodes of acute myocardial infarction while pregnant. During the period 1 January 1955 to 31 December 1966 at least 40,000 patients attended the antenatal clinics of the Belfast City Hospital. The five patients already mentioned were selected from approximately 800 pregnant women referred to the cardiac department for assessment. They were all multigravidae, with an age range of 36–41 years. There was no maternal mortality in connexion with the pregnancies or puerperia. All but one (Case 5) pro-

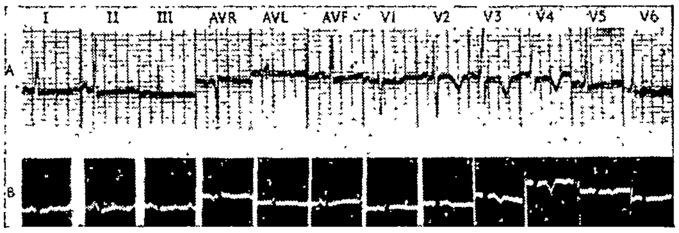


FIG. 1.—Case 1. A (29th week of 4th pregnancy). Sinus rhythm. Abnormal S-T segment and T-wave displacement with grossly abnormal T waves, most pronounced in leads V2–V6. The tracing is consistent with the acute phase of anteroseptal ischaemia or infarction. B (16 days after A). In the interval between the tracings there has been some correction of repolarization, but the underlying myocardium remains abnormal.

Summary of Relevant Data in Five Cases

Case No.	Age	No. of Pregnancies	Week of Onset	Symptoms	Preceding Hypertension	Pre-eclamptic Toxaemia	Biochemical Findings				Follow-up
							S.G.O.T. (units)	S.G.P.T. (units)	Cholesterol (mg./100 ml.)	β-Lipoproteins (mm.)	
1	38	4	29	Dyspnoea for one week, followed by severe crushing retrosternal pain radiating to neck and left arm. Pain lasted 1½ hours	No	No	150		280		Normal delivery of living child at 38 weeks. Puerperium uneventful. Persistent angina of effort over 7 years. Remains normotensive
2	36	7	30	No symptoms referable to C.V.S. before onset of this pregnancy. Sudden attack of severe substernal pain lasting several hours. Pain accompanied by sweating and dyspnoea	No	Yes. All previous 6 pregnancies resulted in stillbirths before 7th month on account of hypertension oedema and albuminuria	50		280		Living child by caesarean section at 40 weeks. Puerperium uneventful. Persistent angina of effort over 2 years 3 months Sudden death after severe episode of retrosternal pain. E.C.G. a few hours before death confirmed a fresh extensive myocardial infarction
3	36	4	32	Epigastric discomfort on exertion relieved by rest, followed 10 days later by crushing retrosternal pain radiating to both arms. Pain awakened patient from sleep and lasted 3 hours	No	No	95		280		Normal delivery of living child at 40 weeks. Puerperium uneventful. No recurrence of ischaemic cardiac pain during 2-year follow-up
4	38	2	30	Dyspnoea for 2 weeks followed by sudden onset of retrosternal tightness associated with flatulence	No	No	50				Normal delivery of living child at 38 weeks. Puerperium uneventful. No follow-up after discharge
5	41	22	13	2-year history of angina of effort before onset of this pregnancy. Awakened from sleep with crushing retrosternal pain radiating to left arm. Pain lasted five hours	Yes	Yes (onset at 28 weeks)	107	32	412	4·2	Intrauterine death at 29 weeks. Normal delivery of macerated foetus at 33 weeks. Puerperium uneventful. Still angina of effort during three-month follow-up

---

* Cardiovascular Unit, Belfast City Hospital, Belfast 9.

duced healthy children. The cause of the single foetal death was severe pre-eclamptic toxaemia. It was not related to the cardiac status of the mother. Two patients (Cases 2 and 5) had severe pre-eclamptic toxaemia of pregnancy, and this might be a contributing factor for the occurrence of coronary atherosclerosis. The other three women had no general medical condition likely to predispose them to coronary artery disease. The relevant clinical obstetric and biochemical data for each patient are summarized in the Table. Serial electrocardiograms were recorded in each case, and these are shown in Figs. 1–5.

Discussion

In a review of 45 cases of coronary artery disease associated with pregnancy by Mendelson (1960) 19 had systemic hypertension, 9 had cardiovascular syphilis, and 2 had diabetes mellitus. Two of our patients (Cases 2 and 5) had a systemic disease likely to predispose to coronary atherosclerosis—that is, a long history of recurrent toxaemia of pregnancy with hypertension. The underlying disorder in all five cases appears to have been coronary atherosclerosis. In all but one of them the acute infarctions occurred in the third trimester, when the oxygen demand of the tissues is increased and the work load of the heart is at its maximum. During pregnancy the blood chemistry alters significantly; the total cholesterol increases and more is attached to the beta-lipoproteins. The pattern resembles that found in men with ischaemic heart disease (Oliver and Boyd, 1955). These changes are maximal about the thirty-third week, and they take place in spite of the great increase in circulating oestrogens, known effective agents in restoring the non-atherosclerotic plasma lipid pattern (Barr, 1953).

The dynamic factors and biochemical changes referred to above may have predisposed some of our patients to coronary occlusion at the critical weeks of gestation, on the assumption that they already suffered from coronary atherosclerosis. They are not, however, the whole answer, since one patient (Case 5)

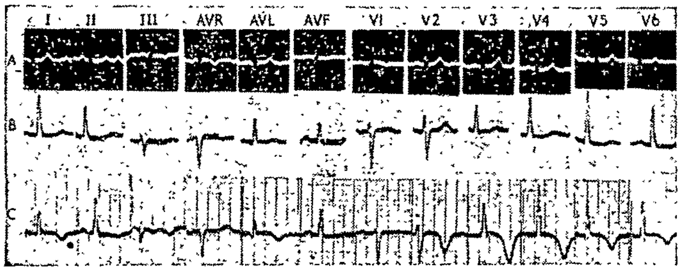


Fig. 2.—Case 2. A (20th week of 7th pregnancy). Normal tracing. B (10 weeks after A). Sinus rhythm. Abnormal S-T segment depression in leads I, II, and V4 V6. An abnormal tracing when compared with A. C (two weeks after B). Abnormal S–T segment displacement in the limb leads with increased polarity of T waves in leads I, AVL, and V2–V6. The tracing is consistent with recent anterolateral infarction.

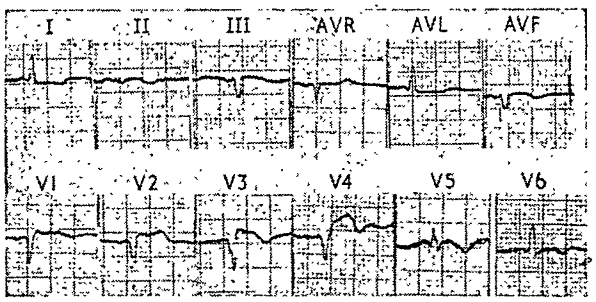


Fig. 3.—Case 3 (32nd week of 4th pregnancy). Sinus rhythm. Abnormal Q–S deflections in leads V1–V4. S–T segment and T-wave displacement upwards due to injury current in these leads and also in leads II, III, and AVF. The tracing is consistent with acute myocardial infarction.

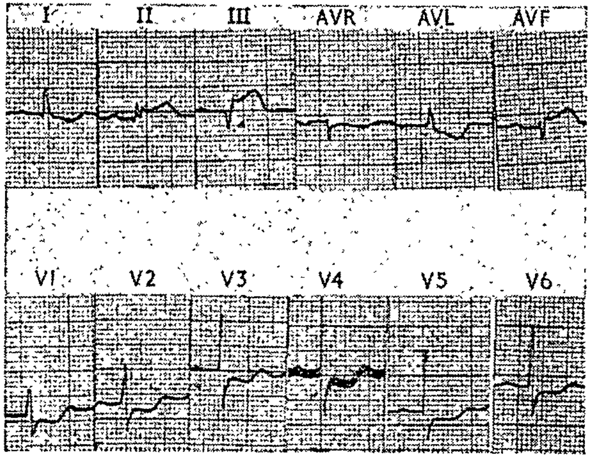


Fig. 4.—Case 4 (30th week of 2nd pregnancy). Sinus rhythm. P–R interval 0.22 second. Abnormal S–T segment and T-wave displacement upwards, due to injury current in leads II, III, and AVF, and downwards in leads I, AVL, and V1–V6. The tracing is consistent with acute postero-diaphragmatic infarction and anterior-wall ischaemia.

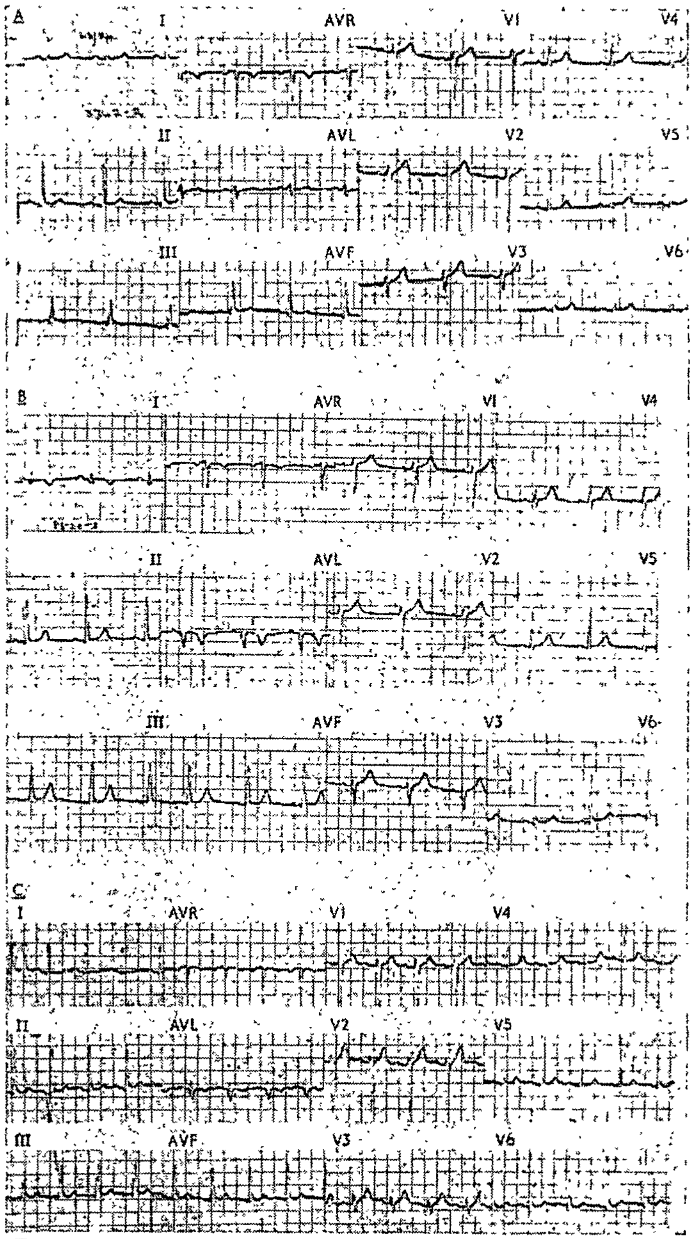


Fig. 5.—Case 5. A (10 months before B). Normal tracing. B (13th week of 22nd pregnancy—10 months after A). Sinus rhythm. Abnormal S–T segment and T-wave displacement with increased polarity of T waves in leads I and AVL. Abnormal Q–S deflection in lead AVL. The tracing is consistent with recent anterolateral infarction. C (4 months after B). In interval following B considerable correction of repolarization has taken place but the tracing still remains abnormal.

developed her episode of coronary occlusion as early as the thirteenth week of gestation and she was the only one in our series in whom the serum cholesterol was significantly raised.

The diagnosis of myocardial infarction during pregnancy presents clinical and electrocardiographic difficulties. Accessory laboratory investigations for myocardial necrosis have to be interpreted with reservations. Upper abdominal pain, flatulence, and even chest discomfort are so common during normal pregnancy that they may mask ischaemic heart pain. The true nature of such symptoms may be obvious only retrospectively when an incidental electrocardiogram is recorded, as in the case reported by Watson *et al.* (1960). Normally the erythrocyte sedimentation rate increases progressively, reflecting changes in plasma proteins. Leucocytosis occurs, and at term the white cell count may be as high as 15,000/cu. mm. (Tysoe and Lowenstein, 1950). There is evidence that normally the serum aspartate aminotransferase activity does not deviate, though it may be elevated in toxaemia of pregnancy (Crisp *et al.*, 1959). Serum lactic dehydrogenase is a much less reliable index of myocardial necrosis, as it may be raised *in normal* pregnancy, and in particular during the puerperium. According to Smith and Gatenby (1958) this enzyme is elevated in 18% of antepartum patients and in 100% of postpartum patients.

Objective evidence of myocardial infarction, therefore, will depend on electrocardiographic analysis, and account must be taken of the electrocardiographic changes which may occur during pregnancy when the heart is not primarily involved. In the later months the mean QRS axis may rotate leftwards owing to elevation of the diaphragm (Hollander and Crawford, 1943) and a deep Q deflection may appear in lead III (Thomson *et al.*, 1938). Acute pulmonary embolism may produce abnormal Q deflections, especially in lead III and S-T segment and T-wave changes, which may mimic postero-diaphragmatic infarction. In addition, electrolyte imbalance may alter the voltage and polarity of the T waves. Intrinsic myocardial disease other than infarction, such as myocarditis of pregnancy, may produce electrocardiographic changes indistinguishable from infarction. In short, electrocardiographic abnormalities must be correlated with all the clinical data. The subsequent history of our patients supports the view that the grossly abnormal tracings were in fact due to myocardial infarction.

Summary

Acute myocardial infarction is rare in pregnancy. The cases of five elderly multigravidae suffering from this condition are described. The diagnosis during pregnancy may present clinical and electrocardiographic difficulties. The increased load on the heart and changes in the blood lipids may predispose to acute infarction in late pregnancy in women with pre-existing coronary atherosclerosis.

Our thanks are due to our obstetric colleagues of the Jubilee and Gardner Robb Maternity Hospitals, who kindly referred their patients to us for cardiac assessment.

REFERENCES

Barr, D. P. (1953). *Circulation*, **8**, 641.
Bedford, J. R. D. (1964). *J. Obstet. Gynaec. Brit. Cwlth*, **71**, 459.
Crisp, W. E., Miesfeld, R. L., and Frajola, W. J. (1959). *Obstet. and Gynec.*, **13**, 487.
Hollander, A. G., and Crawford, J. H. (1943). *Amer. Heart J.*, **26**, 364.
Katz, H. (1921). *Arch. Gynäk.*, **115**, 283.
Magner, D. (1961). *J. Obstet. Gynaec. Brit. Cwlth*, **68**, 128.
Mendelson, C. L. (1960). *Cardiac Disease in Pregnancy*. Philadelphia.
Oliver, M. F., and Boyd, G. S. (1955). *Clin. Sci.*, **14**, 15.
Reis, R. A., and Frankenthal, L. E. (1935). *Amer. J. Obstet. Gynec.*, **29**, 44.
Smith, W. S., and Gatenby, P. B. B. (1958). *Irish J. med. Sci.*, p. 457.
Thomson, K. J., Cohen, M. E., and Hamilton, B. E. (1938). *Amer. J. med. Sci.*, **196**, 819.
Tysoe, F. W., and Lowenstein, L. (1950). *Amer. J. Obstet. Gynec.*, **60**, 1187.
Watson, H., Emslie-Smith, D., Herring, J., and Hill, I. G. W. (1960). *Lancet*, **2**, 523.

Oil Mist Hazard and Piped Air Supplies

JOHN A. BUSHMAN,* L.M.S.S.A.; PETER A. CLARK,† M.B., M.C.PATH.

Brit. med. J., 1967, **3**, 588–590

During recent years there has been a considerable increase in the use of piped air supplies in hospitals. In intensive therapy units this air may often be used to ventilate patients directly.

A system of this type was installed in the intensive therapy unit at Barnet General Hospital and has been in regular use from January 1965. The supply was provided by duplicate oil-lubricated Lacey–Hulbert compressors, each capable of delivering 5½ cu. ft. (0.156 cu. m.) of air per minute at 100 lb./sq. in. (7 kg./sq. cm.). These compressors were installed in the cellar below the intensive therapy unit, together with a reservoir of 33 cu. ft. (0.935 cu. m.) capacity. A Hymatic "rectifier" was installed to remove water. The compressed air was delivered by copper piping to five bedside outlets each equipped with B.O.C. flowmeters.

Some months later it was noticed that some of the flowmeter bobbins were inclined to stick. One of the flowmeters appeared to be slightly oily, and the possibility of oil mist contamination was considered. When the valve of this flowmeter was completely opened to a point far beyond its normal setting, a ripple of oil could be seen on the side of the meter tube (Fig. 1). This excessive air flow had presumably dislodged a quantity of oil trapped below the valve.

An investigation to find the extent of this oil contamination was started. In view of the extremely small quantities of oil mist likely to be present in the air, it was decided to use a fluorimetric technique for oil estimation (Parker and Barnes, 1960).

Methods

Oil mist was collected by passing a known volume of air through filter paper held in a special device consisting of two recessed flanges fitted with hose connexions between which pairs of filter paper discs were held by washers and a spacer. The filter papers used in this work were Whatman paper No. 41, which will cope with low-pressure flows of at least 10 litres per minute. Owing to the rather open nature of the paper, two discs were used in each flange. The papers were

---

* Anaesthetic Registrar, Barnet General Hospital, Barnet, Herts. Research Fellow, Department of Anaesthesia, University of Birmingham.
† Consultant Pathologist, Barnet General Hospital, Barnet, Herts.

prepared by washing twice with spectroscopic quality cyclohexane (Spectrosol grade—Hopkins & Williams Limited).

The collection device was attached by plastic tubing to the outlet of a flowmeter previously cleaned by washing with cyclohexane. The compressed air was allowed to flow at a known rate for varying periods of time, depending on the amount of oil expected to be present. The collection periods varied from one hour after starting the compressor, following emptying the reservoir, to five days after the fitting of the filter system for the removal of oil mist.

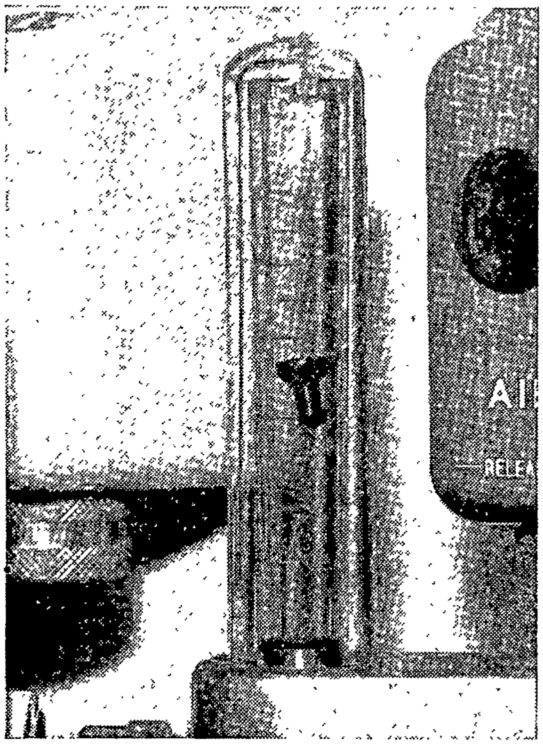


FIG. 1.—Air flowmeter showing ripple of oil when valve fully opened.

After the collection period the central areas of the filter papers which had been in contact with the air channel of the collecting device were cut out and shaken with cyclohexane to extract any trapped oil. The fluorescence of the resulting extracts was read in a Baird-Atomic Fluorescence Spectrophotometer, model SF.1. Under the conditions used it was found that the fluorescence of Shell Talpa 40 oil used in the compressors was maximal at a wavelength of 350 mμ using excitation at 300 mμ (Fig. 2).

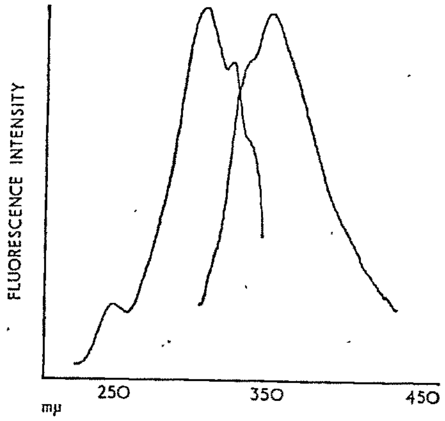


FIG 2.—Excitation (*left-hand curve*) and fluorescence (*right-hand curve*) spectra of crankcase oil.

As it was thought possible that the wick-feed lubrication system concentrated oil in the compressor cylinders after a period of rest, an oil collection was made from air in the reservoir after a 24-hour period during which the compressors had not been run. The reservoir was then emptied and a second sample taken immediately after the compressors had refilled the reservoir.

When the possibility of oil contamination had been confirmed, the British Oxygen Company (who had installed the system) were informed, and they carried out considerable work on the system. This involved the complete cleaning of all equipment, copper piping being replaced wherever easily accessible. The compressors were serviced and arrangements made to drain the excess oil from the sumps at daily intervals. In addition Vokes SPL 10 filters were fitted into the system at points where the air lines entered the intensive therapy unit.

Results

All estimations were made with an air flow of 10 litres per minute. Under the ordinary working conditions of the unit the average amount of oil leaving each flowmeter was 18 μg. per hour. Under the same conditions the amount of oil trapped in the flowmeter was 230 μg. per hour.

After the compressors had been switched off for 24 hours only 6 μg. of oil per hour could be detected in the air leaving a flowmeter attached to the reservoir. After emptying and refilling the reservoir the oil level rose to 70 μg. per hour. After fitting the Vokes SPL 10 filter system, no oil could be detected even in collections lasting 120 hours. After six months' use of the filters no oil could be detected in a 120-hour collection.

Discussion

It seems probable that oil mist contamination of piped air supplies may be a real problem. There appears to have been relatively little work on the problem of oil contamination, though Gerarde (1962) and Cushing and Miller (1965) indicate that chemical pneumonitis may well occur. Although our work has not included any specific estimation of oil particle size, it seems likely, from the relatively small amounts of oil being found, that particle size must be very small.

The provision of oil-free air can be made in two ways—by prevention of oil entering the air at the compressor or by removal of oil found in the compressed air. It is possible to provide oil-free air direct from certain types of compressor, but these are either very expensive or of limited capacity. Compressed air can, of course, be provided from a battery of commercially supplied cylinders, this air having been compressed by a water-lubricated pump and therefore free from oil. However, this is a most expensive method and the cost would be prohibitive in a unit such as ours, where several patients may be ventilated for periods of weeks or even months.

The technology of oil-lubricated pumps is well understood. They are very reliable, relatively cheap, and readily available. Once the use of oil-lubricated pumps is accepted, the problem becomes one of removing the oil mist, either by filtration or by other means.

To be acceptable, a filter, in addition to efficiently removing the oil, must cause a relatively small pressure drop, be able to operate at a flow rate well in excess of the maximum demand, and be safe at the working pressure of the system. From a practical point of view, it is also essential that the filters should be arranged in such a way that they may be changed while the system is in operation. To this end the British Oxygen Company have fitted a system using Vokes SPL 10 filters equipped with replaceable cartridges No. C.74247. Two of these filters are arranged in parallel, so that the air supply can be maintained while one of the filters is being removed for inspection. These filters deal with oil particles. Oil vapour can be removed by techniques based on absorption, but the cost and maintenance of apparatus of this type make their use impracticable.

During the course of several months, usage of this system has proved satisfactory, and we regard this as an acceptable technique for the removal of oil contamination. Though the filters do not appear to be passing detectable oil after several months' use, it seems reasonable to change the filter elements, costing about 30s. each, at quarterly intervals.

Summary

Patients in an intensive therapy unit were being directly ventilated with air from a piped system. It was suspected that this air could be contaminated by oil mist from the compressors used in the system.

By passing the compressed air through a collection device, it was possible to extract oil in microgram quantities, which were subsequently estimated by spectrofluorimetry. Oil contamination was studied under various working conditions.

Because of the implication of oil mist contamination, successful modifications were made to the air-supply system. Even when collections have been made for several days, oil contamination is now below the level of detection.

We would like to acknowledge the co-operation of the British Oxygen Company, and in particular Messrs. J. Cartwright and V. Owen, who have shown the greatest interest in this problem.

Requests for reprints to be made to Dr. P. A. Clark, consultant pathologist, Barnet General Hospital, Wellhouse Lane, Barnet, Herts.

REFERENCES

Cushing, I. E., and Miller, W. F. (1965). *Respiratory Therapy*, edited by P. Safar, p. 186. Oxford.

Gerarde, H. W. (1962). *Industrial Hygiene and Toxicology*, vol. 2, 2nd ed., edited by F. A. Patty, p. 1201.

Parker, C. A., and Barnes, W. J. (1960). *Analyst*, 85, 3.

Bronchial Carcinoma with Hypercalcaemia Simulating Cerebral Metastases

N. J. STRICKLAND,[*] M.A., M.B., B.CHIR.; A. M. BOLD,[†] M.A., B.M., B.CH.; W. E. MEDD,[‡] M.D., M.R.C.P.

Brit. med. J., 1967, 3, 590–592

The occurrence of hypercalcaemia in patients with a neoplasm without bony metastases has been recognized for some years. The symptoms and signs of hypercalcaemia may dominate the clinical picture. In particular, vomiting and mental disturbance might lead to an erroneous diagnosis of cerebral metastases, so that surgical removal of the primary growth is not attempted and a hopeless prognosis is given. Correct diagnosis with excision of the neoplasm may lead to symptomatic and biochemical recovery. The following case illustrates these points.

Case Report

A woman aged 54 complained of nausea and vomiting since an attack of diarrhoea three weeks previously. The vomiting occurred regardless of eating, and there was no abdominal pain or indigestion. She had also noticed lethargy, weakness, impairment of concentration and reasoning, and had had hiccups on and off for a month. She had always been constipated, and had passed urine once nightly for six months. She had lost 1 stone (6.4 kg.) in weight. She had had a cough since an episode of influenza eight months previously, and had smoked 30 cigarettes a day until 18 months before admission.

On examination there was moderately severe weakness of hip flexion and knee extension, and slight weakness of knee flexion on both sides. Her mental concentration was impaired. She sometimes used the wrong words, and her performance at "serial sevens" was impaired.

Investigations

The serum calcium and phosphorus results are given in the Table. Hb 13.9 g./100 ml.; W.B.C. 9,200/cu. mm.; E.S.R. 70 mm. in one hour; blood urea 28 mg./100 ml. Plasma electrolytes: sodium 144 mEq/l.; potassium 3.6 mEq/l.; chloride 94 mEq/l.; bicarbonate 34 mEq/l. Liver-function tests: total bilirubin less than 0.5 mg./100 ml.; thymol turbidity 2.5 units; cholesterol 260 mg./100 ml.; alkaline phosphatase 11 K.A. units; S.G.O.T. 15 sigma units; S.G.P.T. 10 sigma units; serum albumin 4.9 g./100 ml.; serum globulin 2.9 g./100 ml.; electrophoresis: increase in α_1- and α_2-globulin and mucoprotein.

Results of Serum Calcium and Phosphorus Determinations Before and After Operation

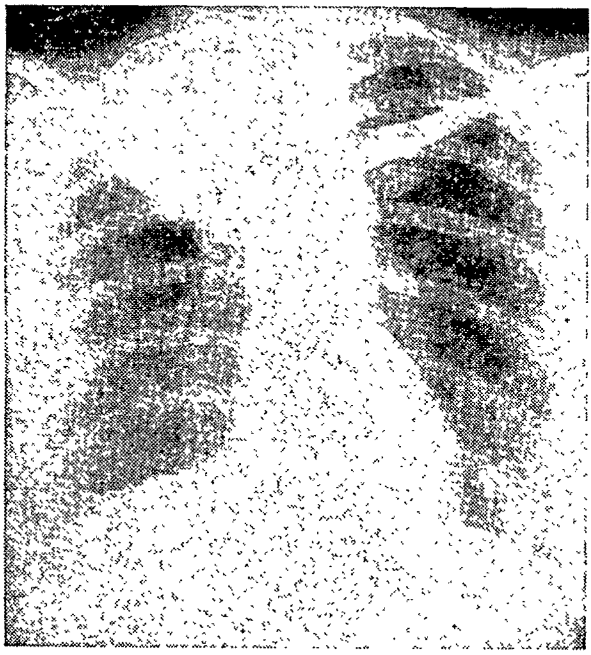
Date	Serum Calcium (mg./100 ml.)	Serum Phosphorus (mg./100 ml.)
3/9/64	16·4	—
5/9/64	15·7	2·1
7/9/64	16·9	1·9
19/9/64 Preop.	Broken	2·3
Postop. (4 p.m.)	11·8	—
Midnight	11·3	3·1
20/9/64	10·3	2·4
21/9/64	10·4	2·1
22/9/64	9·1	1·9
25/9/64	9·1	—
26/9/64	8·8	3·4
28/9/64	9·1	3·3
30/9/64	9·1	3·2
2/10/64	9·5	—
12/11/64	10·3	4·1
15/2/65	10·1	3·6
26/6/65	10·5	4·4
24/8/65	10·0	4·1
15/2/66	9·8	4·0

Creatinine clearance 84 ml./min.; urine calcium 136 mg./24 hours; renal phosphate excretion index, +0.09 (normal 0±0.09—Nordin and Fraser, 1960).

The sputum showed numerous malignant cells, probably squamous in origin. Chest *x*-ray film (see Figure) showed a large tumour in the right upper lobe obstructing the upper-lobe bronchus with some deflation of the upper lobe. No lesion in the oesophagus, stomach, or duodenum was found on barium-meal examination. A radiological skeletal survey showed no bony metastases. *X*-ray examination of hands, feet, and teeth revealed moderate generalized decrease in bone density but no cortical erosions in the phalanges. There was some irregularity of the lateral parts of the lower radii and lower part of the humeri resembling hypertrophic pulmonary osteoarthropathy. The periodontal membrane in the lower jaw was slightly ill-defined. Bronchoscopy (Miss M. C. Waterfall) showed pus coming from the right upper lobe.

---

[*] Medical Registrar, Kingston Hospital, Kingston-upon-Thames, Surrey.
[†] Senior Registrar in Biochemistry, Kingston Hospital, Kingston-upon-Thames, Surrey.
[‡] Consultant Physician, Kingston Hospital, Kingston-upon-Thames, Surrey.



X-ray film of chest showing tumour in right upper lobe.

Lumbar puncture produced clear fluid at a pressure of 90 mm. H_2O. There were 283 R.B.C.s/cu. mm., 60 mg. of protein per 100 ml., with excess of globulin, and 100 mg. of sugar per 100 ml. An electroencephalogram (E.E.G.) (Dr. D. Williams, Atkinson Morley's Hospital) was reported as showing very abnormal records, with recurrent phases of 1 c/s rhythms occurring equally throughout both hemispheres (possibly the result of high pressure), with evidence of extensive local damage also in the right temporal lobe, compatible with a tumour.

An electromyogram (E.M.G.) was reported by Dr. R. G. Willison (National Hospital, Queen Square) as follows: "Right quadriceps and tibialis anterior were sampled with a concentric needle electrode. There was no fibrillation, and the motor unit potentials on voluntary effort did not appear to be abnormal. On maximum voluntary effort a full pattern was seen, but there was striking fatigue after a few seconds and the pattern became rapidly reduced. Surface electrodes were placed over the left extensor digiti brevis. On stimulation of the anterior tibial nerve the muscle action potential measured over 5 mV with normal latency. In conclusion the only abnormality is the rapid fatigue during voluntary effort."

Course and Treatment

Prednisone 20 mg. twice daily was given for only two days, when it was decided to remove the tumour. In the two weeks before operation her vomiting improved, though it did not stop. On 19 September 1964 she had a right upper lobectomy (Miss M. C. Waterfall). The specimen was reported on by Dr. M. E. A. Powell as follows: "Virtually the whole of the upper lobe was distorted by solid tumour, and histology showed that all but a small part of the base of the upper lobe was replaced by a nodular rounded growth. Microscopy showed an anaplastic carcinoma with a suggestion of a squamous pattern."

Her serum calcium returned to normal levels within 24 hours of the operation (see Table). Her mental state gradually became normal. The power in her legs improved, and three weeks after operation she had only slight weakness of left hip flexion and left knee flexion, all other movements being normal. Two months after operation there were no abnormal neurological signs. Nine months after operation she was symptom-free and there was no clinical or radiological evidence of recurrence of the neoplasm. She was back at her skilled clerical duties and was again solving a daily crossword which she had had to give up preoperatively. She was still symptom-free 18 months after operation.

A postoperative E.E.G. on 18 January 1965 (Dr. F. G. Campbell, Guy's Hospital) was reported on as follows: "Symmetrical 10 c/s alpha rhythm posteriorly, much fast activity which was widespread, and occasional runs of 8 c/s rhythm in the temporal areas. At rest, and more so during overbreathing, small sharp waves were seen in the right frontotemporal channels, and less often independently on the left, where low-voltage irregular theta waves also occurred. Thus the original gross abnormality of the E.E.G. had cleared up, but the second record showed a different type of abnormality suggestive of possible epileptogenic discharges in both temporal lobes." A postoperative E.M.G. on 22 July (Dr. R. G. Willison) was reported on as follows: "Right tibialis anterior and quadriceps were sampled with a concentric needle electrode. The appearances of motor units and the pattern on volition were normal. In particular, the pattern was well sustained, in marked contrast to the appearances preoperatively."

Discussion

The common clinical features of hypercalcaemia are mental disturbance, weakness, anorexia, and vomiting. Additional features may be too nonspecific to arouse much attention—for example, vague abdominal pains, constipation, mild polyuria, loss of weight, lethargy, drowsiness, or cardiac irregularities. Renal calculi, uraemia, and calcific or band keratitis seem to be uncommon in malignant cases, possibly because of the short duration of the hypercalcaemia. In the present case it seems likely that the mental symptoms, vomiting, and weakness of the legs were caused by the hypercalcaemia, though it is impossible to exclude an effect of the neoplasm on the nervous system mediated in other ways. Certainly the E.M.G. findings were similar to those in a patient with hypercalcaemia due to a parathyroid adenoma who was recently seen at this hospital.

In hypercalcaemia the E.E.G. may show diffuse alterations (Lehrer and Levitt, 1960; Krane and Roth, 1964) or suggest focal damage without presence of cerebral metastases. In the present case the E.E.G. before operation showed evidence of extensive local as well as diffuse damage. The E.E.G. after operation showed clearing of the original gross abnormality with residual, possibly epileptogenic, discharges in both temporal lobes. The E.M.G. before operation indicated rapid fatigue during voluntary effort. The E.M.G. after operation was normal. There is uncertainty about the significance of the changes in E.E.G. and E.M.G., which are described so that they can be compared with the findings in future cases.

Possible Causes

Of the possible causes of hypercalcaemia in this patient, vitamin-D overdosage, milk-alkali syndrome, and acute bone atrophy were excluded by the history. Serum electrophoresis and bone x-ray examination produced no evidence of multiple myeloma, though a bone-marrow examination was not made. There was no clinical or radiological evidence of sarcoidosis. The hypercalcaemia was thought to be caused either by the lung carcinoma or by coexisting primary hyperparathyroidism (Dent and Watson, 1964). The biochemical findings may be identical in these conditions, and distinction is often impossible. Estimation of plasma chloride has been claimed to be of help in distinguishing hyperparathyroidism from other causes of hypercalcaemia (Wills and McGowan, 1964). The presence of vomiting, however, as in this patient, might invalidate its usefulness. It was decided first to operate on the lung carcinoma. The fall in serum calcium to normal within 24 hours of the operation, and the persistently normal serum calcium and phosphorus in the next nine months, indicated that the lung carcinoma was the cause of the hypercalcaemia.

Bronchial carcinoma (squamous-cell type) is the commonest neoplasm to cause hypercalcaemia in the absence of bone metastases (Locks, 1962; Krane and Roth, 1964). In a series of 119 cases of carcinoma of the bronchus, Locks (1962) reported that 11% had a moderately raised serum calcium (11.5–13 mg./100 ml.) without symptoms of hypercalcaemia, but 50% of this group had radiologically demonstrable skeletal metastases; 2% had a serum calcium around 16 mg./100 ml., with classical symptoms of hypercalcaemia, and no skeletal metastases; and 9% of those with a normal serum calcium had skeletal metastases. Neoplasms in a wide variety of organs have also been reported to cause hypercalcaemia (Plimpton and Gellhorn, 1956; Watson, 1963; Krane and Roth, 1964).

Biochemical investigation characteristically shows a raised serum calcium, the serum inorganic phosphate tending to be low (Plimpton and Gellhorn, 1956). The proportion of ionized calcium is said to be normal, and there is no increase in the complexed fraction (Walser, 1962; Watson, 1963). Corticosteroids in some cases reduce hypercalcaemia (Lucas, 1960; Locks, 1962), but in others they have little or no effect (Krane and Roth, 1964). This suggests that the two groups have a different pathogenesis.

Possible Mechanisms

Several mechanisms for the hypercalcaemia have been proposed. Of these the production of a vitamin-D-like substance is unlikely. Successful treatment of the causative neoplasm is usually followed by a fall in the serum calcium to normal within four days, which would not be expected with cessation of production of a relatively long-acting substance such as vitamin D (Howard and Thomas, 1963). The second possible mechanism is that the tumour produces a substance, "X," which stimulates the parathyroids (Stone *et al.*, 1961; Krane and Roth, 1964). Supporting evidence is that some tumours are associated with chief cell hyperplasia of the parathyroid glands (Massaro and Owen, 1962; Krane and Roth, 1964), and subtotal parathyroidectomy has caused lowering of the serum calcium (Stone *et al.*, 1961). Evidence against this view is that several authors have reported that the parathyroids are histologically normal, though this does not exclude hyperplasia (Plimpton and Gellhorn, 1956; Massachusetts General Hospital, 1961).

In addition, Goldberg *et al.* (1964) commented that the parathyroids at necropsy of one of their patients weighed much less than normal. The most probable mechanism is that the tumour produces a parathyroid-hormone-like substance as first suggested by Albright and Reifenstein (1948). Direct evidence in favour of this hypothesis has been provided by quantitative complement-fixation tests (Goldberg *et al.*, 1964; Tashjian *et al.*, 1964). These authors reported that extracts of primary and secondary carcinoma causing hypercalcaemia contain an antigen indistinguishable from parathyroid hormone. The concentration of this parathyroid-hormone-like substance has been much lower than that found in the parathyroid, but with large tumours the total amount has been comparable to the total in the parathyroid glands. It is possible, however, that there may be more than one mechanism for the hypercalcaemia in these patients.

In the present case the high serum calcium and low serum inorganic phosphate suggest increased production of a parathyroid-hormone-like substance. In the absence of examination of the parathyroid glands and humoral assay of the tumour removed it is not possible to decide whether the tumour was producing a substance having the activity of parathyroid hormone or a "parathyrotropic" hormone.

The urine calcium in this patient was unusually low (136 mg./day) in relation to a serum calcium of about 16 mg./100 ml. and a creatinine clearance of 84 ml./minute, though the patient's calcium intake may have been on the low side because of anorexia. Parathyroid hormone is thought to increase renal tubular reabsorption of calcium, but this action is normally insufficient to compensate for the increased filtered load of calcium in hypercalcaemia. Indeed, nearly all the reported cases of hypercalcaemia due to malignant disease have a raised urinary calcium (Plimpton and Gellhorn, 1956; Goldberg *et al.*, 1964) though unexplained low excretion of urine calcium has been reported (Massachusetts General Hospital, 1961; Goldberg *et al.*, 1964). Ionized and complexed calcium fractions were not measured in this patient, but the serum proteins were normal, so there is no reason to suspect that the proportion of ionized calcium was abnormal. The occasional finding of an unexpectedly low excretion of urinary calcium in patients with hypercalcaemia due to malignant disease is of interest, as it raises the possibility of another factor affecting urinary calcium excretion.

Summary

A case of hypercalcaemia from carcinoma of the bronchus without bony metastases is described in which some of the symptoms of hypercalcaemia resembled those of cerebral metastases. Removal of the tumour resulted in a rapid return of the serum calcium to normal, with relief of symptoms.

Our thanks are due to Dr. M. J. McArdle for his neurological assessment of the patient before and after operation; to Dr. B. W. Meade and Dr. M. E. A. Powell for advice on the biochemical and morbid anatomical aspects respectively; and to Dr. S. Holesh for advice on the radiology.

REFERENCES

Albright, F., and Reifenstein, E. C. (1948). *The Parathyroid Glands and Metabolic Bone Disease.* Baltimore.
Dent, C. E., and Watson, L. C. A. (1964). *Brit. med. J.*, 2, 218.
Goldberg, M. F., Tashjian, A. H., Order, S. E., and Dammin, G. J. (1964). *Amer. J. Med.*, 36, 805.
Howard, J. E., and Thomas, W. C. (1963). *Medicine (Baltimore)*, 42, 25.
Krane, S. M., and Roth, S. I. (1964). *New Engl. J. Med.*, 270, 898.
Lehrer, G. M., and Levitt, M. F. (1960). *J. Mt Sinai Hosp.*, 27, 10.
Locks, M. O. (1962). *J.-Lancet*, 82, 165.
Lucas, P. F. (1960). *Brit. med. J.*, 1, 1330.
Massachusetts General Hospital (1961). *New Engl. J. Med.*, 264, 242.
Massaro, D. J., and Owen, J. A. (1962). *Amer. Rev. resp. Dis.*, 85, 727.
Nordin, B. E. C., and Fraser, R. (1960). *Lancet*, 1, 947.
Plimpton, C. H., and Gellhorn, A. (1956). *Amer. J. Med.*, 21, 750.
Stone, G. E., Waterhouse, C., and Terry, R. (1961). *Ann. intern. Med.*, 54, 977.
Tashjian, A. H., Levine, L., and Munson, P. L. (1964). *J. exp. Med.*, 119, 467.
Walser, M. (1962). *J. clin. Invest.*, 41, 1454.
Watson, L. (1963). *Postgrad. med. J.*, 39, 646.
Wills, M. R., and McGowan, G. K. (1964). *Brit. med. J.*, 1, 1153.

Choice of Method for Administration of Oxygen

I. D. GREEN,* M.B., M.R.C.P.

Brit. med. J., 1967, 3, 593–596

The need for carefully controlled continuous oxygen therapy for patients with chronic obstructive airways disease has been amply stated (Campbell, 1960; Hutchison *et al.*, 1964). Further, it has been suggested that patients with cardiogenic shock require as high a concentration of oxygen as possible in the inspired air (MacKenzie *et al.*, 1964). It is surprising, therefore, that, with the exception of the Ventimask, little or no information is provided by the manufacturers of the many devices at present available in regard to the concentrations of oxygen likely to be delivered to the patient. Few data have been published comparing the performance of these various pieces of equipment in an attempt to define which is the most appropriate to use in a given set of circumstances.

Campbell (1960) pointed out the danger of intermittent oxygen therapy and the need for continuous administration, and it is not uncommon for a patient to be treated continuously with oxygen for several days. Clearly, then, the method used should be comfortable for the patient and should interfere with his activities and those of his attendants as little as possible. This aspect of oxygen therapy has been largely ignored by those writing on the subject.

This paper describes the investigation of a number of methods of oxygen administration commonly employed. The aspects that have been particularly examined are: (1) how accurately the concentration of oxygen that each delivers can be predicted; (2) to what extent rebreathing occurs; and (3) how comfortable and convenient the methods are.

Recommendations are made about which device is likely to be the most appropriate one for the condition being treated. The methods that have been examined in detail are: (1) the Addis nasal cannula made by Portex Ltd. (Addis, 1963); (2) the Bardic nasal cannula made by Bard Inc.; (3) the Edinburgh mask made by British Oxygen Co. (Flenley *et al.*, 1963); (4) the Ventimask made by Oxygenaire Ltd. (Campbell and Gebbie, 1966); (5) the Polymask made by British Oxygen Co.; and (6) the Pneumask made by Oxygenaire Ltd.

Methods

To Determine the Concentration of Oxygen Delivered

No direct measurement could be made of the inspired oxygen concentration (F_IO_2) when the nasal cannulae or the Edinburgh mask were worn. A method of human tomometry was therefore employed. Four normal men aged 28 to 34 acted as subjects. After an initial period of rest of 15 minutes each breathed in succession five mixtures of oxygen in nitrogen. The concentrations of oxygen ranged from 21 to 48%. They breathed each gas for half an hour through a close-fitting oronasal mask. Over the last three minutes of each half-hour blood was withdrawn from an indwelling brachial artery catheter and analysed for its oxygen partial pressure (Pao_2) with a Clark electrode (S.D. ± 1.13 mm. Hg) (Bishop, 1960). The $Paco_2$ was also measured with a Severinghaus electrode and compared with the resting value to ensure that no significant hyperventilation had occurred. A graph was then constructed for each subject relating Pao_2 to the impaired oxygen concentration as a percentage (F_IO_2). The same subjects then each wore a nasal cannula and the Edinburgh mask in turn, and the blood gases were again measured after the same length of time. (It had previously been shown that the two nasal cannulae gave identical results.) It was then possible to read from the subject's calibration curve what his F_IO_2 had been. Three measurements were made at oxygen flows of 1, 2, and 4 l./min. for each of the devices.

The same procedure was carried out with the subjects wearing a 27% Ventimask with oxygen flows of 1, 2, and 4 l./min. As the mask was also assessed by direct measurement this served as a means of checking the accuracy of the blood gas method.

In two subjects wearing the nasal cannulae a comparison of the blood gas values was made during nose-breathing and mouth-breathing.

It was possible to make direct measurements of the F_IO_2 with the three other masks. The same four subjects were used for the Ventimask. Four other normal men aged 23–31 years were used for the polyethylene masks. A respiratory mass spectrometer was used to obtain breath-by-breath measurements of the F_IO_2 and F_ICO_2 at 2, 4, 6, and 8 l./min. of oxygen flow. The probe was inserted into a very short mouthpiece, a hole being cut in the two polyethylene masks for the purpose in such a way that it did not interfere with the mask's action. The nostrils were blocked. Recordings were made for three minutes at the end of half an hour at each level of oxygen flow. The minimum inspired CO_2 concentration was measured from the traces and an estimate of the mean inspired CO_2 was made.

Comfort and Convenience

Six male patients between the ages of 45 and 68 years took part to assess the comfort of the devices. Three suffered from chronic bronchitis and had had previous experience of wearing oxygen masks. At the time of the study they were in a quiescent phase of their disease and were not hypercarbic. The other three patients did not have pulmonary disease and had never worn a mask before.

Each patient wore the six devices for an hour each. The order in which they wore them was devised so that any one particular device was worn immediately after any other on as few occasions as possible. The patients were given at least three hours' rest between masks, and were never asked to assess more than two in one day. At the end of each hour they were given a piece of paper on which there was drawn a line 10 cm. in length. This was marked at one end "No discomfort" and at the other "Intolerable discomfort." They were asked to put a cross on the line at a point which they thought represented the degree of discomfort they had experienced during the preceding hour. The distance in millimetres of this cross from the end marked "No discomfort" was taken as a measure of the degree of discomfort (Gedye *et al.*, 1961). None of the six patients found any difficulty in understanding the method. They were also invited to make comments against or in favour of the device they had just tested.

Blood gas measurements were made in patients wearing some of the devices tested.

---

* Lecturer in Clinical Medicine, Department of Medicine, Queen Elizabeth Hospital, University of Birmingham, Birmingham 15.

Finally, three types of oxygen tents were evaluated; the findings are discussed below.

Results

Inspired Oxygen Concentration.—The calculated F_IO_2 values for the nasal cannulae, the Edinburgh mask, and those of the Ventimask determined by the blood gas method are given in Table I. The mean values for nasal cannulae at 1, 2, and 4 l./min. were 27, 31 and 36% respectively, for the Edinburgh mask 28, 33, and 37%, and for the Ventimask 26, 27, and 28%. By direct measurement the inspired oxygen concentrations provided by the Ventimask at all flows did not alter from 27% by more than ±1% (Table II). The mean values for the Polymask were 36, 52, 70, and 77% at 2, 4, 6, and 8 l./min. flow, and for the Pneumask, 30, 50, 69, and 75%.

TABLE I.—*Inspired O_2 Concentrations of the Three Devices as Estimated From the Blood Gas Measurements of Subjects A, B, C, and D*

Method of Administration	O_2 Flow (l./min.)	Inspired O_2 Concentration				
		A	B	C	D	Means
Nasal cannula	1	27	25	29	27	27
	2	29	29	35	30	31
	4	36	32	39	38	36
Edinburgh mask	1	27	26	29	29	28
	2	29	31	36	35	33
	4	33	39	38	38	37
27% ventimask	1	27	27	27	24	26
	2	26	26	28	26	27
	4	28	27	28	27	28

TABLE II.—*Inspired Oxygen Concentrations, as Measured Directly by the Mass Spectrometer, of Three of the Masks Worn by Subjects A to H*

	O_2 Flow (l./min.)	Inspired O_2 Concentration				
		A	B	C	D	Means
Ventimask ..	2	27	27	26	27	27
	4	27	27	27	27	27
	6	28	27	27	27	27
	8	27	27	27	28	27
		E	F	G	H	
Polymask ..	2	34	34	36	39	36
	4	49	49	56	56	52
	6	62	65	74	78	70
	8	72	76	77	83	77
Pneumask ..	2	27	29	30	32	30
	4	46	49	52	54	50
	6	60	65	70	82	69
	8	61	72	76	84	73

Effect of Mouth-breathing.—In one subject the PaO_2 was 10 mm. Hg higher when he was nose-breathing than when breathing through the mouth wearing a nasal cannula. This corresponded to a difference of 1.4% in his F_IO_2. In the other subject there was no difference.

Rebreathing.—The nasal cannulae could not have caused rebreathing. The Edinburgh mask was most unlikely to have done so, and that with the Ventimask proved to be negligible. The two polyethylene masks, on the other hand, caused a very significant degree of rebreathing. The mean *minimum* F_ICO_2s are given in Table III. The *mean* F_ICO_2s while the subjects were wearing the Pneumask at oxygen flows of over 4 l./min. were as high as 3%.

TABLE III.—*Minimum Inspired O_2 Concentrations in Subjects E, F, G, and H Wearing the Pneumask and Polymask at Various Oxygen Flows*

	Polymask				Pneumask			
O_2 flow (l./min.) ..	2	4	6	8	2	4	6	8
Mean minimum F_ICO_2	1·5	0·8	0·4	0·3	1·3	1·8	1·9	1·9

Comfort

The distances of the patients' marks indicating their discomfiture from the end of the lines are shown as the "degree of discomfort" in Fig. 1, together with the mean values. All the patients clearly preferred the nasal cannulae. The order of preference for the masks was, Edinburgh mask, Polymask, Ventimask, and Pneumask. The mean scores for these masks were not greatly different from each other, however, and it would be wrong to place too much emphasis on this order. The additional remarks made by the patients were interesting. Such comments as "I didn't know I had it on," "Would wear it for any length of time with pleasure," "Very comfortable" were made about the cannulae. Almost without exception the patients made the point that they could get to their face and feed with comfort, and all three bronchitics noticed that they could spit. During the F_IO_2 measurements it had been found necessary to humidify the gas with a Wright nebulizer, otherwise the subjects had a burning feeling in the nostrils at 4 l./min. flow.

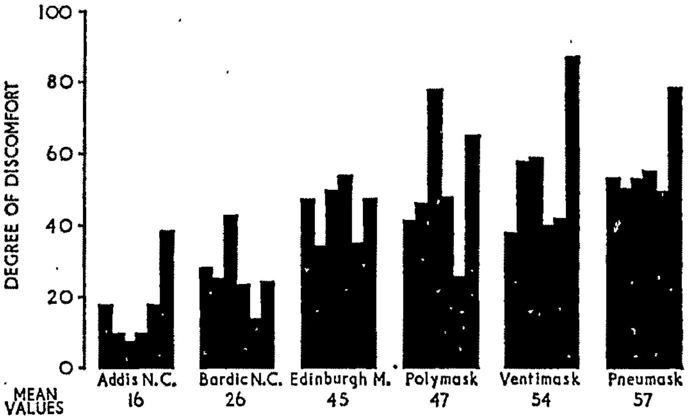


FIG. 1.—Results of six patients' assessment of the comfort of the six devices. Mean values are given—the higher the value the greater the discomfort.

The main objections to the masks were that they all, with the exception of the Ventimask, became hot and sweaty. Most patients noticed discomfort over the bridge of the nose with the Edinburgh mask, the Polymask, and the Ventimask. They all obscured vision to some extent—probably not a serious drawback in a very ill patient. For some the polyethylene masks caused an uncomfortable flow of gas into the eyes. One patient commented that he liked the flow of gas from the Ventimask into his face, but another objected to it. By far the most common objection to the masks was that the patients were unable to get to their face.

Discussion

One striking finding which emerged from the trial was the patients' strong preference for the nasal cannulae. As regards their efficiency as a method, the cannulae proved as reliable as the Edinburgh mask in providing inspired oxygen concentrations between 25 and 39% at flows of 1 to 4 l./min. There was a subject-variation at each flow, this variation being related to the tidal volume. The larger this volume the lower the F_IO_2 owing to greater dilution of the oxygen with inspired air. A patient with chronic obstructive airways will therefore tend to have an F_IO_2 near the upper end of each range given in Table I for the cannulae and Edinburgh mask, and it should be remembered that such a patient wearing either of these devices may have an F_IO_2 of as much as 30% at a flow of only 1 l./min.

In spite of the variation between subjects the nasal cannulae gave reproducible values in the same patient. Fig. 2 shows the results obtained in one patient with chronic hypercapnia whose blood gases were measured before and after being given oxygen for an hour by cannula at 4 l./min. on three successive days.

The Ventimask gave a concentration of oxygen that could be predicted with great accuracy. Both methods of assessment gave similar results, which indicated that the indirect blood gas method was valid. Ventimasks are also available that provide an F_IO_2 of 24, 28, and 35%. Six of each of these have been tested in this unit with the mass spectrometer and have proved equally reliable.

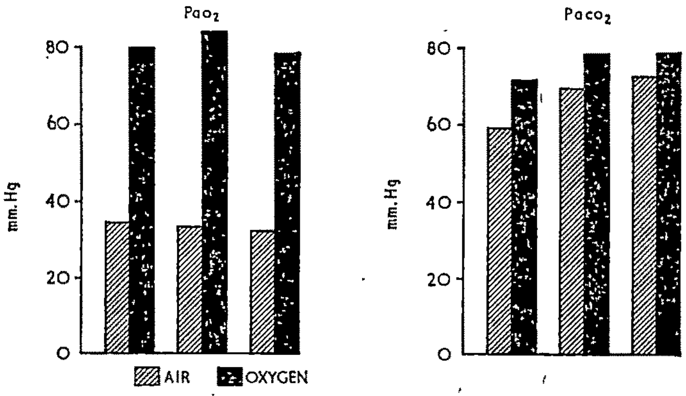


FIG. 2.—PaO_2 and $PaCO_2$ values in one patient measured on three successive days before and after oxygen through a normal cannula at 4 l./min.

The Ventimask's drawback is its lack of comfort. In order to assess whether its ability to control the F_IO_2 accurately outweighs the patient's dislike, consideration has been given to the blood gas results of 38 patients, with chronic obstructive airways disease while in an acute exacerbation, who were treated with oxygen. The measurements were made when the patient was breathing air and after he had received oxygen at 1, 2, or 4 l.min. through a nasal cannula. It can be seen in the oxygen/carbon dioxide diagram in Fig. 3 that if the air-breathing $Paco_2$ was below 60 mm. Hg and the Pao_2 above 45 mm. Hg serious hypercapnia did not develop. With more pronounced blood gas disturbance before oxygen administration a significant rise in $Paco_2$ did sometimes occur. In five patients with a flow of only 1 l./min. $Paco_2$ levels of over 80 mm. Hg were reached. In each case the value on air had been above 70 mm. Hg and the Pao_2 30 mm. Hg or less. Clearly, then, these five patients required less oxygen than could be provided by a cannula to prevent serious hypercapnia and only the 24% Ventimask could have reliably done this. In spite of receiving a lower concentration of oxygen, however, three out of the five patients subsequently required assisted ventilation.

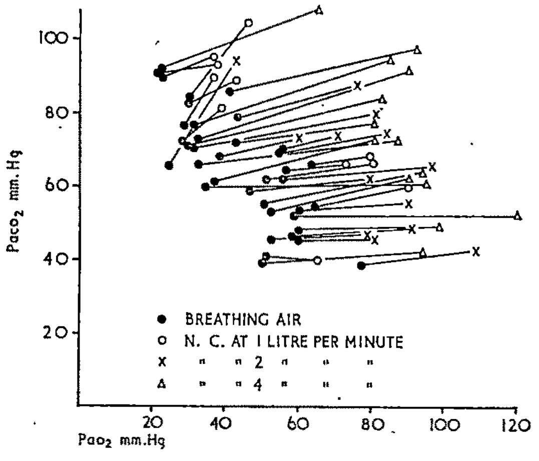


FIG. 3.—Changes in blood gases of 38 patients with obstructive airways disease when breathing oxygen through a nasal cannula at 1, 2, or 4 l./min.

Little information is available on what is the lower level of Pao_2 at which significant harm is done to vital organs. Until detailed studies have been made of regional function in combined anoxia and hypercapnia the safe level can only be guessed at. Hutchison *et al.* (1964) have suggested that the aim should be 50 mm. Hg. In none of the five patients given oxygen by nasal cannula at 1 l./min. did the Pao_2 reach this figure, and the value with the 24% Ventimasks would therefore have been even lower. Nevertheless this mask may be of value in treating those patients with the most severely affected blood gases, especially when assisted ventilation is contraindicated or not available, and perhaps in conjunction with respiratory stimulants. The experience of this department suggests that the facility to deliver 28% or 35% with the same degree of accuracy is not necessary in the management of respiratory failure.

Oxygen Tents

With the exception of their use in very disturbed patients and children, oxygen tents have little value. There are available full-sized tents such as the Oxygenaire MK6 tent and the head tent described by Campbell and Gebbie (1966), that both work on the Venturi principle. These provide constant low concentrations of oxygen with few or no problems of humidity or temperature. However, they do enclose the patient so that he is less accessible and less easy to observe. Patients who need carefully controlled low concentrations of oxygen to prevent hypercapnia will be ill enough to require constant observation and attention, and are better treated with the 24% Ventimask.

At least 6 l./min. of oxygen must be delivered through the Polymask or Pneumask if they are not to be sucked on to the face. In Table II it can be seen that at least 60% oxygen will then be delivered to the patient. Such a high concentration would be likely to induce coma in a patient liable to hypercapnia. At 8 l./min. both masks provide about 80% oxygen. This makes them suitable for treating patients with cardiogenic shock and other conditions requiring a high F_IO_2. Apart from the British Oxygen B.L.B. mask there is no other suitable device commercially available for giving higher concentrations to such patients. Nasal cannulae are unsuitable when a high concentration of oxygen is required, as flows of above 4 l./min. for long periods cause discomfort in the nose. It is therefore unlikely that concentrations in excess of about 40% can be achieved with them. No tents that we have tested have proved satisfactory for giving high concentrations of oxygen. The best that has been achieved by initial flushing and very careful sealing of the tent sides is about 50% inspired oxygen after an hour at 8 l./min.

Care in Prescribing

Any significant degree of rebreathing can be discounted with the cannulae, the Edinburgh mask, and the Ventimask. However, both polyethylene bag masks, in particular the Pneumask, are capable of producing very significant elevations of the F_ICO_2. It should be noted that Table III gives only the minimum values of F_ICO_2, the mean values for the Pneumask being in the region of 3% in the working range. For this reason and because of the high concentrations of oxygen delivered by these two masks they should never be used in the treatment of patients with chronic obstructive airways disease or acute asthma.

A physician must prescribe oxygen with the same care as with any other dangerous drug. The dose should be written on the case sheet in the same way and the nursing staff made aware of its side-effects. The trial has indicated that to provide oxygen to a patient with respiratory failure and hypercapnia—the most difficult situation to prescribe for—the intelligent use of a nasal cannula and a 24% Ventimask, backed up by blood gas measurement or the measurement of the Pco_2 by the rebreathing method, is all that is required, short of assisted ventilation. Furthermore, if such low concentrations as 24% are required, then it is likely that assisted ventilation will be necessary.

In treating patients with other forms of anoxia, when high concentrations of oxygen are needed, the only devices tested that are of value are the Polymask and Pneumask. In such cases the rebreathing they cause is probably not important provided there is no underlying chronic lung disease. There may well be need for the development of a mask that will provide even higher concentrations of oxygen. If such a device becomes available we will still have to prescribe with care because of the dangers of oxygen poisoning and absorption atelectasis.

Summary

A number of devices for delivering oxygen have been evaluated with special regard to what extent the concentration of oxygen they supply is predictable, whether or not they cause rebreathing, and how comfortable and convenient they are. The following conclusions have been drawn:

(1) Oxygen should always be prescribed with care and never left to the whims of untrained staff.

(2) Where there is a likelihood of serious hypercapnia, especially if there is a disturbance of consciousness, P_{CO_2} measurements must be made by one or other of the available methods, and the concentration of oxygen the patient receives should be adjusted according to these measurements.

(3) The vast majority of patients with hypercapnia will tolerate oxygen at 1 litre/min. through a nasal cannula, increasing flows being given if there is no serious rise in Pa_{CO_2} or a lowering of the level of consciousness.

(4) The oxygen must be adequately humidified if given by cannula.

(5) If serious hypercapnia is present—that is, in the region of 70 mm. Hg—a 24% Ventimask may be necessary, but such a patient is likely to need assisted ventilation.

(6) For the delivery of high concentrations of oxygen, but only when hypercapnia is not a problem, either the Polymask or the Pneumask is the most practical method available at present.

It is a pleasure to acknowledge the encouragement and helpful criticism of Professor J. M. Bishop and the technical assistance of Mrs. Anne Hollyhock and Miss Susan Pepper. I would also like to thank Miss Susan Wall for her help in the preparation of the text.

REFERENCES

Addis, G. J. (1963). *Lancet*, **1**, 1084.
Bishop, J. M. (1960). *Proc. roy. Soc. Med.*, **53**, 177.
Campbell, E. J. M. (1960). *Lancet*, **2**, 10.
—— and Gebbie, T. (1966). Ibid., **1**, 468.
Flenley, D. C., Hutchison, D. C. S., and Donald, K. W. (1963). *Brit. med. J.*, **2**, 1081.
Gedye, J. L., Aitken, R. C. B., and Ferres, H. M. (1961). Ibid., **1**, 1828.
Hutchison, D. C. S., Flenley, D. C., and Donald, K. W. (1964). Ibid., **2**, 1159.
MacKenzie, G. J., Taylor, S. H., Flenley, D. C., McDonald, A. H., Staunton, H. P., and Donald, K. W. (1964). *Lancet*, **2**, 825.

Preliminary Communications

Phagocytosis by Polymorphonuclear Leucocytes from Patients with Renal Failure

Brit. med. J., 1967, 3, 596–599

Acute infections are a common problem in the management of renal failure, though their incidence has not been investigated to the same extent as that of infection in other metabolic disorders such as diabetes mellitus. Experience of infective conditions in renal failure is summed up by Schreiner (1964), who states that "infection is the single leading cause of death even in the well-managed uraemic patient." The infective conditions to which this category of patients is prone are usually those caused by *Staphylococcus pyogenes*, Enterobacteriaceae, and *Pseudomonas* species. These pathogens are resisted principally by the non-specific defences of the host. It appeared worth while, therefore, to examine the phagocytic activity of polymorphonuclear leucocytes from uraemic patients to determine whether renal failure in any way impairs the performance of this means of defence against infection.

Two mechanisms of phagocytosis have been demonstrated in human polymorphs (Brogan, 1966): one is independent of serum and the other is conditional on the presence in the cell environment of serum factors. The present inquiry was designed to examine various aspects of these two mechanisms of phagocytosis in uraemic patients and to compare the findings with those in a group of patients whose renal function was normal.

MATERIALS AND METHODS

Patients.—Twelve uraemic patients were studied, the majority of whom were in chronic renal failure from a variety of causes, details of which are listed in Table I. In parallel, a series of 17 hospital inpatients with normal kidney function were investigated; almost 50% were suffering from myocardial infarction, and the rest were under treatment for a variety of conditions (Table I). All patients of the control group had a normal blood urea, and their polymorphs were examined during the recovery or quiescent phase of their illnesses.

TABLE I.—*Patients: Clinical Data. Levels of Blood Urea Were Those Recorded at Time of Taking Blood for Testing Phagocytic Activity*

Group with Renal Failure			Group with Normal Renal Function	
Case No.	Diagnosis	Blood Urea (mg./100 ml.)	Case No.	Diagnosis
1	Chronic membranous glomerulonephritis	400	1–8	Myocardial infarction
			9	Anxiety state
2	Chronic urinary retention	300	10	Epilepsy of late onset
3	Polycystic kidneys	280	11, 12	Pyrexia of uncertain origin
4	Cystinuria	250	13	Drug overdose
5	Renal calculi; chronic pyelonephritis	350	14	Idiopathic steatorrhoea
			15	Bronchiectasis
6	Cystinuria; renal calculi	180	16	Spontaneous pneumothorax
	Chronic pyelonephritis	260	17	Acute appendicitis
8	" "	300		
9	" "	405		
10	Chronic urinary retention: bladder diverticulum	395		
11	Staphylococcal septicaemia precipitating acute renal failure	122		
	Acute glomerulonephritis of late onset	440		

Phagocytosis Experiments.—The materials and methods used for the phagocytosis experiments have been described in detail (Brogan, 1964, 1966). Preparations of polymorphs were made by dispersing the buffy layer of heparinized blood in medium 199 (Morgan, Morton, and Parker, 1950) and allowing the white cell suspension to settle on glass coverslips. Red cells and lymphocytes, which do not adhere to glass, were allowed to sediment from the coverslip preparations that were maintained in a vertical plane in medium 199 in a perspex tank. The morphology of the polymorphs was examined by a phase contrast microscope ; the phagocytic activity of the polymorphs was estimated from the proportion of living cells that were seen to contain test particles. Serum-independent phagocytic activity was investigated by determining the percentages of the cell populations that ingested test particles of rice starch in the absence of serum. Serum-dependent phagocytic activity was studied by determining the serum concentration that caused 50% of phagocytosis in the polymorphs under examination. Paraffin wax particles were used as test material because they are ingested by human polymorphs only in the presence of serum components and will therefore test the mechanism of particle ingestion that is entirely dependent on serum factors (Brogan, 1966). The sensitivity of the polymorph preparations to bacterial endotoxin was measured by determining the concentrations of a commercial preparation of lipopolysaccharide from *Salmonella abortus-equi* (Pyrexal) that would cause a 50% depression of phagocytic activity as compared with a control. Rice starch was used as test particle in these experiments, which were carried out in serum-free medium.

Ultrafiltration of Serum.—Ultrafiltrates of serum from individual patients were prepared by using 8/32 Visking tubing.

Complement Titrations.—A series of logarithmic dilutions of the patients' serum were made in 0.75 ml. of Dulbecco solution (Dulbecco and Vogt, 1954) and added to 0.25-ml. aliquots of a 3% suspension of sheep red cells sensitized with rabbit anti-sheep-red-cell serum (Stayne Laboratories Ltd., High Wycombe, Bucks). After incubating the tubes at 37° C. for 30 minutes the red cells were centrifuged at 400 *g*, and the degree of haemolysis in the supernatant was estimated by reading the optical density of a tenfold dilution at 418 mμ on a Unicam S.P. 500 spectrometer in a 1-cm. cuvette, a standard curve being used to calculate the percentage of haemolysis. The concentrations of serum were plotted on the log scale of log-probability paper against the percentages of haemolysis, which were plotted on the probability scale. The concentration of serum causing 50% of haemolysis ($C'H_{50}$) was read directly from the graph.

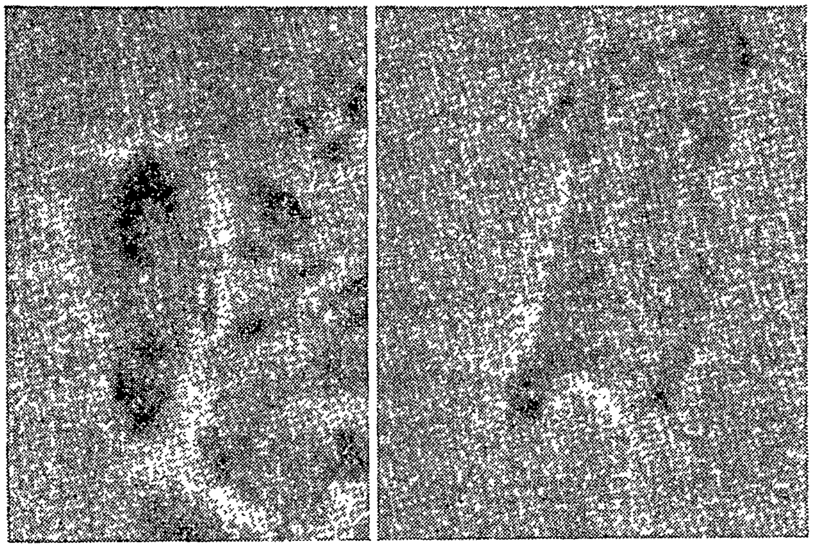


FIG. 1.—Left: Phase contrast photograph of a polymorph from a patient with normal renal function. Right: Phase contrast photograph of a polymorph from a patient with renal failure. (×1,000.)

RESULTS

MORPHOLOGY OF POLYMORPHS FROM URAEMIC PATIENTS

When viewed under phase contrast the morphology of living polymorphs from patients with renal failure was seen to be different from that of cells from patients with normal kidney function. This difference is illustrated in Fig. 1. The cells from uraemic patients appeared to spread on the glass more than those from patients with normal renal function, giving the illusion that the polymorphs from the uraemic patients were the larger of the two. Cytoplasmic granules appeared to be more prominent and vacuoles more common in polymorphs from patients in the renal failure group than in cells from patients with normally functioning kidneys. In addition there was a greater tendency for polymorphs from uraemic patients to form long cytoplasmic processes as compared with cells obtained from the control group of patients.

SERUM-INDEPENDENT PHAGOCYTOSIS

The ability of polymorphs from uraemic patients to ingest rice starch test particles was found to be significantly less ($P<0.005$) than that of polymorphs from patients with normal renal function (Table II). The magnitude of this difference in ability between polymorphs from patients with kidney failure and those from the control group was not large. The results in Table II show that the average phagocytic activity of cells from uraemic patients was almost 90% of that of cells from patients with normal renal function. The variation in the results in cell preparations from individual patients, which was higher in the renal disease group than in the control group, did not appear to be related either to the aetiology of the renal failure or to the level of blood urea at the time of measurement.

TABLE II.—*Phagocytosis of Starch Particles by Polymorphs From a Group of Patients With Renal Failure and From a Group With Normal Renal Function. Tests were Carried Out Either in the Absence of Serum or in Medium Containing Ultrafiltrate of Serum of Individual Patients From Both Groups*

Origin of Cells Tested	Additions to Medium 199	Average Phagocytosis	Limits of Phagocytosis Observed after 1 hr. in Cell Preparations	No. of Patients Tested
Polymorphs from the group with renal failure ..	Nil	*74%	62–84%	10
Polymorphs from the group with normal renal function	”	*83%	77–88%	12
Polymorphs from both groups	50% v/v of serum ultrafiltrate from group with renal failure	74%	47–90%	9
	50% v/v of serum ultrafiltrate from group with normal renal function	78%	67–81%	8

* Difference significant at $P<0{\cdot}005$.

The effect on phagocytosis of adding ultrafiltrates of sera from both groups of patients to the medium was also studied. These experiments were designed to determine whether any low-molecular-weight substances that depressed phagocytosis were present in the sera of uraemic patients. Plasma proteins were therefore removed so that the action of any such substances would not be masked by the phagocytosis-promoting effect of complement (Brogan, 1964). Table II shows that when cells from uraemic patients or from control patients were tested in the presence of 50% of the ultrafiltrate of sera from either group of patients, no significant difference ($P>0.05$) was observed in the percentages of phagocytosing polymorphs. The scatter in results obtained with ultrafiltrates of serum from patients in renal failure was due to a depression in phagocytosis obtained when ultrafiltrates from Cases 1 and 2 were added to the medium ; both these patients were in the terminal phase of their illnesses and died shortly after blood was obtained from them, so it was impossible to repeat the tests. However, depression of phagocytosis was not observed when the ultrafiltrate of serum from another terminally ill patient (Case 9) was added to the medium.

SERUM-DEPENDENT PHAGOCYTOSIS

With the use of paraffin wax test particles normal dose-response curves were obtained when polymorphs from uraemic patients were employed to determine the concentration of serum that caused phagocytosis in 50% of the cells under test (PC_{50}) (Brogan, 1964). It thus appeared that the serum-dependent mechanism of phagocytosis in polymorphs from uraemic patients was unimpaired. In consequence, the complement levels of sera from uraemic patients were determined and compared with those of sera from patients with normal renal function. The results showed that the complement titres of the uraemic group of patients were not significantly lower ($P>0.05$) than those of patients not in renal failure (Table III). Thus the sera of uraemic patients were as capable of promoting phagocytosis in polymorphs as were sera from patients with normally functioning kidneys. The addition of the ultrafiltrates of sera from uraemic patients to a final concentration of 1 : 10 caused no significant depression in the complement titre of sera from either group of patients.

TABLE III.—*Complement Titres of Sera From a Group of Patients With Renal Failure Compared With Those of a Group With Normal Renal Function. Titres are Expressed as Concentration of Serum Required to Haemolyse 50% of a 0.75% Suspension of Sensitized Sheep Red Cells at 37° C. in 30 Minutes ($C'H_{50}$)*

Group with Renal Failure		Group with Normal Renal Function	
Case No.	v/v Concentration of Serum $\times 10^3$ ($C'H_{50}$)	Case No.	v/v Concentration of Serum $\times 10^3$ ($C'H_{50}$)
1	6·4	1	5·0
2	5·1	2	6·0
3	6·3	6	4·9
4	6·1	7	5·0
5	7·2	8	4·1
6	7·6	10	5·8
7	4·9	11	5·5
8	5·7	12	5·1
9	6·9	16	6·3
10	5·1	17	6·9

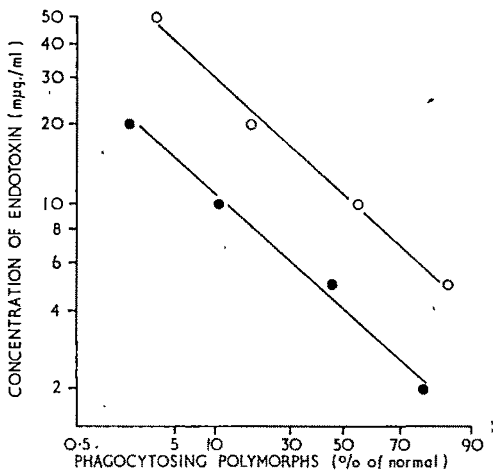


FIG. 2.—Titration of effect of bacterial lipopolysaccharide on polymorph preparations. Concentration of endotoxin, in mμg./ml. (10^{-9} g./ml.), was plotted on a log scale against phagocytosing polymorphs, expressed as percentages of normal phagocytosis in the absence of serum, which were plotted on a probability scale ; rice starch was used as test particle. The concentration that depressed phagocytosis by 50% was read directly from the graph. ○——○——○ Polymorphs from a patient with normal renal function. ●——●——● Polymorphs from a patient with renal failure.

SENSITIVITY TO BACTERIAL ENDOTOXIN

As it had been noted that polymorphs of uraemic patients were different in morphology from those of patients with normal renal function (Fig. 1), the sensitivity of cells from both groups of patients to bacterial endotoxin was determined. These estimations were carried out by plotting the concentrations of lipopolysaccharide on the log scale of log probability paper against phagocytosing polymorphs, expressed as percentages of normal phagocytosis, which were plotted on the probability scale (Fig. 2). Rice starch was used as test particle, and Table IV summarizes the results.

TABLE IV.—*Action of Bacterial Endotoxin on Polymorph Preparations From Uraemic Patients and on Preparations Made From Patients With Normal Renal Function. Effect of Lipopolysaccharide is Expressed as Concentration of Endotoxin Required to Cause a 50% Reduction in Ability of Individual Cell Populations to Ingest Starch Particles*

Polymorphs from Group of Patients with Renal Failure		Polymorphs from Group of Patients with Normal Renal Function	
Case No.	Endotoxin Concentration (mμg./ml.)	Case No.	Endotoxin Concentration (mμg./ml.)
2	4·0	1	11·0
3	2·6	6	10·0
4	1·9	7	12·5
7	1·9	8	9·5
8	4·4	9	8·2
9	2·8	10	8·0
10	3·8	13	9·5
11	1·7	14	8·5

An average concentration of endotoxin of $2.9 \pm 1.1 \times 10^{-9}$ g./ml. was required to depress phagocytosis of polymorphs from uraemic patients by 50% as compared with an average of $9.7 \pm 1.5 \times 10^{-9}$ g./ml. required to produce a similar depression in cells from the control patients. This difference between the effect of bacterial endotoxin on polymorphs from uraemic patients and on cells from patients with normal renal function is highly significant ($P<0.001$). The extent of the difference in the effect of endotoxin is a measure of the far greater sensitivity of polymorphs from uraemic patients to a toxic bacterial product as compared with that of cells from patients with normal kidney function.

DISCUSSION

When the phagocytic activity of polymorphs is under examination in a particular disease the existence of two mechanisms of particle ingestion that are complementary to one another (Brogan, 1966) demands that each is examined in turn lest any effect on one mechanism is masked by the operation of the other. A comparison was made of some aspects of these two mechanisms of phagocytosis in polymorphs from uraemic patients and in polymorphs from hospital inpatients suffering from various illnesses but with normal renal function. The patients with normally functioning kidneys provided a control group that probably avoided bias due to illness alone. Serum-independent phagocytic activity was found to be depressed in polymorphs from uraemic patients as compared with that in cells from the control group, though serum-dependent phagocytosis was not thus lowered. These findings prompted an examination of the cell environment in uraemia for substances that might interfere with phagocytosis, because the extent of this depression in the serum-independent mechanism of phagocytosis was not great. To achieve this, serum proteins were removed by ultrafiltration so that the effect of such substances could be studied in the absence of complement. Ultrafiltration was used for this purpose in preference to the usual procedures for inactivating complement, such as heating at 56° C., because these were thought to be non-physiological.

With the exception of two preparations obtained from patients in the terminal phase of their illnesses, ultrafiltrates of sera from uraemic patients caused no detectable suppression of phagocytosis when polymorphs from either group of patients were tested. Likewise, ultrafiltrates of sera from the uraemic patients did not lower the complement titre of serum.

These results differ from those of Balch (1955), who showed that phagocytosis of staphylococci by polymorphs was not depressed in uraemia of acute onset. Balch, however, tested polymorphs in whole blood so that serum-independent and serum-dependent phagocytosis were not examined separately; depression in serum-independent phagocytic activity therefore could have been missed. Salisbury and Pomeranz (1963) have postulated that toxicity in uraemia is associated with anions which Kramer, Seligson, Baltrush, and Seligson (1965) have identified as aromatic acids. The ultrafiltrates of sera from the uraemic patients in the present investigation probably contained these substances, but little overall effect on serum-independent phagocytosis was produced by their presence; nor had they any effect on the phagocytosis-promoting ability of serum.

It was of interest that the complement levels of sera from uraemic patients were not significantly different from those of patients with normal kidney function. This indicates that the non-specific phagocytosis-promoting activity of serum is not depressed in uraemia. This activity depends on a combination of either the C′1 or the C′2 with the C′4 component of complement (Brogan, 1966), and the complement level of serum is a function of the component in least concentration (Hegedüs and Greiner, 1938). Low-complement levels have been reported in renal disease, particularly in acute glomerulonephritis (Ellis and Walton, 1957), but it would appear that though immunological responses are lowered in uraemia (Wilson, Kirkpatrick, and Talmage, 1965), renal failure as such does not affect the complement level of serum.

The most significant finding of this investigation was the increased sensitivity of polymorphs from uraemic patients to bacterial endotoxin. A 50% depression in phagocytosis was produced in polymorphs from uraemic patients by an average of less than one-third of the concentration of lipopolysaccharide that was required to cause this depression of phagocytosis in cell populations from patients with normal renal function. It is likely that endotoxin stimulates polymorph lysosomes (Brogan, 1966), which are thought by some to be responsible for the self-destruction of cells (de Duve, 1959). It would seem, therefore, that polymorph lysosomes in uraemia are more susceptible to stimulation than normal. This difference is reflected in the difference between the morphology of the cells from patients with and without uraemia; the cytoplasmic granules particularly tend to be more prominent in the cells from uraemic patients than those of the cells from patients whose renal function is unimpaired.

If sensitivity to endotoxin is regarded as a model that indicates how cells respond to toxic bacterial substances in the environment, then polymorphs in uraemia are more susceptible than normal to damage by such substances. The cause of this apparent increase in fragility of polymorphs from uraemic patients is a matter for conjecture. Hypersegmentation has been noted in polymorphs in blood films from uraemic patients (Jensson, 1958), and this could indicate that polymorphs are on the average older in uraemia than in the presence of normal renal function. Whatever the explanation for the apparently increased fragility of polymorphs in uraemia, it may account for the greater than average susceptibility to acute infection in this condition.

SUMMARY

Serum-independent phagocytosis was found to be depressed slightly in polymorphs from uraemic patients, but neither serum-dependent phagocytosis nor the capacity of uraemic serum to promote phagocytosis, as assessed by complement content, was affected. No difference in effect on phagocytosis was found between ultrafiltrates of serum from uraemic patients and from patients not in renal failure. Susceptibility to endotoxin was greater in polymorphs from uraemic patients than in cells from control patients. This difference in sensitivity to a toxic bacterial product may account for the greater than average susceptibility to acute infection in uraemia.

I thank those physicians and surgeons of the Royal Infirmary, Cardiff, who have allowed me access to their patients; and Professor Scott Thomson, Dr. A. W. Asscher, and Dr. M. Sussman for their helpful advice throughout this investigation.

T. D. BROGAN, M.D., PH.D.,
Senior Lecturer in Bacteriology,
Welsh National School of Medicine,
The Royal Infirmary, Cardiff.

REFERENCES

Balch, H. H. (1955). *Ann. Surg.*, **142**, 145.

Brogan, T. D. (1964). *Immunology*, **7**, 626.

—— (1966). Ibid., **10**, 137.

de Duve, C. (1959). In *Subcellular Particles*, edited by T. Hayashi, p. 128. New York.

Dulbecco, R., and Vogt, M. (1954). *J. exp. Med.*, **99**, 167.

Ellis, H. A., and Walton, K. W. (1957). *J. Path. Bact.*, **73**, 315.

Hegedüs, A., and Greiner, H. (1938). *Z. Immun.-Forsch.*, **92**, 1.

Jensson, O. (1958). *Brit. J. Haemat.*, **4**, 422.

Kramer, B., Seligson, H., Baltrush, H., and Seligson, D. (1965). *Clin. chim. Acta*, **11**, 363.

Morgan, J. F., Morton, H. J., and Parker, R. C. (1950). *Proc. Soc. exp. Biol. (N.Y.)*, **73**, 1.

Salisbury, P. F., and Pomeranz, A. A. (1963). Ibid., **114**, 313.

Schreiner, G. E. (1964). In *Diseases of Metabolism*, edited by G. G. Duncan, p. 1130. Philadelphia.

Wilson, W. E. C., Kirkpatrick, C. H., and Talmage, D. W. (1965). *Ann. intern. Med.*, **62**, 1.

Medical Memoranda

Subcutaneous Atrophy after Local Corticosteroid Injection

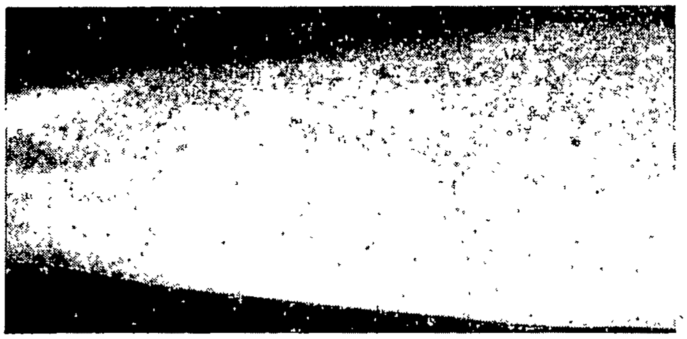
Brit. med. J., 1967, **3**, 600

Atrophy of the skin and subcutaneous tissue at the site of locally applied or injected insoluble corticosteroid preparations was first reported in rats by Baker and Whitaker (1948) and in man by Goldman *et al.* (1953). Since then several further reports of this local complication of corticosteroid therapy have appeared (Goldman, 1955, 1962; Fisherman *et al.*, 1962; Epstein *et al.*, 1963; Meara, 1964; Grice, 1966). All these reports, however, are of patients in whom corticosteroid injections were given for skin diseases or asthma; no reports of this complication occurring in patients treated for arthritis or soft-tissue lesions of the locomotor systems have been found in the literature.

A case in which this complication developed after a local injection of hydrocortisone tertiary butylacetate is described.

CASE REPORT

A woman aged 39 was first seen in June 1965, when she complained of having had pain in the right arm for nine months. Examination showed that she had a right de Quervain's tenosynovitis, and a depressed area of skin about 2 by 1 in. (5 by 2.5 cm.) was noted on the flexor surface of the forearm 4½ in. (11.4 cm.) above the wrist. The overlying skin was of normal colour and consistency and not bound down to the deep tissues. Three small, round, yellow subcutaneous deposits were seen. Clinically the condition appeared to be a small localized area of fat necrosis (see Photograph).



Flexor aspect of forearm, showing depressed area of skin.

The patient had received local corticosteroid injections at another hospital, and subsequent inquiry revealed that when she had been seen eight months previously a diagnosis of de Quervain's tenosynovitis had also been made and treated with two injections of 40 mg. of Depo-Medrone (methylprednisolone acetate) into the tendon sheath of the extensor pollicis longus. There was partial relief of her symptoms, but early in 1965 she complained of pain and numbness along the radial border of the middle third of the forearm, and on 16 March an injection of hydrocortisone acetate was given into this painful area.

Between June 1965 and May 1966 no change in the atrophic area was observed.

On 21 May 1966, because of persistent symptoms, exploration of the right radial nerve and the abductor and extensor pollicis longus tendons was carried out and an extensor tendon release performed by Mr. J. C. R. Madgwick. The patient disliked the appearance of the atrophic area, which was excised at the same time.

Histological examination of this area showed fat necrosis in the subcutaneous tissues and the epidermis was considerably thinned.

DISCUSSION

Animal experiments (Baker and Whitaker, 1948; Castor and Baker, 1950) first showed that local corticosteroids produce thinning of the skin with decrease in the size of sebaceous glands and cessation of hair growth. Later workers showed that very similar changes occur in man.

Goldman *et al.* (1953) reported that deposits of insoluble corticosteroid crystals persist at the site of injection for months and that adjacent skin becomes depressed and atrophic; long-term studies (Goldman, 1955, 1962) confirmed the persistence of the crystals for as long as three years after injection. After their eventual disappearance the skin slowly returned to normal. McKenzie (1962) suggested that these atrophic changes were largely due to ischaemia, as the application of corticosteroids to healthy human skin produced intense vasoconstriction. Schetman *et al.* (1963) studied the effect of local injections of triamcinolone acetate into normal volunteers; they found that long-standing local atrophy was common after intradermal injections and sometimes occurred after subcutaneous injections.

It is suggested that in the case described above the atrophy followed the injection of hydrocortisone into the forearm.

Though local atrophy cannot be regarded as a serious complication of corticosteroid therapy, it is unsightly and may persist for several years. It is suggested that when local injections of insoluble corticosteroids are necessary, deep injections of more dilute suspensions of the corticosteroid, as suggested by Goldman (1962), will lessen the chance of this complication developing.

ANN BEARDWELL, M.B., M.R.C.P.,
Senior Registrar, Department of Physical Medicine and Rheumatology, Royal Free Hospital, London W.C.1.

REFERENCES

Baker, B. L., and Whitaker, W. L. (1948). *Anat. Rec.*, **102**, 333.
Castor, C. W., and Baker, B. L. (1950). *Endocrinology*, **47**, 234.
Epstein, N. N., Epstein, W. L., and Epstein, J. H. (1963). *Arch. Derm.*, **87**, 450.
Fisherman, E. W., Feinberg, A. R., and Feinberg, S. M. (1962). *J. Amer. med. Ass.*, **179**, 971.
Goldman, L. (1955). *Ann. N.Y. Acad. Sci.*, **61**, 520.
—— (1962). *J. Amer. med. Ass.*, **182**, 613.
—— O'Hara, E. H., and Baskett, J. (1953). *J. invest. Derm.*, **20**, 271.
Grice, K. (1966). *Proc. roy. Soc. Med.*, **59**, 254.
McKenzie, A. W. (1962). *Arch. Derm.*, **86**, 611.
Meara, R. H. (1964). *Brit. J. Derm.*, **76**, 481.
Schetman, D., Hambrick, G. W., and Wilson, C. E. (1963). *Arch. Derm.*, **88**, 820.

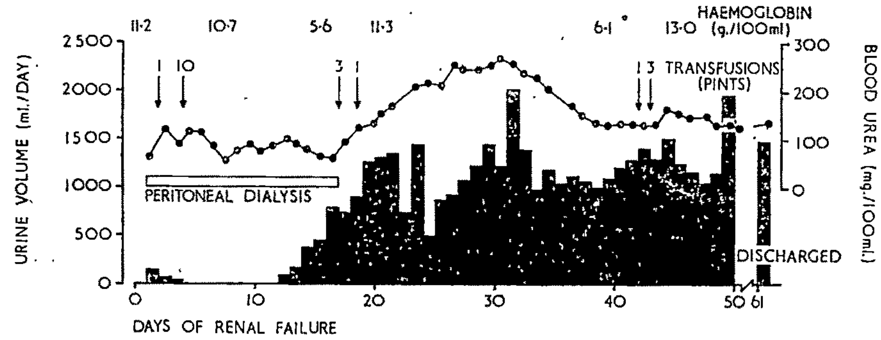
Suicidal Chlorate Poisoning Treated with Peritoneal Dialysis

Brit. med. J., 1967, 3, 601–602

Recovery from chlorate poisoning is rare, and only one case in which dialysis was used has been recorded (Klendshoj *et al.*, 1962). We report here the successful management of a woman who took 40 g. of sodium chlorate in a suicide attempt.

CASE REPORT

The patient, a married woman aged 35, had no history suggestive of renal disease but had a long history of depression. In 1954 and in October 1964 she had been treated for drug overdoses, and in October 1965 for attempted suicide by cutting her wrists. She remained under treatment for three months and was then thought to be well enough to go home. She continued to attend as an outpatient for electric convulsion, which was given at 9 a.m. on 20 December 1965. She walked home alone and took two tablespoonfuls (about 40 g.) of sodium chlorate bought as a weed-killer. She was admitted to Joyce Green Hospital under Dr. P. C. Farrant at 11.15 a.m. Her condition was good, but she began to vomit after arrival. She looked cyanosed and her plasma showed methaemoglobin. She was given methylene blue and vitamin C, and 3 pints (1,700 ml.) of blood were infused and 2 pints (1,140 ml.) removed. She vomited persistently, but by the evening her plasma potassium had risen to 5.4 mEq/l. and her blood urea to 60 mg./100 ml. During the first 18 hours she passed only 90 ml. of urine, and was therefore transferred to Guy's Hospital the next day. Her haemoglobin was 13.5 g./100 ml. and packed cell volume 46%.



The clinical course of the patient.

On arrival during the afternoon of 21 December her condition had deteriorated. She was a khaki colour, with slate-coloured lips and peripheral cyanosis. There were old scars and recent scratches on her wrists and neck. Her pulse was 88/min., blood pressure 120/90 mm. Hg, and respiration rate 22/min. There were no other physical signs. Blood was immediately taken, and had an extraordinary appearance; the plasma was dark opaque muddy brown and the red cells appeared black and shiny like coal dust. Her blood haemoglobin was 10.7 g./100 ml., and spectroscopy showed free haemoglobin, oxyhaemoglobin, methaemoglobin, and methaemalbumin in the plasma. The oxygen saturation was 82% and standard bicarbonate 26 mEq/l. A blood count showed 4% reticulocytes, a white cell count of 52,800/cu. mm., and a platelet count of only 40,000/cu. mm. Though she was anuric, her blood urea was still 60 mg./100 ml.

It was thought that any blood transfused would immediately been oxidized and haemolysed, as her own blood had been, so it was decided to perform a peritoneal dialysis to remove the chlorate before transfusing. An intensive dialysis was begun, being continued (Cameron, 1966) for 24 hours before a 10-pint (5.7-litre) exchange transfusion was started. Throughout these procedures she remained in generally good condition but completely anuric. Her mood seemed normal and she no longer complained of depression. Her subsequent progress is summarized in the Figure.

Her plasma rapidly became free of pigments and was completely clear after six days. Her course was complicated by a number of infections, summarized in the Table. Throughout the whole period of the illness, however, her white blood count remained about 20,000 to 50,000/cu. mm., with a marked left shift even in the absence of serious infection, and continued to be high until day 40.

After a partial diuresis her blood urea remained above 100 mg./100 ml., and after nine weeks in hospital she was discharged with a creatinine clearance of 40 ml./min., urea clearance 9 ml./min., blood urea 118 mg./100 ml., and serum creatinine 4.6 mg./100 ml. When seen at the outpatient department in April she was well, with a blood urea of 46 mg./100 ml., and admission was arranged in May for a full assessment. At that time (five months after admission) there was nothing to find on examination, the blood pressure being normal. Intravenous pyelography showed nothing abnormal, but the creatinine clearance remained low (58 ml./min., serum creatinine 1.3 mg./100 ml.), though the blood urea was normal (32 mg./100 ml.). The urine was sterile and concentration was slightly impaired (1018). Renal biopsy was thought not to be justified at that time.

DISCUSSION

Almost all data on chlorate poisoning concern potassium chlorate rather than sodium chlorate, because of extensive industrial and pharmaceutical use of the potassium salt until about 20 years ago. Witthaus (1911) was able to document 143 cases from the literature then available; Cochrane and Smith (1940) reviewed only a further eight patients, and since publication of their paper 13 cases have been reported (Gordon and Brown, 1947; Oliver *et al.*, 1951; Klendshoj *et al.*, 1962). Ten of these are included in a review of sodium chlorate poisoning by Dérot *et al.* (1948). Apart from these only three case reports (Jacobi, 1879; Stryjzowski, 1931; Klendshoj *et al.*, 1962) refer to sodium chlorate poisoning. The sodium salt may be expected to be even more toxic than the potassium salt, because it contains more chlorate on a weight-for-weight basis (77% as compared with 68%) and is 16 times more soluble in cold water.

Infections

Day	Site	Organism	Antibiotics
1–5	—	—	Benzylpenicillin 500,000 u. q.d.s.
2–4	Lung	?	
2–4	Urine	*Str. faecalis*	
3–14	—	—	Ampicillin 250 mg. q.d.s.
5	*Peritoneum	Atypical *E. coli*	—
7–12	Urine	*Str. faecalis. E. coli.* Proteus	—
12–22	Mouth	*E. coli*	
12	*Peritoneum	Paracolon	
14–19	—	—	Chloramphenicol 1 g. q.d.s.
18–20	*Peritoneum	*E. coli.* Yeast	
18–20	Urine	*E. coli*	
18–22	Lung	*E. coli*	
19	†Blood	*E. coli*	
19–25	—	—	Cephaloridine 0·5 g. q.d.s.
22	Mouth	*E. coli.* Paracolon	—
22–27	—	Candida	Nystatin lozenges
24–27	Urine	*E. coli.* Haemolytic strep.	
26–34	—	—	Ampicillin 250 mg. q.d.s.
32–34	Lung	?	—

* Only on days 18–20 was the dialysate turbid.
† This was the only positive blood culture of many taken.

The fatal dose of chlorate is usually 20–30 g. (Witthaus, 1911). The smallest dose causing the death of an adult is 7.5 g. (Bernstein, 1930) taken in a tooth-paste by a suicidal Army officer ; and the largest dose with survival is 47 g., taken in divided doses over 13 hours (Gesenius, 1882). Previous renal impairment, as in the patient of Cochrane and Smith (1940), would decrease the fatal dose, since 95% of the drug is eliminated in the urine. Few patients survive chlorate poisoning. Blyth (1884) collected 39 cases—28 fatal—and of Witthaus's 143 patients 116 died. The average survival was just over four days, ranging from four hours to 12 days. Renal failure was recorded early. The unfortunate Dr. Fountain took 29.2 g. of potassium chlorate as an experiment to prove its harmlessness in 1858 and died "on the seventh day of nephritis" (Jacobi, 1860).

The symptoms and signs of chlorate poisoning have been well described. After ingestion there is usually a period of one to four hours before vomiting begins, often accompanied by diarrhoea and abdominal pain. Dusky cyanosis and dyspnoea follow, the blood pressure tends to fall, and the heart beat to become irregular. The liver and spleen may be enlarged and tender. The urine is scanty or even absent, is brown or black in colour, and contains casts, red cells, free haemoglobin, and methaemoglobin. The blood is brownish in colour and the plasma contains free haemoglobin and free methaemoglobin. The red count is very low and the white cell count persistently high. Agitation, muscular weakness or twitching, occasionally fits, and a falling blood presure lead to coma and death. Many of these symptoms and signs undoubtedly arise from uraemia and hypoxia. At necropsy the kidneys are brown in colour, hyperaemic, and larger than normal. There are signs of gastro-enteritis, the liver and spleen are enlarged, and the blood is chocolate-coloured.

Apparently chlorate is toxic because it is such a powerful oxidizing agent. It attacks all cells, including liver, kidney, and the circulating red cells (Richardson, 1937). SH groups would be particularly vulnerable. The red cells are largely haemolysed and the released haemoglobin converted to methaemoglobin. The intact red cell has considerable capacity to reduce methaemoglobin to haemoglobin (Jaffé, 1964), but this mechanism presumably cannot operate after haemolysis, and methaemoglobin accumulates. This suggestion is confirmed by Gordon and Brown (1947), who noted that the haemoglobin in the washed red cells of their patient was virtually all true haemoglobin, whereas the free pigment was mostly methaemoglobin. The dangers to the patient are therefore direct tissue toxicity, tissue hypoxia, and haemolysis. The haemolysis could liberate enough free potassium to make the plasma K^+ concentration rise to lethal levels, and this presumably accounts for some of the very rapid deaths. Any patient who goes into immediate renal failure will retain almost all the absorbed dose indefinitely, so that dialysis becomes essential for its removal. The chlorate in the dialysate was not measured, but it is known to be freely dialysable from blood and from tissue in vitro (Witthaus, 1911).

The only other case in which dialysis was performed was that reported in detail by Klendshoj *et al.* (1962) and mentioned by Schreiner (1958) and Doyle (1962). The patient was a 28-year-old Korean physician who took exactly 40 g. of sodium chlorate in mistake for sodium chloride in a laboratory experiment. Haemodialysis was performed on the second day to remove chlorate, and on the eighth and fourteenth days because of renal failure. In addition, an 18-pint (10-l.) exchange transfusion was carried out during the first dialysis. The authors attributed this recovery to prompt exchange transfusion and dialysis. A haemodialysis was begun on one patient (Dérot *et al.*, 1948) but was abandoned after 30 minutes because of clotting problems.

Normally, patients with acute renal failure may be expected to recover renal function completely. The failure of our patient to recover completely presumably reflects some irreversible damage due to direct toxic effect on the renal parenchyma, as well as reversible changes due to the haemoglobinuria. One can only guess whether the peculiar susceptibility of our patient to infection (despite excellent control of blood urea on continuous dialysis) was related to some specific feature of chlorate poisoning.

ADDENDUM.—It has been drawn to our attention that Case 10 of the paper by Pringle and Smith (1964) refers to a 17-year-old youth with renal failure from sodium chlorate poisoning who was treated with peritoneal dialysis for 14 days and who recovered.

R. K. KNIGHT, M.B., M.R.C.P.,
Clinical Tutor.
J. R. TROUNCE, M.D., F.R.C.P.,
Professor of Clinical Pharmacology.
J. S. CAMERON, M.D., B.SC., M.R.C.P.,
Senior Lecturer in Medicine.
Guy's Hospital,
London S.E.1.

REFERENCES

Bernstein, R. (1930). *Samml. Vergiftungsf.*, **1**, 15.
Blyth, A. W. (1884). *Poisons, Their Effects and Detection,* p. 104. London.
Cameron, J. S. (1966). *Brit. med. J.*, **2**, 811.
Cochrane, W. J., and Smith, R. P. (1940). *Canad. med. Ass. J.*, **42**, 23.
Dérot, M., Derobert, L., Girard, M., Dupeyron, T., and Ménager, M. J. (1948). *Sem. Hôp. Paris*, **24**, 719.
Doyle, J. E. (1962). *Extracorporeal Hemodialysis Therapy in Blood Chemistry Disorders*, p. 229. Illinois.
Gesenius, W. (1882). *Dtsch. med. Wschr.*, **8**, 512.
Gordon, S., and Brown, J. A. H. (1947). *Lancet*, **2**, 503.
Jacobi (1860). Cited by Blyth (1884), p. 107.
—— (1879). Cited by Witthaus (1911), p. 690.
Jaffé, E. R. (1964). In *The Red Blood Cell*, edited by C. Bishop and D. M. Surgenor. New York.
Klendshoj, N. C., Burke, W. J., Anthone, R., and Anthone, S. (1962). *J. Amer. med. Ass.*, **180**, 1133.
Oliver, J., MacDowell, M., and Tracy, A. (1951). *J. clin. Invest.*, **30**, 1307.
Pringle, A., and Smith, E. K. M. (1964). *Brit. J. Urol.*, **36**, 493.
Richardson, A. P. (1937). *J. Pharmacol. exp. Ther.*, **59**, 101.
Schreiner, G. E. (1958). *Arch. intern. Med.*, **102**, 896.
Stryjzowski (1931). Cited by Dérot *et al.* (1948).
Witthaus, R. A. (1911). *Manual of Toxicology*, p. 690. New York.

Current Practice

FORENSIC MEDICINE AND TOXICOLOGY

Drug Addiction

THOMAS H. BEWLEY,* M.D., F.R.C.P.I., D.P.M.

During the past ten years there has been a change in the pattern of drug addiction in the United Kingdom. Before 1950 there was relatively little, and virtually none among people who had obtained drugs illicitly. Now cannabis, amphetamines, combinations of amphetamines and barbiturates, lysergic acid diethylamide, cocaine, and heroin are all increasingly obtained illegally. Those who start obtaining drugs illicitly, and become addicted, commonly have a severe personality disorder. They may experiment with any drugs they can obtain.

Sources of Drugs

Heroin and cocaine, each of which has been sold for £1 for 60 mg. for the past ten years, appear to originate from legitimate prescriptions for other addicts who do not always use the amount prescribed. Cannabis (marihuana), commonly known as "pot," "weed," or "hemp," is increasingly widely smoked, and not only by recent immigrants. People generally smuggle it into the country in small amounts for themselves and their friends, though some appears to be smuggled for profit.

Amphetamines and amphetamine-barbiturate combinations are sold widely in capsule and tablet form for 1s. to 2s. each in cafés under such names as "purple hearts," "french blues," or "black bombers." The price is higher at weekends when the demand by young people to become "high" or "blocked" is greater. These have probably been stolen in bulk or otherwise diverted at some stage after manufacture. The current source of L.S.D. is less certain, but until very recently it was legal both to import and to possess the drug.

Control of Drugs

The control of drugs which are liable to be misused is carried out on behalf of the Home Secretary and of the Secretary of State for Scotland by inspectors and other officers. There is a widespread belief that there is a group of addicts who have become "registered," and thus entitled to an indefinite free supply of drugs. This myth is widely fostered by addicts themselves, who often tell doctors that they are "registered," implying that they are entitled to have drugs.

Drugs controlled under the existing Dangerous Drugs Acts may in fact be prescribed by any registered medical practitioner for anyone, and the Home Office index or register is only a list of persons known to be addicted to narcotic drugs. This is chiefly compiled from the routine inspections by the police of retail pharmacists' registers. When, after investigation, cases of drug addiction are found the names are added to the index. The police notify all cases of drug addiction they find, and prisoners who are addicts are also reported. The Home Office also obtains some information from hospitals, doctors, social workers, and similar sources.

Drug Dependence

The new term "drug dependence" is a general term applicable to all types of drug abuse. It is a state of psychic or physical dependence, or both, which may arise after long-term administration of a drug. Describing the type of dependence is an integral part of the new terminology (morphine-type, cannabis-type, amphetamine-type).

TABLE I.—*Summary of Statutory Provisions for Control of Drugs*

	Dangerous Drugs Act (1965) and Dangerous Drugs (No. 2) Regulations (1964)	Drugs (Prevention of Misuse) Act 1964	Pharmacy and Poisons Act 1933, Poisons List Order 1966, and Poisons Rules 1966
Drugs controlled	Opiates Morphine Heroin* Methadone Synthetic analgesics Pethidine, etc. Cocaine* Cannabis*	Amphetamines* and some similar substances Lysergic acid diethylamide (L.S.D.25)* and some similar substances, including mescaline	Barbiturates Many other substances are controlled under these provisions, including drugs controlled under the Dangerous Drugs Act and the Drugs (Prevention of Misuse) Act
Main provisions	(*a*) Offence to possess without authority	(*a*) Offence to possess without authority	(*a*) No offence to possess without authority, but substances in Schedule IV may be sold only by an "authorised seller of poisons" on a prescription from a duly qualified practitioner
	(*b*) Drugs to be kept under lock and key by authorized persons	(*b*) Drugs need not be kept under lock and key	(*b*) Drugs need not be kept under lock and key
	(*c*) Authorized persons have to keep records of drug movements	(*c*) Authorized persons need not keep records of drug movements	(*c*) No records of drug movements, except private prescriptions, have to be copied in prescription book
	(*d*) Offence to import and export except under licence	(*d*) Offence to import except under licence	(*d*) No restrictions on import or export
Penalties	Summary—£250 fine and/or 12 months' imprisonment Indictment—£1,000 fine and/or 10 years' imprisonment	Summary—£200 fine and/or 6 months' imprisonment Indictment—unlimited fine and/or 2 years' imprisonment	£50 fine

* Drugs commonly obtained illegally.

People can become dependent on a wide variety of chemical substances that produce central nervous system effects varying from stimulation to depression. When psychic dependence develops there is a feeling of satisfaction and a drive that requires periodic or continuous use of the drug to produce pleasure or avoid discomfort ("craving"). Some drugs also produce physical dependence, which is an adaptive state that shows itself by intense physical disturbances when the drug is stopped or its action affected by a specific antagonist (withdrawal or abstinence syndromes).

---

* Consultant Psychiatrist, Tooting Bec Hospital, London.

Marihuana

Marihuana is found in this country either as clippings from the dried flowering or fruiting tops of the cannabis plant or in the form of a resin extracted from it, often referred to as "hash," and a more potent source of the active ingredients (probably tetrahydrocannabinols).

When marihuana is smoked there is initially apparent stimulation and exhilaration, followed by sedation, depression, drowsiness, and sleep. The effects, however, are very variable and unpredictable. The neurophysiological effects are clumsiness, incoordination, and frequently ataxia. There may be analgesia of the skin, flushing of the face, pupillary dilatation, and a rise in the pulse rate and blood pressure.

The effects on mood vary from extreme elation and exhilaration to depression, panic, and severe anxiety. In general marihuana promotes a sense of well-being and relaxation. Anxiety and emotional tension may be reduced and critical faculties inhibited. It may induce striking illusions and hallucinations. The distortion of time perception is especially marked, and time appears to pass more slowly. Fantasy and imagination may be stimulated. Ideas may be plentiful but disconnected and disorganized. There may be increased auditory acuity and sensitivity to rhythm. Listening to music after taking the drug may produce unusual aesthetic responses. In general the drug produces an alteration in consciousness and an altered way of feeling and reacting to sensory stimuli. Marihuana is less effective as an analgesic than the opiates and produces less euphoria. Physical dependence does not develop. Like alcohol, but producing more euphoria, it is sought chiefly for casual recreational use and as an escape from reality. The experiences are often described as being "blocked" or "stoned."

The use of marihuana does not in itself cause any mental or physical ill health, though it may lead to social and legal problems. For example, it can be extremely dangerous to drive a car under the influence of marihuana, owing to altered perception.

Amphetamines

Amphetamines and amphetamine-barbiturate compounds are usually taken at weekends by adolescents to produce euphoria and wakefulness, and to increase energy and talkativeness. Occasional weekend use has been called "benign" compared with a "malignant" use, where psychological dependence on amphetamines has developed.

People in this group take more, and are inclined to use a variety of forms of amphetamine in a reckless manner. They start taking the drug during the week as well as the weekend, and their physical health and work suffer. They often have short-lived mental illnesses, which may lead to hospital admission because of agitation, restlessness, and schizophrenic-like psychoses, frequently with persecutory ideas. They may develop depressive reactions ("coming down") when they stop the drug. These are sometimes described as "the horrors" (though this term is also used for the acute psychotic illnesses).

Amphetamines may be taken intravenously by heroin addicts as an alternative to cocaine. Psychological dependence on amphetamine is also seen in patients who first have it prescribed as an antidepressant or appetite suppressant.

Lysergic Acid Diethylamide

Short-lived psychoses are also seen in people who have taken the drug lysergic acid diethylamide (L.S.D.25). It is a potent drug which one would have thought unlikely to be widely misused, because tolerance often develops rapidly while dependence (psychological or physical) does not develop. Also its effects are uncertain and can be exceedingly unpleasant. Nevertheless, it is now widely used (or misused) in the United States and to some extent here. The view that L.S.D. is harmless and safe is not supported by the figures of untoward reactions. Common complications are psychotic reactions with hallucinations, anxiety—which can amount to severe panic—depression, and confusional episodes with disorientation. These may occur at the time the drug is taken, and may sometimes recur, particularly under stress, for several weeks after. Judgement may be so disordered that a person may believe that it is possible and safe to float down from a height.

A patient with acute adverse reactions should be admitted to hospital and treated with intramuscular chlorpromazine.

Heroin and Cocaine

Drug addiction of the morphine type is more serious, because it is more difficult to treat. It is seen increasingly frequently among young people who take heroin, usually combined with cocaine, by intravenous self-administration ("main-lining"). The common pattern is for someone who has previously taken other drugs to experiment with heroin, taking it occasionally subcutaneously or intramuscularly ("skin-" or "joy-popping"). He then takes it more regularly, and finally daily and intravenously. Physical dependence is likely to develop at this stage and may parallel the development of tolerance. When an addict cannot afford enough of the drug to avoid withdrawal symptoms he may try to get drugs prescribed for him by explaining his predicament to a doctor, who (if he believes that maintenance of the addiction is the best treatment) may do so.

Heroin addicts may also seek treatment for a physical illness. Unsterile self-injection with shared syringes can lead to serum hepatitis, multiple abscesses, subacute bacterial endocarditis, or septicaemia. A common emergency is an overdose, and this is the commonest cause of death.

Though the treatment of an overdose is straightforward (resuscitation: artificial respiration, cardiac massage) there are some special problems. If morphine antagonists (such as nalorphine) are used as an antidote the patient will have severe abstinence symptoms when he recovers consciousness, and a further dose of the opiate may be needed to counteract withdrawal. This is clearly undesirable when treating overdosage. Many of these patients have taken cocaine simultaneously, and this may cause ventricular fibrillation. Addicts who take cocaine may also develop short-lived psychoses similar to amphetamine psychoses.

Addicts are apt to be untruthful. The story of a person who states that he is a heroin addict "registered" at the Home Office, that his own doctor is on holiday, and that he is suffering from withdrawal symptoms should be checked. If there are multiple antecubital puncture marks, abscess sites, and tattooing of the veins it is probable that intravenous heroin has been taken. If drugs have been prescribed it is possible, by contacting either the drugs department of the Home Office or the doctor who prescribed or the chemist who dispensed the drug, to confirm what has been prescribed or dispensed.

Treatment of Withdrawal Symptoms

The early signs of opiate withdrawal are craving for drugs, anxiety, restlessness, and running of the nose. These and more serious abstinence signs are shown in Table II. The symptoms are unpleasant but not usually dangerous, and their onset is gradual. It is unnecessary to give heroin immediately to every addict who demands it, and it is always undesirable to give a prescription to an addict who has not been seen before. Treatment is indicated for a known physically dependent addict who is genuinely distressed, has not had any heroin for at least six hours, and is developing withdrawal symptoms. Treatment should be in hospital if possible.

TABLE II.—*Times of Appearance of Abstinence Signs in Physically-dependent Opiate Addicts**

Grade of Abstinence	Signs	Hours After Last Dose		
		Heroin	Morphine	Methadone
0	Craving for drugs, anxiety	4	6	12
1	Yawning, perspiration, running nose, lacrimation	8	14	34–48
2	Increase in above signs plus mydriasis, gooseflesh (piloerection), tremors (muscle twitches), hot and cold flushes, aching bones and muscles, anorexia	12	16	48–72
3	Increased intensity of above plus insomnia, increased blood pressure, increased temperature, increased respiratory rate and depth, increased pulse rate, restlessness, nausea	18–24	24–36	
4	Increased intensity of above plus febrile facies, position (curled up on hard surface), vomiting, diarrhoea, weight loss, spontaneous ejaculation or orgasm, haemoconcentration, leucocytosis, eosinopenia, increased blood sugar	24–36	36–48	

* Modified from a Table by P. H. Blachly, *Amer. J. Psychiat.*, 1966, **122**, 742.

There is no physical dependence on cocaine, so there is no need ever to prescribe or administer it. Heroin withdrawal symptoms can be treated equally well with morphine or methadone (Physeptone). The best way is to use oral methadone, preferably in linctus form so that the patient does not know the amount he is given.

The equivalent in other opiates of methadone 1 mg. are: heroin 1 mg.; morphine 3 mg.; pethidine (meperidine) 20 mg.; codeine 30 mg.; and laudanum (1% morphine) 0.3 ml.

Methadone itself is a drug of addiction and physical dependence to it develops, but withdrawal symptoms are milder. In a doubtful case methadone 10 mg. could be given, and 20 mg. an hour later if there is no improvement. This could be repeated after a further two hours, but 50 mg. should be adequate to cover the next 12 hours, while other arrangements for treatment were made.

Some patients may be dependent on more than one drug. Some take all their prescribed heroin in the morning and barbiturates in the afternoon and evening, when heroin withdrawal symptoms occur. After a time physical dependence on barbiturates develops.

Addicts overstate the dose of opiates they take and underestimate sedatives. A heroin addict can die from inhalation of vomit during a fit from barbiturate withdrawal while being treated for heroin withdrawal symptoms, if concurrent physical dependence on barbiturates is not suspected. Where large amounts of heroin have definitely been taken more methadone will be needed.

Barbiturates

Physical dependence on barbiturates may be found in alcoholics as well as heroin addicts. It may also be found in those who take large amounts of amphetamine-barbiturate combinations. The commonest cause, however, is excessive prescribing of barbiturates as sleeping tablets. The effects of large doses include ataxia, dysarthria, impairment of mental function, confusion, loss of emotional control, poor judgement, and, occasionally, a toxic psychosis. Coma and death may occur.

When physical dependence on barbiturates has developed and the drug is suddenly stopped, the withdrawal symptoms include, in the approximate order of appearance, anxiety, involuntary twitching of the muscles, tremor of hands and fingers, progressive weakness, dizziness, distortion in visual perception, nausea, vomiting, insomnia, loss of weight, a precipitate drop in blood pressure on standing, convulsions of a grand mal type, and a delirium resembling alcoholic delirium tremens or a major psychotic episode. Convulsions and delirium do not usually occur at the same time. Generally a patient may have one or two convulsions during the first 48 hours of withdrawal and then become psychotic during the second or third night.

The barbiturate withdrawal syndrome is best treated in hospital with barbiturates alone. The degree of tolerance must first be determined, by systematically adjusting dosage until intoxication develops, to prevent the development of convulsions from premature withdrawal. Next the physical dependence must gradually be decreased. Physical dependence on barbiturates and other sedative hypnotics (glutethimide, diazepam, chloral) is more severe and dangerous than opiate dependence, and more easily overlooked.

ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Pigmented Naevi in Children

Q.—*Three days after surgical excision of a non-malignant pigmented naevus a child aged 6 developed 10 small pigmented naevi over her trunk. Is this unusual or significant?*

A.—Melanocytic naevi are common skin tumours and tend to appear clinically during infancy and childhood. It is tempting to suggest that in the case in question the 10 pigmented naevi had escaped detection before operation, but they might well have become manifest rather rapidly during an active phase of pigmentation. Whether the "stress" of minor surgery had accelerated this process is a matter for speculation.

The occurrence is unusual but not of any sinister significance, since malignant change in a pigmented naevus is an extreme rarity before puberty. A comprehensive review of juvenile melanoma can be found in the *Year Book of Dermatology.*[1]

REFERENCE

[1] Kopf, A. W., and Andrade, R., *Year Book of Dermatology*, 1965–66. Chicago.

Smallpox Vaccination and D.T.P.

Q.—*It is now recommended that D.T.P. and oral polio vaccine be given at the age of 2 to 6 months, and that a booster dose of these prophylactics should be given at 18 months. Is it advisable to vaccinate against smallpox when giving the booster doses at 18 months?*

A.—Simultaneous administration of D.T.P. and live smallpox vaccines does not affect the antibody response to the diphtheria, tetanus, or smallpox vaccines, but the small risk of encephalitis, which is associated with both pertussus and smallpox vaccines, may be greatly increased if they are given at the same time. It is therefore advisable to allow at least three weeks to elapse between the administration of D.T.P. and smallpox vaccines.

Insulin by Aerosol

Q.—*Has the possibility of administering insulin by metered aerosol inhalation been explored?*

A.—I am not aware of any recent work on administration of insulin by aerosol. Such routes as the oral, lingual, nasal, vaginal, and rectal have been tried,[1 2] but, though absorption of insulin was demonstrated in some cases, none has proved an acceptable alternative to the parenteral route. Nasal and pulmonary absorption could not be unequivocally proved.[2]

REFERENCES

[1] Brahn, B., *Lancet*, 1940, **1**, 829.
[2] *Brit. med. J.*, 1942, **1**, 585.

Book Reviews

Organ Transplantation

Advances in Surgery. Vol. 2. Edited by Claude E. Welch. (Pp. 520; illustrated. £6 12s.) London: Lloyd-Luke. 1967.

One of the truly remarkable phenomena of advances in surgery during the past handful of years has been the explosive development of organ transplantation. This aspect of medicine is of interest not only because of the future possibility of being able to replace any diseased or worn out organ, but also because of the flood of information revealed by clinical and experimental research in the immensely difficult struggle towards this target. Each of the three basic problems in this field—the storage of transplant organs, the pre-operative improvement and then post-operative maintenance of the patient dying of impairment of some vital structure, and the prevention or suppression of the immune rejection process—has evoked quite remarkable advances in fundamental biological knowledge and in practical clinical progress. One may quote tissue typing as an example of the former and progress in extracorporeal liver perfusion in the latter category.

A reflection of the speed of progress in transplantation is the fact that the whole of the second volume of a new series termed "*Advances in Surgery*" has been devoted to this one subject. It is notable that the contributors (apart from Professor Woodruff, who writes the introduction) are all representatives of surgical departments in the U.S.A.—a tribute both to the important part that surgeons have played in this field and to the debt which we owe to the American university medical centres with their lavish equipment and dedicated investigators for many of the major developments in this subject.

The range of topics is comprehensive. There are sections on fundamental studies in leucocyte- and tissue-typing and of immune mechanisms. Experimental work is detailed in the fields of endocrine, gastrointestinal, hepatic, cardiac, and kidney transplantation, as well as experimental limb replantation. Clinical chapters deal with experience in what has already been achieved in organ transplantation in man, notably in kidney grafting (skilfully reviewed by Dr. David Hume), but also describing successful homografting of the parathyroid in hypoparathyroidism and the first attempts at human liver and lung transplantation. There is also an interesting chapter on human upper limb replantation.

This volume can be recommended to any surgeon who wishes to consult an up-to-date and readable account of the field of surgical transplantation. The contributors include most of the surgical leaders in this field in the United States. Most of the chapters have useful summaries and all include exhaustive and up-to-date bibliographies.

HAROLD ELLIS.

Keeping Up with Medicine

The Medical Annual. 84th Year. 1966. Edited by Sir Ronald Bodley Scott, K.C.V.O., M.A., D.M., F.R.C.P., and R. Milnes Walker, C.B.E., M.S., F.R.C.S., F.A.C.S.(Hon.). (Pp. 667+xxxv; illustrated. 52s. 6d.) London: Longmans, Green. 1966.

The form of the 84th issue of this popular annual remains much the same. Nine new names appear, but the true increase in contributors is from 45 to 48, since some are replacements of those who have given up from retirement and other causes (but happily not death).

A review of the year's work occupies most of the book and contains two new sections. Under geriatrics, Dr. A. N. Exton-Smith discusses the current problems of psychogeriatrics and accidental hypothermia, and under general practice Drs. J. H. Hunt and M. J. Linnett (both general practitioners) consider measles prophylaxis and some simple, rapid, pathological tests. Each summary is followed by references and some have editorial comment as well.

The four special articles will be of interest to all doctors. F. T. de Dombal and G. Watkinson conclude that most patients with ulcerative colitis can be kept in reasonable health on medical treatment alone but that surgery is indicated for intractable severe attacks and for patients, especially elderly ones, with total involvement. Multiple sclerosis (the term for disseminated sclerosis now regretfully accepted) is the subject of an excellent review by Professor Henry Miller, who in characteristic style hits out against the professional irresponsibility of much published work about it. Professor A. J. H. Rains's known interest in gallstones is compressed into a most interesting article and the newest ideas about wound healing are discussed by Mr. D. M. Douglas.

Dr. R. M. Mason's usual excellent review on the chronic rheumatic diseases contains up-to-date statements on polymyalgia rheumatica and colitic arthritis. Dr. Oliver Garrod summarizes the work on multiple endocrine adenomatosis, the sex hormones, and on auto-immunity linking endocrine disorders. The section on alimentary disease is the combined work of five distinguished authors, among whom are Professor Sheila Sherlock and Dr. F. Avery Jones. The abandonment of gastric freezing, the Mallory-Weiss syndrome, and Trasylol are among the subjects discussed. The reader will find concise statements on many other current topics, too numerous to mention in detail, such as tetanus prophylaxis, dehydration, osteoporosis, and stereotactic surgery for pain. Among all the specialties, there would seem to be little left under general medicine, but Dr. J. E. Cates has dealt interestingly with his chosen subjects: systemic lupus erythematosus, march haemoglobinuria, and hypercalciuria. The list of "Books of the Year" and the "Practitioners' Index of Drugs and Appliances" are both features which deserve perusal.

Since this book deals with many subjects, it is not to be looked upon as an annual refresher course in any one specialty or a guide to the examination for some special diploma. It is rather an annual presentation of what has recently happened in many fields of medicine and surgery and is a convenient way of keeping the busy doctor "clued up" on the rest of the medical world. It is highly recommended for a place on every doctor's bookshelf.

C. ALLAN BIRCH.

Approach to Old Age

Practical Management of the Elderly. By W. Ferguson Anderson, O.B.E., M.D., F.R.C.P.(Glasg., Edin., Lond.). (Pp. 304 +vii; illustrated. 50s.) Oxford: Blackwell. 1967.

This volume, slim in comparison with the size of the field that it covers, is a welcome addition to the literature on geriatrics. Geriatric trainees and general practitioners will find it of great value.

Professor Anderson's book achieves coverage of the whole field of geriatrics by assuming a sound knowledge of general medicine but concentrating on those aspects of medicine which are specially important in the aged. This is, after all, in accord with the enlightened view of geriatrics, which is the application of general medicine in all its branches to the aged. Since the aged suffer mainly from degenerative disease, he rightly begins with the preventive approach, including a special chapter on work and retirement. Since the object of treatment of the elderly sick is to re-integrate them into society, he then follows with an account of the services available for the elderly.

The main body of the book consists of a consideration of the diagnosis and treatment of disease in the aged, organ by organ, and it is here that space is saved by assuming a sound knowledge of general medicine. At the end is a short appendix on teaching geriatrics and training geriatric physicians which is of great interest because so little has been written on this subject, and most appropriate, coming as it does from the only professor of geriatric medicine in Great Britain.

Throughout the book Professor Anderson clearly speaks of what he knows from personal experience. This is no random collection of other people's thoughts, though his frequent references will be most useful to those who wish to extend their reading of the subject. His pungent and highly personal style of writing is refreshing in these days when it is fashionable to write as if one were a scientific robot; it will hold the reader's interest to the end of the last chapter.

E. WOODFORD-WILLIAMS.

Brain Research

Correlative Neurosciences. Part A: Fundamental Mechanisms. Progress in Brain Research. Vol. 21A. Edited by T. Tokizane and J. P. Schadé. (Pp. 363+xi; illustrated. £5 15s.) Amsterdam, London, and New York: Elsevier. 1966.

Correlative Neurosciences. Part B: Clinical Studies. Progress in Brain Research. Vol. 21B. Edited by T. Tokizane and J. P. Schadé. (Pp. 437+xi; illustrated. £7 5s.) Amsterdam, London, and New York: Elsevier. 1966.

In neurophysiology Japanese workers have made many important contributions, and the manual skill for which they are renowned has made them leaders in some of the most refined investigations, entailing dissection of single nerve units. These two volumes, which contain only articles from Japan, indicate that excellent work in every branch of the neurological sciences is being done in that country at the present time. The first volume contains studies in the basic sciences, while the second is concerned with clinical studies and the applied aspects of physiology, pharmacology, and anatomy. Taken together they cover a wide field of endeavour.

It is of interest to note how much of the basic neuroanatomy and neurophysiology presented in Part A is concerned with functional organization of dendrites. Thus Furakawa, in discussing the functional characteristics of the multitude of synapses on the Mauthner cell of the goldfish, is considering the interaction of post-synaptic events generated at regions of the cell surface which are separated by several hundred microns. And Mannen, presenting some of the most elegant illustrations of neuronal morphology ever published, is attempting to give a quantitative account of the branching of dendrites and the relation between dendritic and somatic surface areas. If applied to many regions of the nervous system, this could provide a most valuable structural basis for physiological theory.

The review by Katsuki of the neural mechanisms of hearing in cats and monkeys is very clear. There are also reports of studies of the central mechanisms of vision and cutaneous sensation as investigated with electrophysiological and anatomical techniques. Brain metabolism and histochemistry, autonomic functions of hypothalamic centres, and studies of neuronal events in relation to the E.E.G. complete the list of topics covered in the basic science section.

Part B is more difficult to review because clinical trials, epidemiological studies, and results of surgical lesions in patients are presented along with experimental investigations of electrical seizure activity in hippocampal tissue, of cortical stimulation in cats, and of paradoxical sleep in rabbits, cats, and man. Yet the reader is impressed by a serious attempt by these Japanese doctors and scientists to use all the methods of study which are available, from classical injection techniques for making anatomical casts of blood vessels in patients who have died of strokes to biochemical studies of central neurones and electrophysiological recording with microelectrodes inside single nerve cells. Pharmacological studies, behavioural studies, and electrical recordings are often used in combination. These researches, approaching many different problems in the neurological sciences from many different points of view, do seem to have some relevance to the study and understanding of clinical neurological problems. This relevance is emphasized by the method of presentation of the chapters in Part B of this work, where the different reports are intermingled.

The articles are beautifully presented, and some of the illustrations are of very high quality. The Progress in Brain Research series is now reaching an impressive size. But the volumes are expensive.

ROBERT PORTER.

Personal View of Paediatric Pathology

Pediatric Pathology. 2nd edition. By Daniel Stowens, M.D. (Pp. 847+ xi; illustrated. £10 12s.) Edinburgh and London: E. & S. Livingstone. 1966.

This book sets out a personal lifetime's experience of paediatric pathology. Although in the preface to the second edition the author says the book is written primarily for doctors who care for and care about sick children, there is no doubt that what he says in the preface to the first edition—that pathologists show an unfamiliarity with the problems of paediatrics—is still true. Therefore the ordinary pathologist should be able to obtain the answer to many of his problems from such a book.

The author deliberately retains in the second edition the emphasis on the morbid anatomical approach to disease. This is unfortunate because so much more could be learnt from a more modern comprehensive approach. While it is true that many of the diseases are reflected in anatomical changes, it is almost impossible to discuss, as he does in so many places, the effects of biochemical change without discussing in more detail the actual biochemical findings. This is particularly true of the nutritional and deficiency disorders as well as in the chapters on the inborn errors of metabolism. In the diseases associated with bacteria there are brief paragraphs included on the morphology of the bacteria. These are really quite useless, as seen in the introductory paragraphs to meningococcal and pneumococcal infections.

In a more original approach the author has transferred the chapter on leukaemia from blood disorders and has placed it into the section dealing with diseases associated with chromosomal abnormalities. This was deliberate but surely unwarranted, and it is unfortunate that paediatricians should be given this impression with leukaemia occupying 13 pages, including almost full-page photomicrographs of kidney infiltration, when Down's syndrome (Mongolism) is dealt with in two pages. (The author has felt impelled to use here nine photomicrographs showing various forms of infiltration from a paper read by him in 1961.) In the inborn errors of metabolism, too, the abnormal haemoglobins, congenital spherocytosis, and Mediterranean anaemia are all introduced in very short sections. All would be better placed in the otherwise very limited chapter on diseases of the blood.

As this book represents the author's own tremendous experience it is inevitable that certain chapters will be extensive at the expense of others. For this reason it will not satisfy the paediatric pathologist as a book of reference. For example, the embryology of congenital malformations of the genitourinary tract, which comprise 30% of all congenital malformations, is dealt with essentially as anomalies of the kidneys, but bladder-neck obstruction in the male, which is certainly of increasing interest, is dealt with in one paragraph.

Nevertheless, it is unfair to criticize this book adversely. It contains an enormous wealth of material, is beautifully produced with excellent photomicrographs and particularly good electron microscope photographs of a renal biopsy, is well arranged, and has an excellent bibliography with easily found references.

The cost of over £10 may, unfortunately, mean that it will be bought by the libraries but probably not by many individual pathologists.

A. GORDON SIGNY.

Genetics of Neurological Disorders

Humangenetik. Vol. 5/1. Krankheiten des Nervensystems. Edited by P. E. Becker. (Pp. 557+xii; illustrated. DM. 174.) Stuttgart: Georg Thieme. 1966.

The high standard of the three volumes of this handbook of human genetics already published is more than maintained by this treatise on the genetics of the neurological disorders. In contrast with the multiple authorship of the earlier volumes, this text is the work of the editor, Dr. P. E. Becker, and only one associate. Dr. Becker contributes three extensive sections which deal systematically with the disorders of the cerebellum and the nervous system below the thalamus. Dr. G. Koch deals equally fully with the diffuse scleroses, the phakomatoses, and various extrapyramidal disorders (such as Huntington's chorea, Parkinson's disease, and nystagmus), and in a concluding chapter with a variety of ill-defined affections.

The text is beautifully illustrated and is supported by exhaustive lists of references, which by themselves are exceedingly valuable, as they are arranged by clinical groupings. The lists on rare affections are particularly admirable. Encyclopaedic in range, the volume carries discussions which are frequently in the nature of monograph surveys based on personal work by the two authors. Because of its comprehensiveness and critical insight into a diffuse and particularly difficult literature this volume is likely to establish itself as the standard work on the subject.

ARNOLD SORSBY.

Hallucinatory Drugs

The Varieties of Psychedelic Experience. By R. E. L. Masters and Jean Houston. (Pp. 326. 84s.) London: Anthony Blond. 1967.

R. E. L. Masters, who is a popular and prolific American writer on matters of sex, has now joined his wife, Jean Houston, in producing a book on an even more immediately topical subject. It discusses their findings in over ten years of giving the psychedelic drugs to a wide variety of people. Then it became illegal in the U.S.A. for L.S.D. to be given or used without medical supervision. Their work has therefore stopped, as neither of the authors is a qualified doctor.

The book does little more than tread all the old ground of those doctors who, for the past 30 years or more, have tested these drugs experimentally and therapeutically, and have recorded their good and bad phenomena and side-effects. Only very limited therapeutic benefits have been obtained. Most of the people given the drug and discussed in this book must come under the heading of "normal," but in the widest range of its meaning. The authors attach great importance to the role of the so-called "guide," who stays with the patient and helps to control what is experienced by the subject under the drug. The guide directs the delusional and hallucinatory material into what are thought to be the best insight channels for each individual. L.S.D., mescaline, and the like are probably the most useful drugs for imposing on others the lessons we feel they need to learn. If the guide is interested in birth trauma most of his subjects tend to obtain startling experience of it. Many will interpret any experiences they get under the drug along such lines—or along Freudian or Jungian lines if that is their guide's own speciality.

The book does not tell us when these drugs should and should not be used, and it gives no advice on the handling of the psychiatric emergencies that are bound to arise. The results of giving hallucinatory drugs, as recorded in this book, remain as speculative as ever in terms of human benefit, especially to those still unconvinced that they do anything but create new delusions and hallucinations for the patient, and mainly serve to encourage abreaction about what is being experienced or supposedly remembered. Moreover, present guides, with their own special beliefs and viewpoints, are rarely the ones best equipped to sort the true from the false.

WILLIAM SARGANT.

Books Received

Review is not precluded by notice here of books recently received.

Symposia Series in Immunobiological Standardization. Vol. 3. International Symposium on Biotechnical Developments in Bacterial Vaccine Production. Edited by R. H. Regamey, H. Hennessen, D. Ikic, and J. Ungar. (Pp. 240 +xii; illustrated. sFr./DM. 52.50.) Basel and New York: S. Karger. 1967.

Nursing Mathematics. By Margaret Rosier, S.R.N., H.V., A.I.H.E. (Pp. 242; illustrated. 13s. 6d.) London: Oxford University Press. 1967.

Principles of Head and Neck Surgery. By H. Robert Freund, M.D., with six contributors. Illustrated by Gottfried W. Goldenberg. (Pp. 337+xi; illustrated. $12.50.) New York: Appleton-Century-Crofts. 1967.

Pesticides and Pollution. The New Naturalist Series. By Kenneth Mellanby. (Pp. 221; illustrated. 30s.) London: Collins. 1967.

Clinical Judgment. By Alvan R. Feinstein, M.D. (Pp. 414+vii; illustrated. 76s.) Edinburgh and London: E. & S. Livingstone. 1967.

Childbearing. Its Social and Psychological Aspects. Edited by Stephen A. Richardson, Ph.D., and Alan F. Guttmacher, M.D. (Pp. 334 +xvii. 68s.) Edinburgh and London: E. & S. Livingstone. 1967.

Roentgen Diagnosis of Diseases of Bone. By Jack Edeiken, M.D., and Philip J. Hodes, M.D. (Pp. 701+v; illustrated. £12 16s.) Edinburgh and London: E. & S. Livingstone. 1967.

Comprehensive Textbook of Psychiatry. Edited by Alfred M. Freedman, M.D., and Harold I. Kaplan, M.D. (Pp. 1666+xxv; illustrated. £9 18s.) Edinburgh and London: E. & S. Livingstone. 1967.

Textbook of Gynecelogy. 4th edition. By John I. Brewer, B.S., M.D., Ph.D., and Edwin J. de Costa, B.S., M.D. (Pp. 918+xxviii; illustrated. £6 16s.) Edinburgh and London: E. & S. Livingstone. 1967.

Medical Shorthand. By Phyllis E. Davis and Nancy V. Hershelman. (Pp. 317+ix. 50s.) London: John Wiley. 1967.

Lectures on Preventive Cardiology. By Jeremiah Stamler, M.D. (Pp. 434+xiv; illustrated. $18.75.) London and New York: Grune & Stratton. 1967.

Nutrition. By Rudolf Hauschka, D.Sc. Translated from the German by Marjorie Spock and Mary T. Richards. (Pp. 212+xi; illustrated. 55s.) London: Stuart & Watkins. 1967.

Molecular Basis of Some Aspects of Mental Activity. Vol. 1. Edited by Otto Walaas. (Pp. 476+xv; illustrated. £5 10s.) London and New York: Academic Press. 1967.

Molecular Basis of Some Aspects of Mental Activity. Vol. 2. Edited by Otto Walaas. (Pp. 515+xv; illustrated. £6 6s.) London and New York: Academic Press. 1967.

Pathologic Physiology. Mechanisms of Disease. 4th edition. By William A. Sodeman, M.D., Sc.D., F.A.C.P., and William Sodeman, jun., M.D. (Pp. 1051+xxi; illustrated. £6 13s.) London: W. B. Saunders. 1967.

The Vesico-Vaginal Fistula. 2nd edition. By J. Chassar Moir, C.B.E., M.D.Edinb., M.A.Oxon., D.M.Oxon., F.R.C.S.(Edinb., F.R.C.O.G., Hon. LL.D. Queen's University, Ontario, Hon. M.M.S.A. (Pp. 196+ix; illustrated. 60s.) London: Baillière, Tindall & Cassell. 1967.

The Use of Antibodies in the Study of Blood Coagulation. By K. W. E. Denson, D.Phil. (Oxon.). Foreword by R. C. MacFarlane, C.B.E., M.A.(Oxon.), M.D.(Lond.), F.R.S. (Pp. 244+ix. 52s. 6d.) Oxford: Blackwell. 1967.

Neurosis in the Ordinary Family. A Psychiatric Survey. By Anthony Ryle, D.M. (Pp. 155. 32s. 6d.) London: Tavistock. 1967.

Histologie und Zytologie des Menschen. Einführung für Ärzte und Studenten. By Professor H. Leonhardt. (Pp. 407+viii; illustrated. DM. 10.80.) Stuttgart: Georg Thieme. 1967.

Anatomische Bildnomenklatur. By Professor Heinz Feneis. (Pp. 438+vi; illustrated. DM. 14.80.) Stuttgart: Georg Thieme. 1967.

Case Development Problems in Hematology. Series 1: The Red Cell, Problems 1–8. By John W. Harris, M.D., and Daniel L. Horrigan, M.D. (Pp. 196. 26s.) London: Oxford University Press. 1967.

The Science Century. By Magnus Pyke. (Pp. 183+x; illustrated. 30s.) London: John Murray. 1967.

The Psycho-Analytical Process. By Donald Meltzer, M.D. (Pp. 109+xvii. 20s.) London: William Heinemann. 1967.

The American Male. By Myron Brenton. (Pp. 252. 28s.) London: George Allen & Unwin. 1967.

Quality Control in the Food Industry. Vol. 1. 1967. Edited by S. M. Herschdoerfer. (Pp. 385+xiv. 90s.) London and New York: Academic Press. 1967.

Elektronenmikroskopische Organpathologie. By Professor Heinz David. (Pp. 711+xx; illustrated. £10 2s. 1d.) Jena: Volk und Gesundheit. 1967.

Alcohol and Traffic Safety. Proceedings of the Fourth International Conference on Alcohol and Traffic Safety. (Pp. 353+xiii. $10.00.) Bloomington, Indiana: Department of Police Administration, Indiana University. 1966.

Personality and Arousal. A psychophysiological Study of Psychiatric Disorder. By Gordon S. Claridge. (Pp. 274+xviii. 70s.) Oxford: Pergamon. 1967.

Advances in Veterinary Science. Vol. 11. Edited by C. A. Brandly and Charles Cornelius. (Pp. 404+xvi; illustrated. £6 16s.) London and New York: Academic Press. 1967.

Gout. 3rd edition. By John H. Talbott, A.B., M.D., D.Sc.(Hon.). (Pp. 296+x; illustrated. $12.50.) London and New York: Grune & Stratton. 1967.

The History of Psychiatry. An Evaluation of Psychiatric Thought and Practice from Prehistoric Times to the Present. By Franz G. Alexander, M.D., and Sheldon T. Selesnick, M.D. (Pp. 471+xiv; illustrated. 63s.) London: George Allen & Unwin. 1967.

Antilymphocytic Serum. Ciba Foundation Study Group. No. 29. Edited by G. E. W. Wolstenholme, O.B.E., M.A., F.R.C.P., F.I.Biol., and Maeve O'Connor, B.A. (Pp. 165+x; illustrated. 24s.) London: J. & A. Churchill. 1967.

The Medical Annual. A Year Book of Treatment and Practitioners' Index. 85th year. Edited by Sir Ronald Bodley Scott, K.C.V.O., M.A., D.M., F.R.C.P., and R. Milnes Walker, C.B.E., M.S., F.R.C.S., F.A.C.S.(Hon.). (Pp. 654+xxiv; illustrated. 52s. 6d.) Bristol: John Wright. 1967.

Myotatic, Kinesthetic and Vestibular Mechanisms. Ciba Foundation Symposium. Edited by A. V. S. de Reuck and Julie Knight. (Pp. 331+xi; illustrated. 65s.) London: J. & A. Churchill. 1967.

Assisting the General Practitioner. A Manual for the Doctor's Secretary, Receptionist, and Surgery Nurse. By M. D. Mackichan, B.A., M.B., B.Chir. (Pp. 264+xii; illustrated. 35s.) London: Pitman. 1967.

Middle Articles

HOSPITAL TOPICS

Clinical Virology: A Year's Experience

J. E. BANATVALA,* M.A., M.D., M.C.PATH., D.P.H., D.C.H.; ELIZABETH A. KENNEDY,* B.A.(MOD.)
JENNIFER M. BEST,* B.SC.

Brit. med. J., 1967, 3, 609–612

Advances in virology over the last decade, mainly resulting from the renaissance of tissue culture techniques and the application of these techniques to the field of diagnostic virology, have led to the discovery of many viruses which have been shown to cause infectious disease.

Hitherto, most diagnostic virology in England and Wales has been performed by the Public Health Laboratory Service. However, the increasing demand for virological investigations has resulted in a few hospitals developing clinical virology laboratories of their own, and it seems possible that this trend may increase. It is important to evaluate such services from time to time in order to see whether or not a useful service is provided, to whom it is of value, and, almost equally important, for both clinicians and virologists to realize its shortcomings and recognize when certain types of investigation are uneconomic or of doubtful value.

This paper presents our first year's experience (21 January 1966 to 20 January 1967) in developing and running a clinical virology laboratory at St. Thomas's Hospital.

Organization and Function of the Laboratory.—The laboratory staff consists of a microbiologist (J. E. B.), assistant microbiologist (E. A. K.), research fellow (J. M. B.), two technicians, a glassware assistant, and a secretary. The function of the laboratory is to provide diagnostic services to the hospital, to conduct research into clinical and epidemiological problems associated with virus infections, and to train both graduates and technicians in diagnostic procedures and research methods. Studies on infection by rubella and herpes simplex viruses have been in progress during the course of the year, the results of which are being presented elsewhere.

Materials and Methods

Selection of Cases.—Patients with possible virus infection were referred for investigation. Before investigations were begun clinical details were discussed; then the microbiologist, whenever possible, visited the wards to see patients and obtain or advise on specimens to be collected. Outpatients were often referred from their respective clinics to the laboratory, where clinical details and specimens were obtained and visits for further specimens, if necessary, arranged.

Identification of Viruses

1. *Isolation.*—Specimens were prepared and processed immediately after arrival in the laboratory (Lenette, 1964), after which they were inoculated into tissue culture. Specimens were then "snap" frozen and stored at −70° C. Cultures of secondary rhesus monkey kidney (M.R.C. Hampstead) and suspensions of primary vervet (M.R.C. Hampstead) and patas monkey kidney cells (Wellcome Research Laboratories) were supplied regularly. In addition, HeLa, WI-38, and RK13 cell cultures were propagated in the laboratory. Reserves of these cells were kept frozen in liquid nitrogen (Linde LNR-25-B, Union Carbide). Rubella virus was detected by the appearance of cytopathic effect in RK13 cell cultures (McCarthy, Taylor-Robinson, and Pillinger, 1963) and the presence of interference phenomena in patas or vervet cell cultures (Parkman, Buescher, and Artenstein, 1962). Specimens from patients with possible enterovirus infections which failed to show cytopathic effect in tissue culture were inoculated into suckling mice in order to detect the presence of Coxsackie A viruses. The identity of all isolates was confirmed by neutralization tests employing virus-specific rabbit antisera. In addition, fertile hens' eggs and an agar-gel diffusion system were kept readily available for the investigation of patients with possible infection with variola virus.

2. *Serology.*—Sera from patients with respiratory infections were tested against the following antigens by complement fixation: influenza A, B, and C; adenovirus; respiratory syncytial virus; parainfluenza 1, 2, and 3 viruses; *Rickettsia burnetii*; psittacosis; and *Mycoplasma pneumoniae*. Overnight fixation at +4° C. was employed (Bradstreet and Taylor, 1962), a microtitre apparatus (Sever, 1962) being used. Antibody titres in sera from pregnant women exposed to or contracting rubella were determined by neutralization (Dudgeon, Butler, and Plotkin, 1964) and complement-fixation tests (Sever *et al.*, 1965). Sera from patients from whom enteroviruses were isolated were, whenever possible, tested for significant rises (fourfold or greater) in antibody titre to the particular virus isolated. Serological evidence of mumps infection was detected by complement fixation, and measles by both complement fixation and haemagglutination inhibition. During the time that influenza was epidemic (January and February 1966) patients with possible influenza virus infection who failed to show significant rises in complement-fixing antibody titre were tested by haemagglutination inhibition (A2Eng. 1964).

Results

From 306 patients referred for virological investigations 741 specimens were obtained. The following patients were excluded: those who were subsequently shown to have disease which was non-viral (13); those from whom adequate specimens were not obtained—for example, because of inability to obtain "convalescent" sera when a serological diagnosis was to be attempted (11); and those referred for estimation of antibody to rubella virus when exposed to possible rubella in early

---

* Clinical Virology Laboratory, Department of Medical Microbiology, St. Thomas's Hospital, London S.E.1.

pregnancy (17). Attempts at diagnosis were completed on 262 patients. An aetiological agent was identified in 96 (36.6%) of these cases. A diagnosis by virus isolation alone was made in 56 (58%) of the 96 cases, by serology in 19 (20%), and by both serology and virus isolation in 21 (22%). However, serum was not obtained from 38 of these patients who attended the departments of venereology and dermatology with vesicular lesions of the skin or mucous membranes caused by herpes simplex virus, nor from five infants with acute respiratory infection from whom respiratory syncytial virus (2 cases), adenovirus (2 cases), and parainfluenza 3 virus (1 case) were isolated.

Table I lists the viruses detected and the principal clinical syndromes with which they were associated. The number of patients referred by different hospital departments and the results of virological investigations on them are shown in Table II. The high proportion of patients referred by the venereology department was partly caused by a survey on patients with herpes genitalis. Herpes simplex virus was isolated from 28 (38%) of 73 patients with clinical herpes genitalis, no other virus being isolated. Though the clinical diagnosis of herpes genitalis may be simple enough when typical vesicles are present, once ulceration has occurred other conditions have to be differentiated. The most important of these is syphilitic chancre, but such diseases as chancroid, lymphogranuloma venereum, candidiasis, and Behçet's syndrome may also have to be considered. Concomitant serological tests (Wassermann reaction and Reiter's protein complement-fixation test) did not reveal any cases of primary syphilis in this series. The detailed results of this investigation are being published elsewhere.

Fifty-two members of the hospital staff, most of whom were nurses, were referred for virological investigation. The high incidence of infectious disease in general, and of acute respiratory and exanthematous disease in particular, is characteristic of communities of young adults living in close quarters. It was possible to obtain specimens from most of these patients within 72 hours of the onset of symptoms, this probably contributing toward the high diagnostic rate (46%) in this group. Rubella was prevalent among the nursing staff from March to April 1966. Since rubella often presents atypically and because of the relation between maternal rubella and congenital malformation, it was thought to be important to confirm the diagnosis of rubella virologically in nurses, not only for their own future reference, but also in order to exclude them from places where they might have contact with pregnant women (for example, children's wards, mothercraft clinics, etc.) until after the period of virus excretion—up to 14 days from the onset of rash (Krugman and Ward, 1964 ; Green *et al.*, 1965).

The paediatric department has 32 medical beds, but is also responsible for the care of newborn babies. A diagnosis was made on 20 (44%) of 45 cases investigated. The admission rate for acute respiratory infections, which is frequently high during winter, often coinciding with the prevalence of respiratory syncytial and parainfluenza viruses in the community (Chanock and Parrott, 1965), showed no marked increase during the winter months of the investigation. It is of interest that studies on 15 infants with congenital defects or neonatal infections revealed six cases of congenital rubella, five infants having many of the characteristic features of the rubella syndrome (Table III). These infants also possessed some of the additional features described as part of the "expanded" rubella syndrome noted after the large rubella epidemic in the U.S.A. in 1964 (American Pediatric Society and Society for Pediatric Research, 1965). Five of these six infants were of West Indian origin, there being a history of maternal rubella in only one of these cases. In hospital these infants were

Table I.—*Principal Clinical Syndromes with Associated Viral Diagnosis*

Clinical Category		Influenza A	Influenza B	Parainfluenza	Adenovirus	R.S.V.	*M. pneumoniae*	E.C.H.O.	Coxsackie	Poliovirus	Rubella	Measles	Mumps	Herpes Simplex	Total
Acute respiratory infection	Adults	8	1				2	2 (E 16)	1 (B 2)					1	15
	Children			1 (P 3)	2 (Ad 1)	4									7
Exanthema								1 (E 16)	*3 (A 16)		13	2			19
Acute C.N.S. infections ..								1 (E 14)		1 (P 1)					2
Congenital malformations											6				6
Genital herpes														28	28
Non-genital herpetic lesions														5	5
Ulcerative stomatitis ..														2	2
Bornholm disease ..								2 (E 1)	1 (B 2)						3
Conjunctivitis/keratoconjunctivitis					2 (Ad 3, 10)									3	5
Mumps													4		4
Total ..		8	1	1	4	4	2	6	5	1	19	2	4	39	96

* Hand, foot, and mouth syndrome. Serotypes identified are given in parentheses.

Table II.—*Departments from which Patients were Referred, Together with Virus Infections Diagnosed*

Department	No. of Cases	No. of Diagnoses	Influenza A	Influenza B	Parainfluenza	Adenovirus	R.S.V.	*M. pneumoniae*	E.C.H.O.	Coxsackie	Poliovirus	Rubella	Measles	Mumps	Herpes Simplex
Venereology ..	73	28 (38·3%)													28
Staff	56	26 (46·4%)	8						2 (E 16)	1 (B 2)		12	1		2
Paediatric ..	45	20 (44·4%)			1 (P 3)	2 (Ad 1)	4		2 (E 14 and 16)			7		2	2
General medicine	53	11 (20·8%)		1				2	2 (E 1)	1 (B 2)	1 (P 1)			2	2
Dermatology ..	15	6 (40·0%)								3 (A 16)			1		2
Ophthalmology ..	20	5 (25·0%)				2 (Ad 3, 10)									3
Total ..	262	96 (36·6%)	8	1	1	4	4	2	6	5	1	19	2	4	39

Table III.—*Principal Clinical and Virological Features in Children with Congenital Rubella*

Case No.	History of Maternal Rubella	Age at Investigation	Principal Clinical Features	Virus Isolation		Neutralizing Antibody	
				Site	Duration of Excretion	Baby	Mother
1	–	6 months	Bilateral cataract, V.S.D.	+ (T.S.)	7 months	1 : 64	1 : 48
2	–	1 month	Neonatal hepatitis, splenomegaly, low birth weight	+ (T.S.)	2 „	1 : 10	N.T.
3	–	3 years	Bilateral perceptive deafness	Not tested	—	1 : 64	1 : 8
4	+	1 week	Apparently healthy baby	+ (T.S.)	Not known	1 : 48	1 : 64
5	–	2 weeks	Hepatosplenomegaly, cloudy corneas, low birth weight, maladsorption	+ (T.S.; C.S.F.; C.S.; urine)	*2 months	1 : 24	1 : 48
6	–	6 days	Bilateral cataract, V.S.D. and P.D.A.	+ (T.S.; C.S.)	*1 month	1 : 48	1 : 48

* Still excreting virus. C.S. = Conjunctival swab. T.S. = Throat swab. V.S.D. = Ventricular septal defect. P.D.A. = Patent ductus arteriosus.

isolated and tested for virus excretion at regular intervals. When at home, mothers were warned not to expose their infants to women who might be pregnant, until such time as tests showed that excretion had ceased. Nevertheless, one infant (Case 4) infected ten nurses during her stay in hospital. No virus other than rubella was recovered from any of the infants with neonatal infection or congenital malformation.

In relation to the number of beds available (298) a disproportionately small number of patients (53) were referred for investigation by the general physicians. Twenty of these patients had had symptoms for one week or longer, thereby making it difficult to be certain that any virus which was isolated was responsible for the patient's illness. Of the 11 patients in this group in whom serological evidence of infection was found or from whom virus was recovered, three had Bornholm disease, and from their stools E.C.H.O. 1 virus (two cases) and Coxsackie B2 virus (one case) were isolated. However, these patients showed neither rising nor elevated antibody titres to the respective viruses recovered, making the relation between virus isolation and illness tenuous.

A diagnosis was made in 19 patients with exanthematous disease (Table I). Generally, apart from cases of rubella, virus studies were not attempted on patients in whom clinical diagnosis was obvious, but only on those who presented a diagnostic problem; examples being a woman of 63 with a respiratory infection, high fever, and maculopapular rash who developed a significant rise in measles antibody titre during the course of her illness, and a child aged 6 months with fever and maculopapular rash from whose throat E.C.H.O. 16 virus was isolated.

Studies were conducted on 17 women exposed during early pregnancy to cases of possible rubella. Four of them were investigated within seven days of exposure, two having been exposed to a child with rubella while visiting their children in hospital. All of these patients were found to have neutralizing antibody to rubella virus, indicating previous infection. They were therefore immune to subsequent infection (Brody *et al.*, 1965; Green *et al.*, 1965). All but one of the remaining patients had neutralizing antibodies ranging from 1:8 to 1:32. However, these women presented at intervals ranging from four to eight weeks after exposure, making the interpretation of results difficult, since it was impossible to say whether their neutralizing antibody titre was acquired as a result of recent or of past infection. More recently, complement-fixation tests were performed in conjunction with neutralization tests, the presence of high titres of complement-fixing antibody being suggestive of recent infection (Sever *et al.*, 1965). Of four patients tested by both neutralization and complement fixation, none had complement-fixing antibody, suggesting that their neutralizing antibody was not a result of recent infection.

Discussion

In contrast to the position a decade or so ago, a virus diagnostic laboratory may be called upon to undertake investigations on an ever-increasing range of viruses. Thus facilities were provided, for example, for the detection of viruses causing acute respiratory and C.N.S. infections; viruses causing neonatal infections or congenital malformations—for example, rubella, cytomegalovirus, herpes simplex; as well as viruses responsible for exanthematous infections—for example, measles, variola, varicella/zoster, and enteroviruses. Such diagnostic procedures required the maintenance of numerous continuous cell-culture lines and the provision of a variety of serological techniques. Furthermore, the deployment of a small staff in both routine and research and the time involved in both seeing patients and discussing these cases with clinicians often imposed considerable strain on the laboratory's resources. Nevertheless, close co-operation between laboratory staff and clinical personnel proved invaluable, saving work in the long run by ensuring that good clinical material was selected for study and that correct specimens were obtained in the best possible condition with the minimum delay.

However, these factors necessitated some restrictions in the number and types of cases investigated. The 262 cases were investigated as a cost of approximately £40 per patient. A more economic figure could have been achieved only by carrying out a more limited range of investigations. An increase in the number of patients investigated or extension of services to neighbouring hospitals in our group would certainly have necessitated the provision of greater space and more personnel, or a regular supply of cell cultures ready for use from a commercial source. These factors would have entailed much greater expense.

Our experience over the past year demonstrated that the laboratory provided a useful service to certain hospital departments, whereas to others it was of less value than we had expected.

For example, virus studies which clinicians thought useful were the investigation of maternal and neonatal rubella, the diagnosis of atypically presenting exanthematous disease, and the differential diagnosis of vesicular lesions in patients referred by the dermatologists and venereologists. However, in contrast to many bacteriological investigations, most virological diagnostic procedures take a long time to complete, and the results can therefore seldom influence clinicians in the management of acutely ill patients. Furthermore, we found that investigations on many patients admitted to general medical wards who presented as "interesting" or "puzzling" cases with perhaps an unexplained fever or haematological features "consistent with viral infection" were usually unrewarding, since by the time such patients were admitted to hospital they were long past the acute phase of their illness, making either positive or negative virus isolation or serology difficult to interpret. Consequently, we investigated and obtained diagnoses on proportionately fewer patients referred by general physicians than on those referred from other departments in the hospital.

Most diagnostic laboratories dealing with large numbers of specimens are attached to the Public Health Laboratory Service, to hospitals for infectious diseases, or to children's hospitals, most of which, unlike our laboratory, can obtain large amounts of suitable clinical material from acutely ill patients. We believe that most value can be obtained from a laboratory such as ours, which is also an integral part of a research department of a teaching hospital, not by providing a fully comprehensive diagnostic service but by specializing in certain fields, working on them in depth, and training personnel in both diagnostic and research methods. General diagnostic services should mainly be restricted to cases where infectious disease provides an urgent public health problem or requires definite action (for example, smallpox, poliomyelitis, maternal and neonatal rubella), or is likely to prove genuinely useful to clinicians (for example, differential diagnosis of acute C.N.S. infections and atypically presenting exanthematous infection). Inevitably, in these circumstances the services of other laboratories would be required to perform additional tests which a small laboratory could not undertake.

Though many virological investigations are at present of limited value to clinicians, a clinical virology laboratory may profitably extend its studies to the investigation of the role of different agents in varying communities, thus "pin-pointing" specific public health and epidemiological problems. In addition, combined clinical and virological studies, conducted on carefully selected clinical material, are also likely to be rewarding if performed as well-defined projects. Though viral chemotherapy is not generally available today, the position may alter in the future. In such an event, increased sensitivity and diagnostic speed may well be essential, and clinical virology laboratories are particularly well placed to undertake work in order to achieve such aims.

Thus, in these ways clinical virology provides fields where routine and research work may profitably coexist hand in hand, much rewarding research stemming from properly collected specimens from well-documented cases.

Summary

A diagnosis was made on 96 (36.6%) of 262 patients referred for virological investigations between 21 January 1966 and 20 January 1967. The highest numbers of patients were referred by the departments of paediatrics and venereology and from the physician in charge of nurses' health. The highest diagnostic rates were achieved on those patients referred by the nurses' physician (46.4%) and by the paediatricians (44.4%). Investigations on women exposed to or contracting rubella in early pregnancy, on infants with congenital malformations or neonatal infections, and on exanthematous infections which presented atypically were thought to be among the most useful studies conducted. Difficulties encountered in providing a fully comprehensive diagnostic service are described, and emphasis is placed on the importance of conducting epidemiological, clinical, and virological studies on carefully selected material alongside routine diagnostic investigations.

We are grateful to the St. Thomas's Hospital Endowment Fund Committee and the Wellcome Trust for generous financial contributions; to Dr. C. M. P. Bradstreet, Standards Laboratory, Central Public Health Laboratories, Colindale, for supplying numerous serological reagents; to the Virus Reference Laboratory at Colindale and Epsom for typing various enteroviruses; and to the consultant staff of St. Thomas's Hospital for permission to investigate patients admitted under their care. One of us (J. M. B.) is in receipt of a grant from the M.R.C. in order to undertake research on rubella virus.

References

American Pediatric Society and Society for Pediatric Research (1965). *Amer. J. Dis. Child.*, **110**, 345.
Bradstreet, C. M. P., and Taylor, C. E. D. (1962). *Mth. Bull. Minist. Hlth Lab. Serv.*, **21**, 96.
Brody, J. A., Sever, J. L., McAlister, R., Schiff, G. M., and Cutting, R. (1965). *J. Amer. med. Ass.*, **191**, 619.
Chanock, R. M., and Parrott, R. H. (1965). *Pediatrics*, **36**, 21.
Dudgeon, J. A., Butler, N. R., and Plotkin, S. A. (1964). *Brit. med. J.*, **2**, 155.
Green, R. H., Balsamo, M. R., Giles, J. P., Krugman, S., and Mirick, G. S. (1965). *Amer. J. Dis. Child.*, **110**, 348.
Krugman, S., and Ward, R. (1964). In *Infectious Diseases of Children*, 3rd ed., **19**, p. 262. St. Louis.
Lenette, E. (1964). In *Diagnostic Procedures for Viral and Rickettsial Diseases*, edited by E. Lenette and N. J. Schmidt, **1**, 1. American Public Health Association.
McCarthy, K., Taylor-Robinson, C. H., and Pillinger, S. E. (1963). *Lancet*, **2**, 593.
Parkman, P. D., Buescher, E. L., and Artenstein, M. S. (1962). *Proc. Soc. exp. Biol. (N.Y.)*, **111**, 225.
Sever, J. L. (1962). *J. Immunol.*, **88**, 320.
—— *et al.* (1965). *Science*, **148**, 385.

COMPUTERS IN MEDICINE

Notification of Death Occurring after Discharge from Hospital

M. R. HUBBARD*; E. D. ACHESON,† M.A., D.M., F.R.C.P.

Brit. med. J., 1967, 3, 612–613

Although the fact of death has been recorded in practically all instances in this country since the Registration Act of 1837, and a quarterly alphabetical index of persons dying is maintained at Somerset House by the Registrar General, it may still be difficult for a doctor to discover which of a group of patients treated by him has since died. This paper describes an experiment in the systematic notification of deaths occurring after discharge to the hospitals in the Oxford area by a computer method.

Material and Method

Since the beginning of 1962 data from records of every birth, admission to hospital, and death in the population of Oxford and the surrounding area have been abstracted, coded, punched on cards, and matched into personal cumulative files (Acheson, 1964, 1967). This paper deals with hospital discharges and deaths in the defined population during 1963 and 1964. During these years the electromechanical system of data-processing set up in 1962 was replaced by a computer system.

Two cards are punched for each event—an identification card, containing the name, date of birth, N.H.S. number (if known), and other identifying data, and a statistics card carrying coded diagnostic and administrative information. The data are read on to magnetic tape, and edited. They are then sorted into sequence by using the Russell–Soundex phonetic code, sex, and initial as the sorting items, and each new record is compared with all records in the equivalent subdivision of the master file. The system of record linkage is based on the principles described by Newcombe, Kennedy, Axford, and James (1959), whereby discrepant records are dealt with by allotting appropriate weighting factors (positive or negative) to agreements and discrepancies.

The product of the record linkage programme is a compound cumulative file which contains one entry for each person encountered by the system, each consisting of identification data and the records of a variable number of the defined events.

The next step was to scan the master file for all patients whose records included a death certificate and to write these records on to a separate magnetic tape. Records were selected from this tape for patients who had died in 1963 or 1964 and who had been discharged from hospital once or more in that period. An item was then formed for each discharge containing the following data: identification of patient, date of discharge, date of death, diagnosis on discharge (hospital record), and cause of death (death certificate).

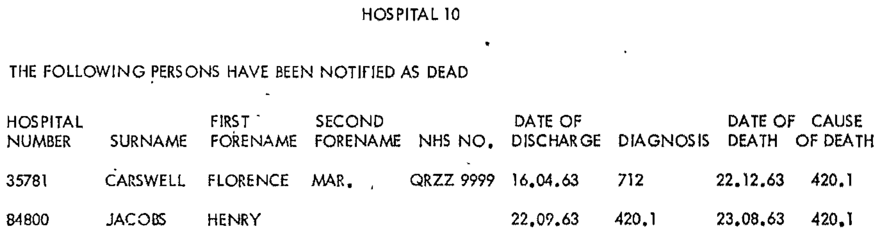
If the patient died while in a hospital all items relating to that hospital were deleted, as it was assumed that the hospital was bound to be aware of the death. To avoid multiple notifications of a death where a patient had been discharged more than once from a hospital, the record of the final discharge was the only one retained. By means of the appropriate sorting lists of persons discharged from hospital within the two-year period who died at home or in another hospital were then prepared for each hospital and printed in alphabetical order of surname. Two years after the last death in the series had occurred—that is, at the end of 1966—the lists were sent to the medical records officer of each hospital in the area.

---

* Computer Scientist.
† May Reader in Medicine.
The Oxford Record Linkage Study, Nuffield Department of Clinical Medicine, University of Oxford.

Results

A facsimile of a section of one of the listings is shown in the accompanying Figure, the surnames having been changed to maintain confidence. From left to right are written the names of the patient, the N.H.S. number, the date of the last discharge from the hospital, the code number of the principal diagnosis reached at that time, the date of death, and the code number of the underlying cause of death as stated on the death certificate.



HOSPITAL 10

THE FOLLOWING PERSONS HAVE BEEN NOTIFIED AS DEAD

HOSPITAL NUMBER	SURNAME	FIRST FORENAME	SECOND FORENAME	NHS NO.	DATE OF DISCHARGE	DIAGNOSIS	DATE OF DEATH	CAUSE OF DEATH
35781	CARSWELL	FLORENCE	MAR.	QRZZ 9999	16.04.63	712	22.12.63	420.1
84800	JACOBS	HENRY			22.09.63	420.1	23.08.63	420.1

Facsimile of section of the record.

Table I shows the proportion of deaths about which the various hospitals had been informed before receipt of the listing. Small country hospitals without records departments were excluded from this analysis. Taken overall, a little more than one-third (38.4%) of the deaths had already been notified. The substantially higher proportion of notified cases in the special hospitals (63.4%) was due to the practice at the hospital for chest diseases of searching a complete return of death certificates supplied quarterly by the medical officer of health for the names of old patients. In a previous analysis (Acheson, 1967) it was shown that the proportions of deaths notified were as great in those not dying of cancer as in those dying of this condition—that is, the deficiency was not due to the assumption of death in terminal cases.

In Table II a sample of the cases has been classified according to the time interval elapsing between discharge and death. Though the trend is irregular, the proportion of deaths known to the hospitals falls off as the time interval between discharge and death increases ($\chi^2 = 15.85$; $P<0.01$). Nevertheless, almost half the deaths *occurring within one month of discharge* had gone unrecorded in the records departments of the hospitals concerned.

Discussion

An interesting feature of this study was that it uncovered a deficiency in communication of which the hospitals themselves were unaware. In the two principal groups considerable pains had been taken to ascertain death when it occurred after discharge, both by following up missed outpatient appointments and by scanning the obituary columns of the local papers. The ineffectiveness of these measures came as a surprise. The only hospital with complete information was the chest hospital, which, perhaps because of a long tradition of following up patients with tuberculosis, made a systematic study of the quarterly death returns from the medical officer of health. Another specialist hospital knew of none of the deaths which had occurred after discharge.

Table I.—*Numbers and Proportions of Deaths Occurring After Discharge from Hospital Not Noted in the Hospital Records*

	Deaths Known to Hospital		Deaths Not Known to Hospital		Total
	No.	%	No.	%	
Teaching hospitals ..	362	35·2	677	64·8	1,039
District hospital ..	58	40·0	87	60·0	145
Mental hospitals ..	16	29·6	38	70·4	54
Specialist hospitals ..	90	63·4	52	36·6	142
All hospitals ..	526	38·4	854	62·3	1,380

Table II.—*Effect of the Interval Between Discharge and Death on the Proportion of Deaths Known to the Hospital*

Interval Between Discharge and Death	Death Known to Hospital		Death Not Known to Hospital	Total
	No.	%		
1 month	52	50·0	52	104
2–3 months	71	39·7	108	179
4–6 months	35	26·7	96	131
7–12 months ..	40	40·1	58	98
1 year + ...	10	27·0	27	37
Total ..	208	37·9	341	549

The possible usefulness of feeding back this type of information to hospitals may be considered under three headings—namely, its administrative value ; its value to research workers ; and its possible importance to the clinician in his evaluation of the correctness of the diagnosis, the effectiveness of the treatment, and the accuracy of the prognosis which he had given.

From the administrator's point of view notification of death means that the patient's dossier can be completed and be retired to relatively inexpensive filing space. The risk of importuning the relatives with correspondence addressed to a person who is dead will be avoided. Also, the advantage of accurate notification of death to the clinical research worker is obvious.

It is more difficult to be certain of the value of the data to the clinician himself, and it is proposed to mount a more detailed clinical study of a sample of the deaths with such an evaluation in mind. Preliminary analysis suggests that the majority of the deaths will prove either to have been more or less inevitable or to be irrelevant from the standpoint of the clinician in charge of the final episode of inpatient treatment. However, a minority of the reports are likely to prove of considerable interest in that they may influence the clinician in the treatment of similar cases in future.

If it were thought desirable to provide this type of service on a regular and extended scale, this could be done either by a system of linked records or by asking for the name of the hospital from which the deceased person had been discharged to be recorded on the death certificate. Table II suggests that the service might reasonably be limited to hospitals from which the patient had been discharged within the 12 months before death.

Summary

Only one-third of the deaths occurring within a two-year period after discharge from a group of hospitals had been recorded in the hospital notes of the patients concerned ; of those occurring within one month of discharge from hospital one-half had been recorded. The possible merits of supplying the missing data are discussed from the administrative and clinical points of view.

The Oxford Record Linkage Study is supported by grants from the Nuffield Foundation, the Ministry of Health, and the Nuffield Provincial Hospitals Trust.

References

Acheson, E. D. (1964). *Brit. J. prev. soc. Med.*, **18**, 8.
—— (1967). *Medical Record Linkage.* Oxford University Press, London.
Newcombe, H. B., Kennedy, J. M., Axford, S. J., and James, A. P. (1959). *Science*, **130**, 954.

Correspondence

Letters to the Editor should not exceed 500 words.

Yearly or Quinquennial Grants?

SIR,—Mr. A. McWilliam (19 August, p. 489) gives a general report on the advantages of the quinquennial grant system of financing universities.

It is often implied that this system might be used with advantage in the National Health Service. Comparatively few people, however, have first-hand experience of the application of both the annual and quinquennial systems. The fact that the two methods have existed for 19 years side by side in teaching hospitals and medical schools may be held to indicate that neither system is wholly satisfactory. In this period if one system had no disadvantage it would have displaced the other.

What are the disadvantages of the quinquennial grant system? I think there are none in an economy in which there is no monetary depreciation. The difficulties arise when there is inflation. Mr. McWilliam says, "The quinquennial block grant, without any supplementation except for proved increased costs (and by no means all of these), is both an incentive to economy and a firm basis for forward planning." The unfortunate fact is that, apart from academic salary increases and the rates on property paid to the local authority, there is no significant supplementation throughout the quinquennium. In any recent five-year period rises in wages and non-academic salaries, particularly of technicians, which have not been reimbursed, have severely hampered planned development. Most of the medical schools in London have ended up quinquennia with considerable deficits, which rightly have been carried over as a first charge on subsequent grants.

The development of medical teaching and research is now so rapid and costs rise so unpredictably that five years is too long a period for medical schools or the University Grants Committee to make realistic financial forecasts of recurrent expenditure. The alternative need not be an annual grant, something in between may well be about right.—I am, etc.,

H. B. MAY.

Esher, Surrey.

Disturbed Geriatric Patients

SIR,—We should like to comment on Dr. H. M. Davies's letter (5 August, p. 367). The need for integration of the services for the aged has been recognized by many of those who work in this field. The problem that awaits solution is how to make some progress towards this logical and desirable objective.

Inquiries carried out in this city[1 2] have shown that considerable overlap existed between patients treated in general hospitals, geriatric wards, psychiatric units, and residential homes. Patients requiring medical treatment, psychiatric care, social support, or in need of help in each of these ways were to some extent found in every kind of unit. In an attempt to overcome this a consultant psychiatrist was appointed jointly to the regional hospital board and the local authority in 1961. In 1962 the local authority health and welfare departments combined, and the consultant in geriatrics was given honorary status within the new health and social services department. In 1963 a senior medical officer was appointed by the local authority specifically to assess the needs of the elderly and handicapped referred for and already in residential homes; the liaison so established has been described elsewhere.[3] With this organization a more integrated and co-ordinated service for the elderly has been possible. A more recent development has been the appointment by the regional board of a consultant psychiatrist with special interest in the mental disorders of old age. Psychogeriatric units and day hospitals are being developed in the general and mental hospitals in the city, and it is planned to employ these new developments so as to bring together at regular intervals all those concerned with the care of elderly patients in different settings and thus take further steps towards integration of the services.

The pattern of co-ordinated work that has evolved demands much patience, hard work, and, above all, tolerance and understanding of others' viewpoints, patterns of professional life, and practical difficulties if it is to succeed. Dr. Davies's suggestion to appoint a single doctor to co-ordinate services is a logical objective, but sets up an ideal which at the present stage of development would be difficult to translate into a practical reality. We feel that it would perhaps be better to modify the Newcastle upon Tyne organization, so that joint appointments in both geriatrics (as described by Wollner[4]) and in psychiatry (as in Newcastle upon Tyne) should be made to the regional hospital board and local authority and both consultants brought into a close working relationship with the senior medical officer (geriatrics), who has reciprocal attachments with the regional hospital board. This triad would then be responsible for the integration, co-ordination, and operation of the geriatric services, perhaps along lines already described.[5]—We are, etc.,

M. R. P. HALL.
R. C. M. PEARSON.
MARTIN ROTH.

Department of Psychological
Medicine,
University of Newcastle upon Tyne.

REFERENCES

[1] Kay, D. W. K., Beamish, P., and Roth, M., *The Sociological Review Monogr.*, No. 5, 1962.
[2] —— —— —— *Brit. J. Psychiat.*, 1964, **110**, 146.
[3] Grant, J., and Hall, M. R. P., in *Proceedings 7th International Congress Geront.*, 1966. Vienna.
[4] Wollner, L., *Geront. clin. (Basel)*, 1964, 6, 65.
[5] Kay, D. W. K., Roth, M., and Hall, M. R. P., *Brit. med. J.*, 1966, 2, 967.

Propranolol in Myxoedema

SIR,—May I direct the attention of your readers to a use of propranolol that appears to be insufficiently known?

Patients are not infrequently seen who are suffering from myxoedema, and therefore need treatment with thyroxine, whose hearts are so sensitive to the β-adrenergic enhancement produced by thyroxine that it cannot be used alone. I have seen many myxoedematous patients who develop on very small doses a dangerous tachycardia or angina and a few who have been precipitated into congestive heart failure.

These patients may be restored to health by combining propranolol with thyroxine. They should be treated first with small doses of the former, followed soon by small doses of the latter. The doses of the two drugs are then raised stepwise, any suggestion of cardiac symptoms heralding a slight temporary decrease in the dose of thyroxine and an increase in that of propranolol before the dose of thyroxine is raised again. In this way these patients can eventually tolerate a dose of thyroxine high enough to correct their metabolic deficit.

I am sure that this method of treatment is used by many physicians, but, as the manufacturers of propranolol know of no publication on the subject, I hope that this letter may be useful.—I am, etc.,

London W.1. RAYMOND GREENE.

Carcinogenicity of Tobacco and Tobacco Smoke

SIR,—I was interested to read (5 August, p. 373) Dr. M. Glass's letter pointing out that cigarette smoker's carcinoma of the finger has never been reported. It is probably not the smoke which seeps through the cigarette paper after the first puff of the cigarette which is dangerous. The very interesting finding that the incidence of bronchogenic carcinoma in those who smoke a given number of cigarettes a day is similar to that in people who smoke half that number but stub out their cigarettes half way through and light them up again later points to the probability that the dangerous part of the cigarette is the part which is raised to a high temperature by the match flame. The carcinogenic factor(s) seem therefore to be contained in the smoke inhaled from the super-heated area. I should like to see an inquiry made into the habits of smokers in order to distinguish those who inhale the first puff of a cigarette from those who reject it before inhaling the subsequent ones.—I am, etc.,

H. DALE BECKETT.

Cane Hill Hospital,
Coulsdon, Surrey.

SIR,—Dr. M. Glass (5 August, p. 373) asks, if tobacco smoke is a carcinogen for man, " Is it not surprising, and indeed significant, that, among the millions of tobacco-stained fingers that have been continually contaminated with tobacco smoke condensates and tars in heavy cigarette smokers . . . not a single instance of cigarette-smoker's finger (papilloma or carcinoma) has ever been seen or reported ? " The shortest answer to this naive question is, " No." Human epidermis is very thick and is protected by a more generous layer of keratin (Figs. 1 and 2) in comparison with the epidermis of the mouse (Fig. 3), which develops cancers very readily in response to the application of tobacco smoke condensates. In terms of thicknesses the epidermis of the mouse and of the epithelium of the human bronchus are not dissimilar.—We are, etc.,

F. J. C. ROE.
A. LEVENE.

Institute of Cancer Research
and Royal Marsden Hospital,
London S.W.3.

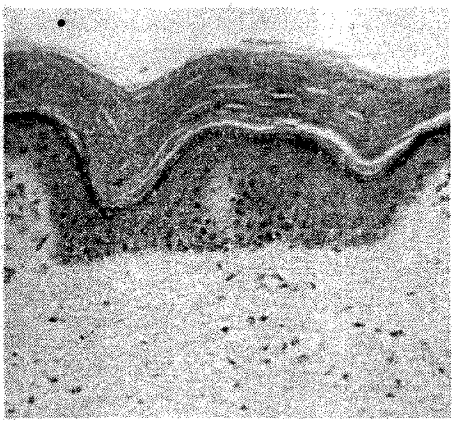


FIG. 1.—Epidermis from dorsal surface of human finger. (H. and E. ×180.)

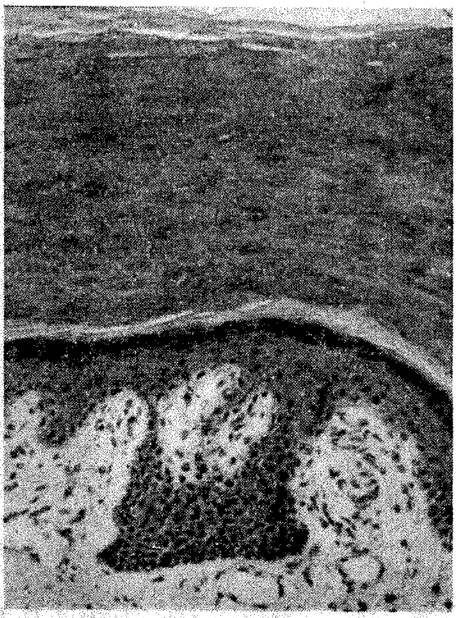


FIG. 2.—Epidermis from palmar surface of human finger. (H. and E. ×180.)

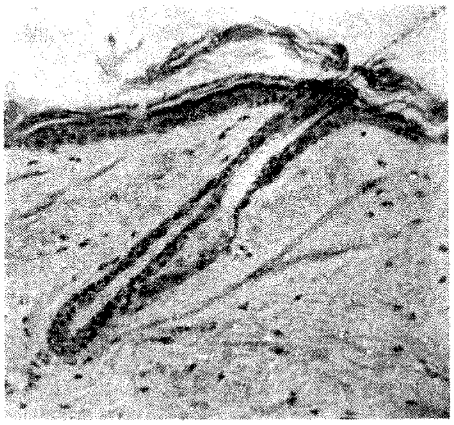


FIG. 3.—Epidermis from dorsal skin of mouse. (H. and E. ×180.)

Carcinogenic Properties of Ortho-dianisidine

SIR,—I do not have any special knowledge of the carcinogenic bases used in laboratories, nor have I done more than discuss with some knowledgeable colleagues the practical problems involved. The following represents the opinion of a chemical pathologist who has used these substances extensively in various analytical procedures during the last 30 years.

Of the dangerous substances few are used in the clinical laboratory. The most important are: (*a*) Benzidine and all its derivatives, including ortho-tolidine and ortho-dianisidine ; (*b*) amino-nitro- and nitroso-naphthalenes, of which the most used are 1-nitroso-2-naphthol for the estimation of urinary 5-hydroxyindole acetic acid, and 1-naphthylethylene diamine, the Bratton and Marshall coupling reagent.

There are a few other reagents incriminated, notably the dyes auramine and magenta, and possibly the nitrophenols ; but these are used relatively little except in the fluorescent staining of tubercle bacilli. Richards and Miller[1] have investigated other fluorochromes, but, as far as I can judge, use for staining would lead to minimal exposure.

Serious danger is due to contamination gross by any analytical standards, such as is unlikely in any clinical laboratory. Reasonable precautions should suffice ; such are the avoidance of pipetting using direct mouth suction, and the use of disposable plastic gloves to handle containers on the outside of which solutions of ortho-tolidine have crept and evaporated. However, we are advised that no threshold dose seems to exist, and, if this is so, it is our moral duty to remove all these carcinogens from routine use as soon as is possible. Fortunately many alternatives are available or will soon become so.

In testing for occult blood benzidine and ortho-tolidine tests have been popular because they are very sensitive and easy to perform. Many observers find their sensitivity too great.[2-4] Indeed, some have concluded that if enough tests were done positive results would occur in every healthy individual. These very sensitive reagents have therefore been modified so that their full sensitivity is not used.[2 5 6] Other less sensitive tests using " safe " reagents, though frequently proposed, are all less convenient ; but in future we shall have to tolerate the inconvenience. Those most popular are the amidopyrin test[7] and the reduced phenolphthalein or phenolphthalein test of Kastle and Meyer, either in its direct form[8] or in the modification described by Varley.[9] The chemoluminescence test of McGrath[10] is inconvenient, though it seems possible that it, alone of the known methods, could be adapted to give an objective reading.

My own experiments with the leuco-bases of green dyes have not produced satisfactory results. I suggest, therefore, that some form of the phenolphthalein test should become standard practice: it is slightly less sensitive than the benzidine test.[11] To avoid the use of ortho-dianisidine or ortho-tolidine in the glucose-oxidase procedures, Trinder[12] has used adrenaline as a chromogen ; his procedure uses nearly twice as much blood as does that of Dick,[13] but even so it is easy to obtain capillary blood in sufficient volume. The Bratton and Marshall reagent can be replaced by a number of phenols ; β-naphthol is possible, and thymol was used in the early days of sulphonamides ; of course such phenols must be coupled in alkaline solution. There appears to be no substitute for 1-nitroso-2-naphthol, but it is possible that a reagent could be prepared extemporaneously, by mixing either an inorganic nitrite with β-naphthol, or hydroxylamine with ortho-naphthoquinone. In this case it could easily be washed down the sink without endangering anyone.—I am, etc.,

GEORGE DISCOMBE.

Central Middlesex Hospital,
London N.W.10.

REFERENCES

[1] Richards, O. W., and Miller, D. K., *Amer. J. clin. Path.*, 1941, **11**, Tech. Section, 1.
[2] Gregersen, J. P., *Arch. Verdau.*, 1919, **25**, 169.
[3] Ross, G., Gray, C. H., de Silva, S., and Newman, J., *Brit. med. J.*, 1964, **1**, 1351.
[4] Sagan, L. A., and Seigel, D., *Atomic Bomb Casualty Commission Technical Report*, 1964, Japan.
[5] Hughes, A., *Brit. med. J.*, 1952, **2**, 970.
[6] Kohn, J., and O'Kelly, T., *J. clin. Path.*, 1955, **8**, 249.
[7] Forshaw, J. W. B., and Mason, G. M., *Lancet*, 1954, **2**, 470.
[8] Gettler, A. O., and Kaye, S., *Amer. J. clin. Path.*, 1943, **13**, Tech. Section 77.
[9] Varley, H., *Practical clinical Biochemistry*, 1962, 3rd. ed., p. 275, London.
[10] McGrath, J., *Brit. med. J.*, 1942, **2**, 156.
[11] Caplan, H., and Discombe, G., ibid., 1951, **2**, 774.
[12] Trinder, P., personal communication, 1967.
[13] Dick, M., *J. clin. Path.*, 1965, **18**, 249, 485.

Lead Absorption in Children

SIR,—The object of our paper (20 May, p. 480) was to ascertain if, within a certain community, there was any evidence that mentally handicapped children were at greater risk from lead intoxication than children of normal intelligence ; and this we failed to demonstrate. There can be no doubt that it is of the utmost importance to consider lead poisoning when examining children showing evidence of either acute and chronic damage to the nervous system. The co-operation of the Nuffield Department of Occupational Health in carrying out estimations of blood lead levels has made it possible to include this investigation whenever necessary. However, we could not confirm the claim of Sir Alan Moncrieff and his colleagues[1] that the incidence of diagnosed cases of lead poisoning "has risen enormously when the estimation of blood lead becomes freely available." They state that blood lead levels between 40 and 60 µg./100 ml. should be carefully considered in the light of other clinical findings, especially among children under 5 years of age; if levels of over 36 µg./100 ml. of blood are regarded as abnormal, such a finding must raise the question of treatment with chelating agents. At the moment the position seems to be unproved. There is no doubt that everyone in this modern age is exposed to great risks of lead intoxication. Filling the kettle from the hot tap, for instance, can be hazardous.[2] It would therefore be surprising if occasional raised blood lead levels were not demonstrated among the general population. The significance of these in terms of chronic lead poisoning must be further studied.

Sir Alan Moncrieff and his colleagues in their paper did suggest that lead poisoning was commoner among mentally handicapped children than had been realized, and, although they did not say that it was of primary aetiological significance, they stressed that it may add to the brain damage of a child already retarded. In their letter (15 July, p. 174) they state that mentally retarded children with pica are clearly more liable to lead poisoning if there is lead in the environment, and this is true. However, in their paper the 20 mentally handicapped children studied in detail, and treated with chelating agents, did not all have pica. The child with a blood lead level of 48 µg./100 ml. blood was improved after treatment, but may have improved clinically from other factors. There was only a slight change in the assessments on the Griffiths mental development scale before and after treatment, and, depending on the profile, a D.Q. of 43 on this scale at the age of 3 may not be strictly comparable with an I.Q. of 56 on the Stanford–Binet, Form L-M, at the age of 4.

In spite of present legislation in this country there are still many dangers of lead intoxication. Surely much can be done in terms of prevention, and for the protection of children particularly at risk. The treatment of individual children must remain a clinical decision, but an isolated blood level only slightly raised above the accepted level for normal in a particular area would seem an insufficient indication for treatment in the absence of other symptoms and signs supporting the diagnosis of lead poisoning. We are certainly in agreement with the need to know at what level lead becomes actively toxic.—We are, etc.,

N. S. GORDON.
E. KING.
R. I. MACKAY.

Royal Manchester
Children's Hospital,
Pendlebury,
Nr. Manchester.

REFERENCES

[1] Moncrieff, A. A., Koumides, O. P., Clayton, B. E., Patrick, A. D., Renwick, A. G. C., and Roberts, G. E., *Arch. Dis. Childh.*, 1964, **39**, 1.

[2] Wilson, A. T., *Lancet*, 1967, **1**, 9[illegible].

Dermatitis from Occlusion Plasters

SIR,—Children who are having one eye occluded as part of the treatment of squint occasionally develop local dermatitis resulting from the plaster. Sometimes, with or without the advice of the family doctor, the occlusion is stopped. This seriously hampers the treatment of a squint, because occlusion should almost invariably be total. There are several other types of plaster available; rarely even these prove to be unacceptable.

There are two types of plaster which can be used in such special cases: Micropore, made by the 3M Co., and Dermicel, made by Johnson & Johnson. Both of these are expensive and cannot be prescribed on an E.C.10; they can, however, be obtained from the hospital. Family doctors should therefore in the circumstances where no other plaster is tolerated insist that the occlusion be continued and advise the mother to obtain a supply of one of these plasters from the hospital forthwith. It is strongly recommended that hospitals should carry stocks of one of these plasters, and should advise parents of squinting children that this type of plaster is available if necessary.

Probably most people are aware of this, but there may be some who are as ignorant as I was.—I am, etc.,

Portsmouth, Hants. NIGEL CRIDLAND.

Experiments on Man

SIR,—The report of the special committee of the Royal College of Physicians on this subject (12 August, p. 429) calls for comment. It is a white-washing, worthless document, purposely vague, and adding nothing to the publicized but often ignored recommendations of the Medical Research Council and the World Health Organization. The R.C.P. not initiating, organizing, or supervising any clinical research, how can its recommendations have any force, and how can they be implemented? What punishments will be meted out to any who flagrantly disregard its recommendations?

The committee divides clinical research into two groups: "the first is that which has direct diagnostic or therapeutic relevance to the individual patient, and which therefore seldom poses serious ethical problems." But it is within this very group that the R.C.P. could have given guidance. The real problem is what constitutes routine investigation. For example, what routine investigations are acceptable for a patient with hypertension? Is either renal biopsy or renal angiography an acceptable routine? What are the acceptable routine investigations in an intensive-care unit? One professor of medicine apparently considers that the insertion of three cardiac catheters into ascending aorta, pulmonary artery, and right atrium respectively to be a justifiable routine in such a unit. Would the committee agree?

The problem can be discussed another way. What are the indications for various investigations—for example, liver puncture, coronary angiography, combined right- and left-heart catheterization, renal angiography, etc.? Does not the committee realize that much questionable research is done under the guise of routine investigation? Does the committee seriously advise, as they appear to do in the report, that a doctor "could sometimes be said to have failed in his duty" if he did not perform any one of the investigations listed above? I wonder how many of the committee have actually read my book *Human Guinea Pigs*.[1]

We are informed: "even the most experienced workers would often welcome the opinion and advice of their peers." The words "peers" was no doubt carefully chosen as the most apt for an R.C.P. report. But who are the peers from whom the various professors, who are primarily research workers, are likely to seek advice?

I agree that the board of governors "has a responsibility to ensure that all clinical investigations carried out within its hospital or institution are ethical. . . ." But do the governors know of and understand the clinical research going on in their hospital?—I am, etc.,

London W.1. M. H. PAPPWORTH.

REFERENCE

[1] Pappworth, M. H., *Human Guinea Pigs*, 1967. London.

Digital Ischaemia and Malignant Disease

SIR,—I was interested to see the article by Mr. P. R. Hawley and colleagues (22 July, p. 208). The following case adds a further diagnosis to the association between digital ischaemia and malignant disease.

A 51-year-old quantity surveyor was seen in hospital on 25 September 1961. He gave a history of pain, blanching, and coldness of the left middle finger starting about the beginning of August 1961. On examination he was found to have incipient gangrene of the tip of the left middle finger. On 23 February 1962 the top of the left middle finger came off spontaneously and the pain was subsequently relieved.

Shortly afterwards, however, he felt unwell. He reported at outpatients on 30 April 1962, complaining of diarrhoea, sore throat, and loss of weight of 1 stone. On examination he was found to have generalized tender lymphadenopathy and the liver and spleen were just palpable. He was admitted to hospital, and a biopsy of glands from the groin and axilla showed a reticulosarcoma with total loss of normal lymph node architecture and replacement by sheets of pleomorphic cells and giant cells; there was increase in coarse reticulin. He died on 23 June 1962.

Post-mortem examination showed reticulum-celled sarcoma involving widespread lymph nodes, liver, kidneys, and gastric, intestinal and vesical mucosae. Death was ultimately due to bronchopneumonia.

This case would support Hawley *et al.* in their premise that unexplained, spontaneous digital ischaemia, particularly in those over 50, warrants very thorough investigation to exclude a malignant condition.—I am, etc.,

Dorchester,
Dorset. EDWARD JARRETT.

Safer Dental Anaesthesia

SIR,—Intravenous anaesthesia represents for the patient nothing less than a revolution in dental treatment and is one of the greatest advances in dentistry of modern times. But is it safe? This is an all-important question that must be answered.

The present death rate from dental anaesthesia, all methods included, is stated in a recent leading article comment in the *British Medical Journal*[1] to be at about four to six a year in this country, a marked improvement on the not-so-distant past. In 1952 22 lives were lost. Similar comment in the *Lancet*[2] puts the yearly total of administrations for extraction of teeth in the National Health Service at 1.7 million; to which, it says, must be added a large number given in private practice for this purpose, and an increasing number given for conservative dental work. It thus appears that in present-day practice the risk incurred in dentistry by the use of a general anaesthetic is exceedingly small. And most of these deaths occur in patients anaesthetized in hospitals, the mortality in dentists' surgeries being about one in a million.[3] Unfortunately, there are no figures to show to what extent, if any, the intravenous method is contributing to this mortality. My own views on this question[4] were based on an analysis of 37 deaths about which I had collected such information as there was; and on more than 100 cases, described to me by the dentists in whose surgeries they had occurred, of patients who came to the very brink of death but survived. I concluded that it made little difference what anaesthetic was used or who gave it; the problem was the traditional upright position of the patient, and the only effective remedy was to abandon that position.

At a recent demonstration I attended the patient took her place in the chair, which was promptly lowered into the horizontal position, forming in effect a level couch. The dentist gave an initial injection of anaesthetic intravenously, leaving the needle in situ, and then seated himself at the head of the patient. On either side of him sat his nurse assistants. The patient's colour was a healthy pink, her breathing was free and rhythmical, and she had all the appearances of being quietly asleep. A mouth pack was carefully placed in position, the nurse on the dentist's left directed the suction nozzle to the site of operation, and work began. At intervals of about two minutes further small increments of anaesthetic were given by one of the nurses until, about 12 minutes after the start, the dentist had finished. Two minutes later the patient was awake. At no time had any help been needed with the airway, and the dentist had been able to proceed with his work untroubled and without interruption. About 20 patients were treated in similar fashion.

The smoothness of the whole performance raised the query of what is the role of the second practitioner whose presence is strongly advocated by many people. Complications are rare, and, with the patient in the supine position, they present little difficulty, either in recognition, diagnosis, or treatment. There are three of major importance: obstructed airway, laryngeal spasm, and vomiting; and the persons best placed to spot them at once and deal with them effectively are the dentist and his nurses, poised, as they are, straight over the patient's face. The second practitioner's function could be to assess the patient's fitness for anaesthesia. There would be some point in this if he is required to be medically qualified, but this is not stipulated by those who insist on his presence.

What then can be the role of the second practitioner? I believe it is this: to help dentists who are unable to give the anaesthetic themselves. Anaesthesia is a demanding responsibility and training for the dual role is hard and expensive. The standards required are the highest attainable. And it is in fact to safeguard these standards that the Society for the Advancement of Anaesthesia in Dentistry has long desired teaching to be placed on an official basis, under the aegis of the Faculty of Anaesthetists, with a diploma for successful candidates. There is therefore plenty of room for the second practitioner; and dentists and doctors (and perhaps others, as I have suggested in a recent publication[5]) should be trained for this work.

The intravenous method is, I believe, inherently safe for the dentist who wishes to give his own anaesthetics, with certain provisos. Firstly, the dental work for which the anaesthetic is given must not be unduly prolonged, and require no more than the lightest levels of unconsciousness; secondly, the dentist must have been properly trained in the use of the intravenous method; thirdly, he must employ at least two nurses of suitable status and training to assist him; fourthly, his patients must be recumbent; and, finally, he must use always the smallest amounts of anaesthetic that meet the requirements. With such doses the patient is never more than two minutes from being virtually awake.—I am, etc.,

Salisbury,
Wilts.

J. G. BOURNE.

REFERENCES

[1] *Brit. med. J.*, 1967, 1, 447.
[2] *Lancet*, 1967, 1, 487.
[3] *Dental Anaesthesia*, Report of a Joint Subcommittee of the Standing Medical and Dental Advisory Committee, Ministry of Health, 1967, London.
[4] Bourne, J. G., *Lancet*, 1966, 1, 879.
[5] —— *Studies in Anaesthetics: Including Intravenous Dental Anaesthesia*, 1967, p. 159. London.

SIR,—Your correspondent Mr. S. L. Drummond-Jackson (12 August, p. 436) condemns the Government Report on Dental Anaesthesia[1] on the grounds that it lacks "conciseness and clarity" to such an extent that the British Dental Association has mistakenly expressed agreement with two important points made in the report, with which Mr. Drummond-Jackson feels they could not possibly have agreed had the report made its real meaning clear.

The first of these points is contained in paragraph 31 of the report, and this paragraph Mr. Drummond-Jackson interprets as implying that "dental students should receive no practical training in anaesthetics." Paragraph 31 contains the following sentence: "It seems to us that undergraduate instruction, including any clinical practice, should concentrate at an elementary level on the principles of anaesthesia, on the pharmacology of the drugs used and the risks inherent in their administration, on the basic conditions for safety, and on resuscitation." It is difficult to see why the British Dental Association should find this recommendation neither concise nor clear, and it is even more difficult to see why Mr. Drummond-Jackson should interpret the phrase "including any clinical practice" as meaning that no practical training should be given. The recommendation seems concise and clear enough to me. Furthermore, in a recent conference on general anaesthesia in dentistry called by the British Dental Association the following exchange is recorded.[2]

"Dr. Coplans asked if undergraduates entered any of the classifications or were they to be taught nothing at all? Dr. Bourne replied 'theory only.'"

Mr. Drummond-Jackson, who was sitting opposite me at this conference, raised neither an eyebrow nor any objection to this reply; no more did any of the five British Dental Association Representatives present, and indeed there was absolute agreement expressed by all parties represented that undergraduate training no longer fitted a doctor or dentist to administer anaesthetics routinely, nor should it attempt to do so—a view at least as extreme as any suggested by the report itself.

The second point is said to be contained in paragraphs 33, 34, and 35 of the report, which Mr. Drummond-Jackson interprets as implying that "dental graduates could not receive any postgraduate training which would enable them to provide a service." In fact the paragraphs in question simply suggest a number of different forms of postgraduate course designed to meet different needs, the details of which the report quite rightly leaves open for further discussion between the relevant medical and dental bodies. In the first of these discussions, the conference already referred to, the only positively restrictive idea emanated surprisingly enough from Mr. Drummond-Jackson himself, who suggested that in the future "the only man who could give dental anaesthetics was the man who attended such and such a course." [2]

Let us hope that the British Dental Association's agreement with large and important sections of the report will continue on the basis of the report's actual content, rather than be destroyed by careless misinterpretations of its main recommendations.—I am, etc.,

St. George's Hospital,
London S.W.1.

M. P. COPLANS.

REFERENCES

[1] *Dental Anaesthesia*, Report of a Joint Subcommittee of the Standing Medical and Dental Advisory Committees on Dental Anaesthesia, Ministry of Health, 1967, H.M.S.O.
[2] Supplement to *Brit. dent. J.*, Conference on General Anaesthesia in Dentistry, 20 June, 1967.

Holiday Camps for the Disabled

SIR,—This is a plea for careful medical examination of any disabled who are recommended even for a short holiday at a camp for disabled. The benefits of such a holiday are obviously great for disabled persons and also for relatives who may have to look after them for the rest of the year.

A good example of this was one cripple, unable to get about except in a wheel chair, who had been entirely dependent on and never left his mother's care for 40 years. After a holiday at one of our camps his whole personality changed; he took to going about by himself, learnt to type, and became secretary of the local disabled club. Imagine the relief for his mother.

But it is only fair to ask that cases should be selected with care and with a knowledge of the conditions at a particular camp and of the voluntary personnel available to look after them there.

The camps are made available to the Red Cross at much reduced rates by the generosity of the owners and by the unstinted personal generosity of camp managers and camp staff, who often freely give of their own holiday periods or own off duty hours to help these disabled. The personnel of the voluntary organizations who undertake these holiday duties, although fully trained to the highest Red Cross and St. John nursing standards, are not professionally qualified nurses and may have had little hospital nursing experience; the personnel, women and men, are often in full-time employment, in shops, offices, or homes, and only able to give part-time help in their spare time or even in their own holiday periods. We have several men who give 7–10 days of their own annual fortnight's leave period to help with this.

We make a point of always having at least one or two fully qualified nurses on the roster of duties, but it is only fair that all cases should be carefully selected, and disabled who require heavy continuous hospital care and attention should not be recommended for a holiday at one of the camps for the disabled.

Having been associated for nearly 20 years with the holiday camps for disabled my plea is that those who are asked to examine and recommend any disabled for a holiday should realize the conditions involved.—I am, etc.,

Chulmleigh,
N. Devon.
Treffry O. Thompson.

Mental Illness in Foreign Nationals

Sir,—There have been many studies in Britain on immigrant populations,[1-3] but the amount of mental illness among them is uncertain. This preliminary report draws attention to some of the features of mental illness as seen in this hospital.

During recent years the number of foreign national patients admitted here has increased (geographical distribution is shown in Table I and diagnosis in Table III). These patients were treated and in the main discharged to their relatives or homes in Britain within a few weeks or months. However, a number have remained in hospital, and it seems probable that this number will increase. In March 1966 there were 135 long-stay patients of foreign nationality in Banstead Hospital, of whom 21 probably could be rehabilitated. The rest even with only residual psychotic symptoms proved resistant to rehabilitation because of, among other things, a formidable language barrier and lack of relatives or friends.

Table I.—*Foreign National Admissions During* 1966

	Male	Female
European	23 (Poland 12)	7 (Poland 8, Spain/ Portugal 9)
Asiatic	17 (India/ Pakistan 11)	8 (Ceylon/ India 4)
Western Hemisphere	19 (West Indies 11)	2 (West Indies 10)
African	16 (Nigeria 7)	2 (Nigeria 6)
Australasian	4	8
Eire	42	9

Table II.—*Foreign National Inpatients in March* 1967

	Male		Female	
	Short-stay*	Long-stay†	Short-stay	Long-stay
European	7	52 (Poland 33)	5	22 (Poland 7)
Asiatic	1	5	3	3
Western Hemisphere	4	3	2	0
African	1	1	2	0
Australasian	0	1	1	0
Eire	5	10	3	3

* Less than six months. † More than six months.

Table III.—*Diagnoses in* 115 *Foreign Nationals in Hospital*

Diagnosis	Male		Female	
	Short-stay	Long-stay	Short-stay	Long-stay
Paranoid Schizophrenia ..	4	29	2	12
Schizophrenia (unspecified) ..	4	24	8	9
Organic	2	7	1	4
Affective disorders and others ..	5	1	2	1

Table IV.—*Repatriation in Longstay Patients*

	Male	Female
Definite wishes not to return to country of origin	8	8
Vaguer wishes/changeable/ psychotic	11	2
Unknown	43	16
Definite wish to return ..	8	1

There are other difficulties peculiar to these patients. Correspondence with their embassies is often protracted with long delays; sometimes relatives deliberately try to prevent the patient returning home; occasionally the patient is reluctant to return to his country because his judgement is poor and he may be quite unrealistic about his ability to adjust to life in this country. Two case histories illustrate some of these points.

Case 1.—The patient was born in Freetown, Sierra Leone, and is aged 34. He came to Britain in 1960 to study medicine. He failed his first M.B. three times in all subjects, had to leave, and drifted to London, where he has failed to adjust to any work or life in general. He has had a number of mental hospital admissions and some minor difficulties with the police—for example, failing to pay his fare on the train. He expresses a number of simple wish-fulfilling delusions. For example, when he travels he feels he need not pay because he is related to the Royal Family; at times he believes he is a prince of one country, while at times a prince of another quite distinct country. He is in fact a well-preserved young African, well-spoken, in touch with his surroundings, if rather aloof and solitary.

This illness would seem to be related to his inability to adjust to any way of life in England because he has no family here nor any real prospects.

Case 2.—The patient was born in Poland and is aged 46. He came to Britain with the Polish Forces in 1946, and following his discharge from the Army worked as a labourer intermittently until he was admitted to Banstead Hospital in 1951 with paranoid schizophrenia. He has had the usual range of treatment and remains on his optimum dose of phenothiazines. He believes he is being persecuted by the Communists, and so in spite of repeated requests by his father in Poland for his son's repatriation the patient refuses to consider it. In spite of the residual delusions he has been rehabilitated as far as working outside the hospital for the last five years, but resists any efforts to help him live outside. He is physically fit, has an adequate command of English, but is settled within the hospital and seems content as things are.

We have a large number of Poles who, in the main, became ill within a few months or years of coming to this country after the last war (Table II). Obviously for them repatriation is now hardly a possibility. Patients' views on repatriation are shown in Table IV. Psychiatric patients have a specific disability in adjusting to their environment, as distinct from patients who are physically ill. It is generally agreed that foreign culture is itself a stress and may make readjustment after psychiatric illness more difficult. For this reason it is to be expected that the long-stay chronic schizophrenic population could well increase with the years ahead.—I am, etc.,

Banstead Hospital,
Sutton, Surrey.
H. R. George.

References

[1] Gordon, E. B., *Brit. J. Psychol.*, 1965, **111**, 877.
[2] Mezey, A. G., *J. ment. Sci.*, 1960, **106**, 628.
[3] Pinsent, R. J. F. H., *Lancet*, 1963, **1**, 437.

"Swallowed" Endotracheal Tube

Sir,—Following the recent article on "swallowed" endotracheal tubes in neonates by Mr. J. A. S. Dickson and Mr. G. C. Fraser (24 June, p. 811), and the further report by Mr. M. G. Prinn (15 July, p. 176), I would like to report a similar case.

A mother was admitted to the Nuffield Maternity Department, Oxford, with severe pre-eclamptic toxaemia at 37 weeks and had a low forceps delivery of a male infant weighing 5 lb. 8½ oz. (2.5 kg.). Endotracheal intubation with a Portsmouth tube proved necessary, but momentary relaxation of the hold on the tube caused it to become gripped by oesophageal peristalsis and lost. The infant was admitted to the special care baby unit in good condition, respirations were slightly grunting, and rather frequent mucus extraction was required. A plain *x*-ray was unhelpful owing to the radiolucency of the tube. An oesophagoscope was passed without anaesthetic by Mr. A. J. Gunning, who found the tube lying just below the cricopharyngeus, from where it was easily removed. The infant's subsequent progress was uneventful.

It would be a great advantage if the tubes could be made opaque to *x*-rays by the inclusion of a radio-opaque salt, as is done already in the case of the Liverpool Holter valve tube.[1]—I am, etc.,

Paediatric Department,
Radcliffe Infirmary,
Oxford.
E. S. Mucklow.

Reference

[1] Rickham, P. P., *Develop. med. Child. Neurol.*, 1967, in press.

What is Psychosomatic Disease?

Sir,—Dr. J. W. Todd's letter (5 August, p. 368) following the paper by Dr. F. Feldman *et al.* and your leading article (1 July, pp. 14 and 1) resurrects a semantic misconception which some of us have laboured long, and we might have hoped fruitfully, to resolve. The adjective psychosomatic is properly used to describe either an approach to clinical medicine or research, or the mechanism whereby certain reactions occur in patients. Since the vast majority of human beings are conscious and react through their autonomic and neuroendocrine systems to their experience and their environment, all disorders of health are to some extent properly regarded as containing a psychosomatic element. To disregard this is to equate medicine with mechanics; an even older historical blunder than that adduced in Dr. Todd's telling examples.

The basically indisputable case for including a psychosomatic appreciation in the clinical approach to any illness has been painstakingly elaborated in innumerable publications, and is succinctly summarized in terms which leave no room for doubt in two reviews of the subject included in a recent textbook and the revised edition of an original paperback.[1] [2]—I am, etc.,

DAVID STAFFORD-CLARK.

London S.E.1.

REFERENCES

[1] Stafford-Clark, D., *Psychiatry for Students*, 2nd revised edition, 1966, pp. 134 to 143. Unwin University Books.

[2] —— *Psychiatry Today*, 2nd edition, pp. 239 to 242. Pelican Books.

SIR,—Dr. John W. Todd (5 August, p. 368) claims that the use of the term psychosomatic can be justified only if a disease is invariable—and he quoted a *B.M.J.* leading article: "an illness in which the organic lesions are the consequence of emotional disturbances." This is, I agree, the sense in which the term is most commonly used by doctors. But surely, where the organic lesions are the consequence of emotional disturbances, the correct description is "psychogenic"?

Psychosomatic has in fact a wider connotation; it embraces those disorders where mind and body interact to cause symptoms. For example, Kissen[1] was able to show that a break, or a serious threat of break, in a romance, engagement, or marriage was significantly often associated with the onset of tuberculosis. Nobody in his senses would argue, from that evidence, that the break *caused* tuberculosis. But if, say, a broken romance weakens resistance, in some way, to tuberculosis, then tuberculosis is to that extent psychosomatic.—I am, etc.,

BRIAN INGLIS.

London W.2.

REFERENCE

[1] Kissen, D. M., *Int. J. soc. Psychiat.*, 1958, 3, No. 4, 252.

Court Lees School

SIR,—Three matters about this disturbing case puzzle me. Firstly, did the pathologists have no opportunity to make a clinical examination of the boys? Secondly, was there an adequate check of the accuracy of the colour reproduction in the photographs? Thirdly, was an examination made to establish the date on which all bruising had disappeared?

Perhaps the pathologists can reassure your readers on these points.—I am, etc.,

J. H. LANKESTER.

Oxted, Surrey.

Coroners' Jurisdiction

SIR,—Mr. H. A. Kidd (5 August, p. 372) contends that there was a failure to consult the Central Consultants and Specialists Committee before the submission of evidence to the Brodrick Committee and also that the members of the Association were given no opportunity "of deciding whether they would continue to support the present system of coroners' jurisdiction or would prefer a system similar to the procurator fiscal in Scotland." These contentions are false, as the following account of the sequence of events shows.

"Deaths in the Community" was produced in 1963, and was fully discussed by all the interested Committees, including the Central Consultants and Specialists Committee and the G.M.S. Committee, before being accepted by the Council. Indeed, detailed comments prepared by the Medico-Legal Subcommittee of the Central Consultants and Specialists Committee were considered by the Private Practice Committee on 10 April 1963, prior to the submission of the final document to the Council. The report, which deals very fully with the defects of the procurator fiscal system, was included as an appendix to the Annual Report of Council in 1963, when, on a specific Motion, it received the approval of the Representative Body and thus became Association policy. The unaltered, published report was submitted to the Brodrick Committee in 1964 as the Association's written evidence.

In May 1965 the Brodrick Committee invited the Association to reply to a questionary. This task was remitted to the Private Practice Committee, which referred the matter to its Forensic Medicine Subcommittee. The Central Consultants and Specialists Committee and the G.M.S. Committee were again consulted and, so far as the Central Consultants and Specialists Committee is concerned, replies to the questionary drafted by its Medico-Legal Subcommittee were incorporated in the replies finally sent on behalf of the Association with the approval of the Council. In fact, before the replies were finalized the Forensic Medicine Subcommittee had considered a memorandum prepared by Mr. Kidd and forwarded by the Central Consultants and Specialists Committee. It was decided that Mr. Kidd's paper produced no additional points which ought to be forwarded to the Brodrick Committee on behalf of the Association. No dissentient voice was raised in the Council on behalf of the Central Consultants and Specialists Committee.

There followed a long interval of time before the Association was invited to give oral evidence to the Brodrick Committee. Meanwhile, in May 1966, a further memorandum was received from the Central Consultants and Specialists Committee, prepared by Mr. Kidd, and considered by the Executive Subcommittee of the Central Consultants and Specialists Committee on 25 April 1966. This memorandum differed slightly from the one which had been rejected in 1965, and in submitting it the Executive Subcommittee asked if the Forensic Medicine Subcommittee would give Mr. Kidd an opportunity of attending personally and speaking to his paper. On 10 January 1967 Mr. Kidd duly attended a meeting of the Forensic Medicine Subcommittee, which decided that it could not support his views. This action was subsequently approved by the Private Practice Committee and on 1 February 1967 by the Council, prior to the attendance of the Association's representatives before the Brodrick Committee. All the relevant facts were brought out during the debate in Council on 1 February 1967, when an earlier request from the Central Consultants and Specialists Committee that some support should be given to Mr. Kidd's views was withdrawn. During this debate I agreed, at the request of Dr. Skene, to invite one consultant engaged in clinical medicine or surgery to join the deputation to the Brodrick Committee. The Council approved my statement that this could only be done on the understanding that there would be no departure from the general tenor of the evidence which had already been submitted. To have done otherwise would have been unfaithful to the Representative Body.

In light of these facts, I am surprised to see Mr. Kidd's statement that the Central Consultants and Specialists Committee subsequently sent his rejected memorandum to the Brodrick Committee. If the statement is true, I must question the propriety of such action.—I am, etc.,

IVOR M. JONES,
Chairman,
Private Practice Committee, B.M.A.
Chairman,
Forensic Medicine Subcommittee.

Sunderland.

"Long-acting" Corticotrophin

SIR,—We are interested to see Dr. M. Friedman's study using plasma 11-hydroxycorticosteroid levels to measure the relative activities of two long-acting A.C.T.H. preparations (12 August, p. 409). Undoubtedly this study demonstrates that the duration of the increase in plasma 11-OHCS levels in response to A.C.T.H. gelatin is greater than that seen with the same dose of A.C.T.H./c.m.c. used in this experiment by a difference which is small but significant.

Gelatin is added to A.C.T.H. to delay its release and to prevent its breakdown at the site of injection. The clinical duration of activity of a long-acting A.C.T.H. preparation may range from less than 24 hours to more than 72 hours; this has been borne out in clinical practice with A.C.T.H./c.m.c.[1] It is not our intention to develop an A.C.T.H. preparation which lasts exactly as long or longer than any of the A.C.T.H. preparations already available. We are as yet uncertain of what significance can be placed on the exact duration of elevation of 11-OHCS or plasma cortisol following A.C.T.H. and how this ties up with the results seen in clinical practice.

The Mattingly method[2] of plasma 11-OHCS estimation is recognized as a good and useful indication of changes in plasma levels of a certain fluorescing fraction largely comprising cortisol, but should perhaps not be used as an accurate means of comparing response to different A.C.T.H. preparations when one does not know what proportion of the fluorescent response is due to cortisol and what proportion is due to other factors. It has been shown that 27–55% of the fluorescence obtained during the Mattingly procedure may in fact be due to substances other than cortisol.[3] When one measures the plasma 11-OHCS levels it would be useful to know exactly what is being measured and to be able to correlate these figures with clinical activity.

We are as yet not aware of how long the ideal prolongated preparation should act. Each individual patient varies in his requirements, perhaps owing to differences in rate and degree of inactivation of the A.C.T.H. injection, cortisol turnover rate and distribution, and the disease process involved. Clinical observations of therapeutic effects and side-effects are of more use in practical A.C.T.H.

therapy than biochemical estimations alone. We would therefore respectfully suggest that before reaching a conclusion on Dr. Friedman's study with regard to clinical activity one must first correlate this latter with the plasma 11-OHCS curves described. We would, however, repeat that we have no desire to produce a long-acting A.C.T.H. preparation which has an identical duration of action to any other prolonged A.C.T.H. at present available.

We would maintain that A.C.T.H./c.m.c. represents a highly purified long-acting A.C.T.H. preparation with a therapeutic action which is similar to A.C.T.H. gelatin and every other natural A.C.T.H. preparation, but which has two additional practical advantages—the first is its liquid nature and the second is its stability. These properties facilitate subcutaneous injection and make self-administration a more practical form of A.C.T.H. therapy for the outpatient. The necessity of warming a heat labile compound before administration is avoided.—I am, etc.,

M. J. FLYNN,
Medical Adviser,
Crookes Laboratories Limited.

Basingstoke,
Hants.

REFERENCES

[1] Geda, P. O., and Spongsveen, K. L., Symposium on Rheumatology, Sandefjord, June 1966.
[2] Mattingly, D., *J. clin. Path.*, 1962, 15, 374.
[3] James, V. H. T., Townsend, J., and Fraser, R., *J. Endocr.*, 1967, 37, 28.

Disinfectants and Plastic Mop Heads

SIR,—We have read with interest the letter from Dr. D. A. Leigh and Miss Christine Whittaker (12 August, p. 435) on the interference with the disinfectant property of Hycolin and Roccal by plastic mop heads. They found much less interference with Sudol, and recommend that this disinfectant be used with these mops. Adsorption of quarternary ammonium compounds, such as Roccal, by plastics (and many other materials) is well known. Such an occurrence in respect of phenolic disinfectants is less well known.

Our own observations in this connexion may be of interest, since they extend those reported by Dr. Leigh and Miss Whittaker. Using the same plastic sponge (which the manufacturers of this mop inform us is composed of polyvinyl acetate) we have found that both Hycolin and Sudol disappear from solutions in which it is immersed. In the case of Hycolin, using just sufficient of a 1 in 20 dilution to cover the sponge on all sides, rather more than 75% of the disinfectant disappears from the solution in 24 hours. With Sudol about 50% so disappears. Replacing the disinfectants with fresh solutions daily, we have found that the rate of disappearance slows down, and ceases in the case of Hycolin after eight days, but can still be shown to occur with Sudol after 40 days.

Both Hycolin and Sudol can be recovered from treated sponge for a considerable time. This recovery continues even when the sponges are washed out thoroughly under a running tap daily before being immersed in water to test for elution of disinfectant. In the case of Hycolin recovery continued for eight consecutive days under such circumstances. With Sudol recovery continued for at least 10 days. It seems likely, therefore, that the disappearance of these substances from solution can be entirely explained by this adsorption by the sponge.

We observed that Sudol makes the sponge material soft and "mushy" after prolonged immersion. Contrary to the suggestion made by Dr. Leigh and Miss Whittaker, we feel, therefore, that Hycolin is more suitable for the disinfection of this mop head, particularly since within a few days it becomes saturated with the disinfectant, and the adsorbed disinfectant appears to retain its bactericidal activity. Our work is being continued, and we hope to publish it in full, with technical details, at a later date.—We are, etc.,

L. STEINGOLD.
L. J. DUNN.
S. HENMAN.

St. Andrew's Hospital,
London E.3.

Opportunities in British Medicine

SIR,—Having read the leading article entitled "But eastward, look, the land is bright" (15 July, p. 128), I viewed with considerable concern the presidential address delivered at the 135th Annual Meeting at Bristol, entitled "One Profession, One Purpose" (15 July, p. 129). The repetition of numerous platitudes in a situation in which the practice of medicine no longer remains attractive to the younger graduate in Britain will not in any way prevent the ever-increasing flood of emigration to a more free system of practice. The comments with regard to loans and "an enforced period of service," whether this be in Egypt or in the United Kingdom, are typical of the lack of constructive thinking by the establishment on how to prevent emigration. The obvious answer is to improve conditions of practice and to offer an attractive career in a free profession.

The Minister of Health has made it clear that he will not allow an expansion of private practice at the present time, as this will cause a further decrease in the standards of National Health practice. The interpretation is that a universal steadily deteriorating standard of medicine will continue in Britain.

As always, the issues have been, and remain, crystal clear. Medical men are as anxious as politicians to ensure that no financial barrier should deter the sick person from consulting the physician. The duty of the doctor, whether general practitioner or specialist, is prevention and treatment of illness, and a private system of contracting between patient and doctor is the most satisfactory method of ensuring rewards for diligence, efficiency, further training, ability, or a manner which inspires confidence. The duty of Government is to reimburse the patient according to individual need, and for this the politician must answer to the electorate. These two matters are entirely separate, and unfortunately the leaders of the British medical profession are aiding and abetting successive Governments in confusing for political ends the profession and the public. From this side of the Atlantic the prospects of the young doctor in Britain remain apalling, as the basic issues are as yet untackled.

In a hospital in which approximately 50% of the specialist staff are from Britain, my colleagues and I feel it our bounden duty to advise and encourage our younger colleagues to emigrate from the United Kingdom. On this Continent the leaders of the profession are determined to preserve a fee-per-item-of-service basis of remuneration, contracted privately between the individual doctor and the patient, and we look forward to increasing the medical personnel with more graduates from the United Kingdom, whose value to the community will be suitably rewarded.—I am, etc.,

J. W. DAVIDSON.

Toronto,
Canada.

Impression of General Practice

SIR,—In this group practice we are becoming increasingly concerned and alarmed at the present image of general practice and community medicine that exists in the minds of medical students.

Undergraduates come to our practice for training from one provincial and two London medical schools. Virtually none of them is considering general practice as a career, although the majority have not decided on a specialty. They appear to have formed the impression, without any first-hand knowledge, that proper medicine is done purely within the confines of a hospital, and that general practice is for failed specialists.

The situation might be described as farcical, were it not for the fact that general practice needs a considerable increase in recruits over the next few years. Until these false impressions are corrected in the minds of tomorrow's doctors the increase will not come. Many general practitioners are anxious to widen their undergraduate teaching programme considerably. The medical schools, however, do not seem to encourage their students, nor do the educational planners appear to sense the urgency of remedying this unfortunate attitude, both in the minds of the students and in those of some of their clinical teachers.—We are, etc.,

A. R. H. WILLIAMSON,
P. M. R. HEMPHILL,
J. C. FOSTER,
T. I. STEWART,
A. J. PIM,
J. C. HASLER.

Nettlebed and
Sonning Common,
Oxon.

Points from Letters

Psychological Factors and Ulcerative Colitis

Dr. IAIN DUNCAN (Annan, Dumfries-shire) writes: It is interesting that Dr. H. Gainsborough's salutary reminder (19 August, p. 499) of the importance of understanding the patient fully, in all the ramifications of his personal being, is given in relation to ulcerative colitis. However, it applies cogently to two other subjects in the same columns—namely, asthma and enuresis, and indeed to every disease with which we deal. A general practitioner in particular is privileged to have the opportunity of really knowing the patient as a person, since he has contact with him in a variety of situations and relationships, and sees him against the background of his work, his community contacts, and in the exposed intimacy of the very home where he performs the fundamental process of existence. As Dr. Gainsborough says, evidence based on this kind of observation is subjective but none the less valid and should not be discounted just because we do not measure it in terms of absolute values.

Obituary Notices

GREGORY PINCUS, D.SC.

Dr. G. Pincus, the eminent biologist best known for his work in developing the contraceptive pill, died in a Boston hospital on 22 August. He was 64.

Gregory Pincus was born on 9 April 1903 at Woodbine, in New Jersey, U.S.A. He studied firstly at Cornell University, where he took a bachelor's degree in science, and then at Harvard, where he gained successively a mastership and a doctorate of science. He travelled to Europe, first to the Kaiser Wilhelm Institute in Berlin, and came to England in 1930 to study at Cambridge. He went back to the United States a year later, and became successively lecturer and assistant professor in the department of biology at Harvard. He returned to Cambridge in 1937, where he was a visiting investigator, after which he held posts at Clark University and Tufts Medical School in the United States, and was finally appointed research professor of biology in Boston in 1951, a post he held until his death.

[Keystone Press Agency, Ltd.

His interest in the biology of reproduction was manifest as early as 1936, when he published *The Eggs of Mammals*. His interest became more and more focused on the role of the steroid hormones. With the introduction of orally active synthetic progesterone in the early 1950s Dr. Pincus saw the possibility of using this as an oral contraceptive agent. With colleagues at the Worcester Foundation for Experimental Biology, Shrewsbury, Massachusetts, where he was research director, he tested the inhibitory activity of a large number of compounds. Having narrowed his choice to a selected few, he, together with Dr. John Rock, began clinical trials on Puerto Rican women.

Their remarkable results were published three years later and established the contraceptive pill as far superior to any other method of contraception currently in use. His interest in reproductive physiology continued, and he made a number of important contributions to the literature on this subject.

Many honours were bestowed upon him. In 1957 he received the Oliver Bird Prize for his contributions to the study of fertility control, and the Lasker Award for Planned Parenthood was bestowed upon him in 1960. The University of Edinburgh awarded him the Cameron Prize in 1966. He was elected fellow of many scientific societies in the United States, South America, Japan, and Europe.

He is survived by his wife, a son, and a daughter.

A. K. writes: Gregory Pincus has to his credit three great accomplishments, any one of which would have fulfilled the life of a lesser man. He was the chief creator of the Worcester Foundation for Experimental Biology, which from a very modest beginning grew to be a Mecca for endocrinologists from all over the world. The Laurentian Hormone Conference was his brain child and he edited the yearly volume of *Recent Progress in Hormone Research* that came from it. To be asked to give a paper at the Laurentian is the highest accolade in the endocrinological world, and the standards set by Gregory Pincus made it so. No man in science now stands alone, and Gregory Pincus would be the first to acknowledge that others have a share in the development of oral contraceptives, but to him rightly belongs the main credit for the invention that has touched closely the fabric of society in the Western world and goes far to meet one of the most pressing problems of our times.

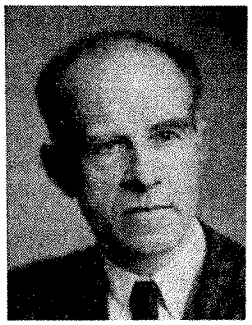
Gregory Pincus had in abundant measure the American gift for informality, but his relaxed air went with a formidable professionalism. Under his guidance it was always shirt sleeves and christian names at the Laurentian, but the arrangements ran with a smoothness which was no accident, and *Recent Progress in Hormone Research* appeared on time every year and with the references correct. He had a sardonic humour which was a perfect foil for the Russian ebullience of his wife Liz. They kept open-house in Shrewsbury, and many British endocrinologists have enjoyed the hospitality of their beautiful home.

Although Gregory and his friends all knew he had not long to live, he did not desist from starting new ventures. Negotiations for an academic connexion for the Foundation were in hand, and a few days before his death letters went out to endocrinologists all over the world arranging for the foundation of an international society for the study of reproductive physiology, the project long close to his heart. Medicine owes much to this man who was not medically qualified, and British endocrinologists grieve for the loss of a great master and a stout friend.

E. B. VERNEY, M.A., M.D., F.R.C.P., F.R.S.

Professor E. B. Verney, emeritus professor of pharmacology in the University of Cambridge, died on 19 August after a short illness.

Ernest Basil Verney was born on 22 August 1894, and after attending Tonbridge School entered Downing College, Cambridge, as a scholar. There he obtained a first-class in the Natural Sciences Tripos, and qualified with the Conjoint diploma at St. Bartholomew's Hospital in 1918. He graduated M.B., B.Ch. in 1921. He spent two years in the R.A.M.C., and after the usual house posts became an assistant in physiology at University College and later an assistant in the medical unit at University College Hospital. It was at this period that he worked with E. H. Starling on the systematic study of cardiovascular control that the flexibility of the heart-lung preparation made possible. It was immediately evident that Verney had gifts of a quite exceptional order as an experimental physiologist, and he soon achieved wide recognition. In 1926, when the chair of pharmacology at University College fell vacant, he was elected to it, and during the subsequent years his interests gradually shifted to the control of urinary secretion, at first using methods similar to those previously used in his study of the circulation. In 1934 he was invited to succeed Walter Dixon as Sheild Reader in Pharmacology at Cambridge, and he was also elected a fellow of his old college, Downing. He became the first Sheild Professor of Pharmacology in 1946. During the period in Cambridge he turned more to studies on urinary secretion in conscious animals. This led to the very important discovery that the major control of antidiuretic hormone secretion was by the osmolarity of the blood. This very elegant study has become one of the great classics of physiology, and was presented in a brilliantly lucid fashion in the Croonian Lectures delivered to the Royal Society in 1947. He continued to work on various aspects of the control of kidney function up to his retirement in 1961. He was then offered a research professorship in physiology at the University of Melbourne, where he spent the years 1961 to 1964 working with undiminished enthusiasm on renal problems. He returned to Cambridge in 1964 and settled down to write a book on the physiology of the kidney, in which he could draw upon his own vast experience of the subject. It was a task he was still engaged on at the time of his death. Verney was a fine teacher, and in particular the magnificent demonstrations he gave were an exciting part of his teaching. He had a great sense of fun, and there can be few of his colleagues who were not vastly entertained by his stories or stimulated by his wit. This may be illustrated by his entry in *Who's Who*: "Recreation: administration and tax evasion."


[Walter Stoneman

Many honours came his way. He was elected F.R.C.P. in 1928 and F.R.S. in 1936. After his retirement he became an emeritus professor of the University of Cambridge and an honorary fellow of his college. He was the Sharpey–Schafer lecturer, University of Edinburgh, in 1945; Croonian lecturer, Royal Society, 1947; William Withering lecturer, Birmingham, 1949; Dunham lecturer, Harvard, 1951; and elected a member of many foreign medical societies.

He is survived by his wife, Ruth Conway, whom he married in 1923, and by two sons and a daughter.—A. S. V. B.

GAETANO MARTINO, M.D.

Professor Gaetano Martino, eminent Italian physiologist and statesman, died at his home in Rome on 21 July, after a long illness. He was 67.

[Universal Pictorial

Gaetano Martino came from a distinguished Sicilian family. He was born at Messina on 25 November 1900, and graduated as doctor of medicine from the University of Rome in 1923. After a four-year period of scientific training spent at the Berlin University II Medical Clinic, the St. Antoine Hospital in Paris, the University Institute of Vegetative Physiology in Frankfurt, and in the University of London, he was appointed assistant professor of physiology at the university of Messina. From 1930 to 1934 he held the appointment of professor of physiology at the University of Asunción, Paraguay, and from 1934 to 1956 was professor of biochemistry and physiology, as well as director of the Institute of Human Physiology, at the Messina University. From 1957 until his death he held these same offices at the University of Rome. A pupil of Giuseppe Amantea—one of the most distinguished disciples of the world-famous physiologist Luigi Luciani—Gaetano Martino became a most original and versatile research worker in the fields of physiology and biochemistry. He published more than a hundred scientific papers, among which those on the hyperglycaemic factor of the pancreas and on the mechanism of reflex epilepsy are worthy of special mention.

In addition to his merit as a research worker and teacher Professor Martino was internationally known as an able politician and statesman. He was a member of the Italian Parliament from 1946 until his death, and was its vice-President between 1948 and 1954. In 1954 he was Minister of Education and from 1948 to 1957 Minister of Foreign Affairs. It was in this latter post that he displayed the full measure of his wisdom and political talent. Largely by his efforts Trieste was returned to Italy in 1954, Italy gained admission to the United Nations in 1959, and the creation of the European Economic Community and Euratom owe much to him. In 1960 he led the Italian delegation at the Geneva Disarmament Conference and also led the Italian Delegation at the United Nations General Assembly on two occasions. From 1962 to 1964 he was president of the European Parliament and from 1961 until his death was president of the Italian Liberal Party.

In recognition of his work of teacher and scientist Gaetano Martino was elected successively rector of Messina University and of the University of Rome. He was a member of many learned societies including the Accademia Nazionale dei Lincei, the Accademia Nazionale dei Quaranta and the World Academy of Art and Science. Numerous honours were bestowed upon him, both in Italy and abroad, including the Légion d'Honneur of France and the Order of Merit of the Federal Republic of Germany. He was an enthusiastic worker for the promotion of the European Economic Community and a tireless worker to secure the admission of Great Britain, as he regarded her membership as an essential factor in the process of political and economic integration of Europe.

He is survived by his wife Donna Alberta, a daughter of the Prince Stagno d'Alcontres, and by his daughter and two sons.—S. C.

J. B. S. GUY, C.B.E., T.D., D.L.
M.B., B.S.

Dr. J. B. S. Guy, formerly in general practice at Loftus, Yorks, died in the King Edward VII Hospital, Windsor, on 22 July. He was 67.

John Baden Strickland Guy was born at Widnes, Lancashire, on 5 June 1900. His early years were spent in Sheffield, and in 1912 he moved to Newcastle upon Tyne. He was educated at the Royal Grammar School, Newcastle upon Tyne, and the University of Durham College of Medicine. After a short time at the College of Medicine in 1917 he left and served in the Royal Flying Corps until the end of the war, returning to Newcastle to complete his studies, qualifying M.B., B.S. Dunelm in 1924. After qualifying he became house-surgeon to the late Professor R. J. Willan at the Royal Victoria Infirmary, and on completing this appointment he went into general practice with his uncle at Whickham-on-Tyne. After 12 months there he settled in Loftus, North Yorks, in November 1925, where except for his active service he was to practise for the next 40 years.

In spite of being in a busy single-handed practice he found time to interest himself in medical politics and in Service life. He was vice-chairman of the North Riding Territorial Association, and he served until 1940 as regional medical officer to the D.L.I., T.A. In the late 1920's he became a member of the old North Riding of Yorkshire Local Medical and Panel Committee. He was honorary secretary of the Cleveland Division of the B.M.A. from 1933 to 1938, and was voted chairman of that Division from 1938 to 1940. He was elected President of the North of England Branch of the B.M.A. from 1946 to 1947, when he became chairman of the newly formed local medical committee of the North Riding of Yorkshire. From that committee he was appointed a member of the North Riding of Yorkshire Executive Council, and was soon elected its vice-chairman. He became chairman in 1955 and remained chairman of both until his retirement in November 1965. He was elected President of the Tees-side Branch of the B.M.A. in 1953, and on the institution of the Roll of Fellows of the B.M.A. he became a fellow.

At the outbreak of the second world war Guy was mobilized with his regiment. In 1940 he was posted to the Western Desert in charge of a field hospital, and remained with the Eighth Army throughout hostilities, serving in Egypt, Libya, Sicily, Italy, Greece, and Austria. He was mentioned in dispatches in 1941 and 1943. In the same year he was awarded the O.B.E. and became A.D.M.S. to the 46th Division in Italy. In 1944 he was made a C.B.E. and was awarded the Territorial Decoration.

On retiring from his Territorial Army commitments because of age he was appointed Honorary Colonel of No. 1 General Hospital T.A., Newcastle upon Tyne—an appointment of which he was justly proud—and he was elected vice-chairman of the North Riding of Yorkshire Territorial and Auxiliary Forces Association in 1958, retiring on age in 1965. In 1959 he was appointed Deputy Lieutenant of the North Riding of Yorkshire. On the occasion of the Annual Clinical Meeting of the B.M.A. in Middlesbrough in 1960, at the unanimous request of the members of his Division, John, in spite of poor health, accepted the office of chairman for the second time and greatly helped the success of the meeting.

John was a dominant and forceful personality but never brusque. Although he led a busy life, he was always available to discuss problems and advise his patients and colleagues. In fact it became axiomatic that whenever counsel and guidance were needed we, his colleagues, invariably looked to and asked John—and his vast experience and wise counsel never failed us. He was a man who lived and enjoyed life to the full, but was happiest when he ensured that others enjoyed life too. It is regrettable that he enjoyed his retirement for so short a time. He leaves a widow, two sons, a stepdaughter, and a stepson, to whom we extend our sympathy.—W. M. M.

F. O. G. writes: I met John Guy some 35 years ago. Though not tall, he was a handsome and distinguished man. He was outspoken, but chose his words with care. On first impression some thought him to be very dogmatic, but in point of fact he was always willing to listen to argument. He was never anything but courteous; a characteristic phrase was "Let us be fair." I knew him as a colleague, a friend, and as a patient. That he was a character and a great man in the profession there is no doubt. He did much in the area for the benefit of the practitioners of his immediate vicinity in particular, but also affecting others. The present generation perhaps does not appreciate the amount of work necessitated in the past to obtain a somewhat better system than there used to be. He was worshipped by his patients. I knew of no one who disliked him. He loved a party and he was a difficult man to keep up with in his early days, such was his capacity for life.

After his wonderful military career he returned to his practice but was never really a fit man. He suffered from much pain and increasing disability. He forced himself to complete his 40 years in practice in Loftus. On retirement in November 1965 it was thought that the warm south would give him some comfort. This indeed was the case for a short time. Unfortunately he suffered from increasing anginal attacks and persistent pain from spinal arthritis.

He married twice. He leaves a widow and two children and two stepchildren, to whom our sympathy goes out. John will be remembered by all as a great character, a splendid doctor, and a wonderful friend.

W. H. HARWOOD-YARRED, B.SC. M.B.

Dr. W. H. Harwood-Yarred, a general practitioner in Colchester, Essex, died in St. Thomas's Hospital, London, on 22 July. He was 90.

William Henry Harwood-Yarred was born on 18 January 1877, and was educated at Dulwich College. He went to St. Thomas's Hospital in 1897, where he had an outstanding medical studentship, having already won the First Entrance and William Tite scholarship. At the end of his first year he won the First College prize and repeated this success in the following year. In the winter of 1901-2 his exceptional promise was evident when he won the surgery, pharmacology, and public health prizes, the Cheselden Medal, and the Treasurer's Gold Medal. He graduated B.Sc. and M.B. the same year. In 1904 he won the Murchison scholarship. He was consecutively assistant house-physician, house-physician, junior and then senior obstetric house-physician, and finally resident assistant physician. It was during the time that he was a house-physician that cases of acute appendicitis were first admitted into surgical wards. He also became intensely interested in surgery, and gained great knowledge and expertise in this field.

He bought a waning general practice in High Wycombe, Bucks, and very quickly built it up into a flourishing one and became well known throughout the northern part of the county. He was constantly called into consultation by general practitioners, and did most of the surgery in the area. In 1929 he left High Wycombe and continued practice in Colchester, where he met with equal success until his retirement at well over the age of 70.

He was a member of the B.M.A. for the whole of his medical career. He is survived by his son, Dr. Noel Harwood-Yarred, who is in general practice in Godalming, Surrey.

I first met him in 1926, when he was at the height of his ability. He was a very knowledgeable physician, a wonderful surgeon, as well as being a first-class obstetrician. He had a delightful personality, a reassuring combination of seriousness and gaiety, and could instil confidence into the most fearful of patients. My personal view has always been that he was the greatest "all-rounder" as a general practitioner with whom I have had the good fortune to be associated, and even 35 years later he is well remembered and loved in High Wycombe. —W. B.

P. S. writes: William Harwood-Yarred came to Colchester in the early 1930s to the house where Dr. William Gilbert, P.R.C.P., physician to Queen Elizabeth I and student of electricity and magnetism, had lived and practised. He was a general practitioner of wide experience. Of distinguished appearance, ever calm and courteous in manner, he had a clear analytical approach to medical problems backed by sound clinical intuition and a familiarity with current medical thought. Though somewhat retiring, he was regarded by his colleagues and patients with great affection and respect.

A. GREENHALGH, M.B., B.CH., B.A.O.

Dr. A. Greenhalgh died on 16 August at his home in Grindleton, West Riding, after a long illness. He was 62.

Arthur Greenhalgh was born in Accrington on 7 May 1905 into a medical family. His father was in general practice, and was also medical officer of health for the town, and his mother was the first matron of the Accrington Victoria Hospital. In 1930 he graduated M.B., B.Ch., B.A.O. at Queen's University, Belfast. He joined his father in practice, and eventually succeeded him. He maintained the close family association with the Victoria Hospital and served in turn as honorary anaesthetist, honorary surgeon, and after 1948 as clinical assistant in medicine.

He joined the Royal Navy in 1941, but was invalided out from the Service and spent two years in hospital before returning to practice. Ill-health dogged him throughout his career, but did not curtail his activities. Until his death he was president of the local branch of the British Empire Campaign for Cancer Research, and six years ago he was chairman of the Blackburn and District Division of the B.M.A. He was devoted to the practice of medicine and his skill and clinical acumen earned him the love of his patients and the respect of his colleagues.

Unfortunately deteriorating health brought about his premature retirement in December 1963, and he went to live at Grindleton, just across the border from his native Lancashire. Sadly he was not to enjoy his retirement for long. He suffered greatly in the last year of his life, but he bore his illness with a patience and fortitude which was sustained by the devotion of his wife and family. To his widow Ada and to his son and daughter we offer our deepest sympathy.—H. H. S.

F. D. C. FORD, B.M., B.CH. D.OBST.R.C.O.G.

Dr. F. D. C. Ford, a general practitioner in Shere, Surrey, died suddenly on 12 August. He was 39.

Frank David Chubb Ford was born on 11 June 1928 at Eastbourne. The son of a general practitioner, he was educated at Lancing College; at Hertford College, Oxford, which he entered with a scholarship in classics; and at St. Bartholomew's Hospital, London, qualifying B.M., B.Ch. in 1954. He took the diploma of the Royal College of Obstetricians and Gynaecologists in 1956 and held a number of house jobs. He then became a trainee in general practice in Surrey, and stayed to become an assistant and then a partner in the practice.

G. I. W. writes: David Ford's sudden death has stunned the whole district. We cannot yet believe he will not return from holiday to take up his energetic work among the people for whom he did so much. Many mothers and young families owe much to his obstetric skill and enjoyment of children. Among the sick of heart and mind he moved more surely than most of us. His patience and good humour in easing the burden of chronic illness and age will be missed in more than one old people's home. Truly he was a most likable young man, and still on the threshold of life. He cannot be replaced. He suffered from severe asthma all his life, and we can all learn from his example to be braver in the face of adversity. To Diana his wife, who is a doctor, and his children many helping hands will be stretched out.

W. E. H. BANKS, M.A., M.B., B.CH.

Dr. W. Banks died in Falmouth Hospital on 9 August after a short illness. He was 72.

William Eric Hallamore Banks was the son of a general practitioner in Falmouth. Eric, as he was known to everyone, was educated at Haileybury College, and Clare College, Cambridge, going on to St. Bartholomew's Hospital, London, for his clinical work. He took the Conjoint diploma in 1920 and graduated M.B., B.Ch. in 1921 from Cambridge, gaining a gold medal. In the first world war he saw service in a destroyer as a surgeon. His further surgical experience was at the Halifax Infirmary. On his father's death he returned to Falmouth to take over the practice, as there was no other successor, and from then on Eric Banks served the Falmouth area until his retirement two years ago. He was, until the advent of the National Health Service, surgeon to the Falmouth and District Hospital, and as a general-practitioner surgeon his shrewd analytical mind and his gentleness of hand brought to him a status that he never sought. He was by general acclaim a consultant in the district, and few sought his quiet wisdom without profit to both themselves and their patients. In 1942 he became Justice of the Peace in the borough of Falmouth and served the county in this capacity in 1951. He was a member of the Probation Committee as the representative of the Falmouth Petty Sessional Division from 1948 onwards, and in 1965 became chairman of this committee. He was chairman of the West Cornwall division of the B.M.A. from 1927 to 1929 and a Representative at the A.R.M. in 1934.

Those who came to know Eric Banks found that behind his grave and rather silent façade lay a Gilbertian wit and a capacity to interest his hearers that made an evening in his company a joy to remember. He had a profoundly religious philosophy of life, for he had—to his own satisfaction—examined the Christian credal propositions and found that they could be made to work. His was no narrow sectarian religion, but with an almost Franciscan indifference to the material advantages of his chosen profession he offered his skill and wisdom to humanity as they were needed.

He leaves one daughter. His wife, to whom he was devoted, predeceased him by nearly a year. Both of them will be greatly missed in a community they served so loyally and for so long.—G. E. W.

News and Notes

MEDICO-LEGAL

Who Decides the Standard?

[From our Legal Correspondent]

Though two consultant obstetricians and two general practitioners said they would have done what a defendant general practitioner did in treating an obstetric case, the defendant was found guilty of negligence largely on the evidence of a consultant pathologist.

Mrs. Maureen Audrey Hucks claimed damages for negligence against Dr. John Hugh Cole and Dr. Henry Gordon Peters, practising in partnership at Wellington, in Somerset, after she had contracted fulminating septicaemia following normal delivery of a child on 10 October 1963. The case was heard in the High Court in July 1967, before Mr. Justice Lawton. The case against Dr. Peters was abandoned at an early stage in the trial.

In 1963 Mrs. Hucks was aged 27 and already had two children. In August that year her fingers began to swell. On 4 October her wedding ring was filed off. At her last antenatal examination on 7 October she showed Dr. Cole a reddened area about half an inch in diameter within which there were three tiny spots, each with a yellow centre, under the site of the ring. Dr. Cole told her not to worry about them. He took no steps to find out what organisms were causing the sepsis.

The day after delivery of her child in a maternity home, on 11 October, when Mrs. Hucks was being washed, a nurse noticed the reddened area on her finger, and found another reddened area on a toe which looked like a "shoe-rub." Mrs. Hucks was at once moved into a room on her own and Dr. Cole was informed. Dr. Cole ordered a swab to be taken and sent to a pathological laboratory, and prescribed 250 mg. of tetracycline in tablet form to be taken four times a day for five days.

In the days that followed the general picture was one of healing. On 15 October, when Dr. Cole saw the patient, the finger and toe were both much improved, the finger more improved than the toe. The patient's general condition was good, and she felt well in herself. On that day Dr. Cole saw the pathological report, which showed the presence of *Staphylococcus aureus* resistant to tetracycline and *Streptococcus pyogenes.* Dr. Cole decided to continue the five-day course of tetracycline without prescribing any further drugs, and on 17 October after that course had ended he decided not to prescribe

(Continued on next page)

EPIDEMIOLOGY

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **12 August** (No. 32) and corresponding week 1966.

Figures of *cases* are for the countries shown and for Greater London. Figures of *deaths* and *births* are for the whole of England and Wales (London included), Greater London, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars-General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

	1967					1966				
CASES	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	1	1	0	0		2	0	0	0	
Dysentery ..	226	44	79	2	3	323	79	42	5	8
Encephalitis, acute ..	3	0				3	0		0	
Enteric fever:										
Typhoid ..	9	2	0	1		5	1	6	0	
Paratyphoid	3	1	8	0		6	0	0	0	
Food-poisoning	136	41	65	2		150	28	19	10	
Infective enteritis or diarrhoea under 2 years				19	39				17	44
Measles* ..	3,140	190	9	122	132	8,095	965	77	70	122
Meningococcal infection ..	6	0	3	0		10	2	2	0	
Ophthalmia neonatorum	27	4	1	0		5	2	2	0	
Pneumonia† ..	57	3	87	2		78	8	50	0	
Poliomyelitis, acute:										
Paralytic ..	2	0	0	0		2	0	0	0	
Non-paralytic	0	0	1			0	0	0		
Puerperal fever§	93	52	3	1		109	60	3	0	
Scarlet fever ..	146	21	8	8	3	234	34	7	1	4
Tuberculosis:										
Respiratory ..	236	44	36	5		219	56	32	9	
Non-respiratory ..	43	7	7	1		47	5	9	3	
Whooping-cough	779	110	182	8	49	419	65	26	13	11

	1967					1966				
DEATHS	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0		0		0	0		0	0	0
Dysentery ..	1	0				0	0		0	
Encephalitis, acute ..					0					0
Enteric fever ..	1	0	0			0	0	0	0	
Infective enteritis or diarrhoea under 2 years	4	1	1	0	2	2	0	1	0	0
Influenza ..	3	0	0	1	0	0	0	0	0	0
Measles ..	0		0		0	0		0	0	0
Meningococcal infection ..			0					0		
Pneumonia ..	491	64	20	11	1	532	90	15	15	13
Poliomyelitis, acute ..	0	0			0	0	0		0	0
Scarlet fever ..	0		0		0	0		0	0	0
Tuberculosis:										
Respiratory	31	7	7	0	1	34	8	3	2	2
Non-respiratory ..				0	0				0	0
Whooping-cough	0	0	0	0	0	2	0	0	0	0
Deaths 0-1 year	270	50	9	3	11	282	51	24	8	15
Deaths (excluding stillbirths)	9,128	1456	483	124	107	9,323	1483	512	114	194
LIVE BIRTHS	15,852	2673	876	260	345	16,438	2812	972	261	448
STILLBIRTHS	228	40	15			258	36	17		

* Measles not notifiable in Scotland, whence returns are approximate. † Includes primary and influenzal pneumonia. § Includes puerperal pyrexia.

(Continued from previous page)

any further drugs. The finger and toe had virtually healed, and in his view "it was all over bar the shouting." The nursing reports showed that an antiseptic powder was applied to both finger and toe on 19 October.

Onset of Septicaemia

On 19 October Mrs. Hucks was discharged. She had a pain in her abdomen shortly before she went home, and at home she became ill and was treated by Dr. Peters and then by Dr. Cole, who removed her to hospital, where a diagnosis of fulminating septicaemia was confirmed. The organism was identified as *Str. pyogenes*.

Mrs. Hucks's counsel criticized Dr. Cole on three grounds, firstly because he failed to treat his patient's finger when it was first shown to him, secondly because he failed to change the antibiotic after seeing the laboratory report, and thirdly because he discontinued the administration of antibiotics after 16 October.

Mr. Justice Lawton held that the first two charges of negligence failed. Although Mr. Alec Bourne, Professor F. E. Camps, and Dr. H. B. May all had expressed the view that on seeing the laboratory report Dr. Cole ought to have prescribed penicillin to combat the streptococci and either cloxacillin or erythromycin to combat the staphylococci, Mr. Justice Lawton held that Dr. Cole was not negligent in the light of the experience found in Somerset in October 1963.

So far as the third allegation was concerned, Miss Josephine Barnes, Mr. James Thomson, and two general practitioners practising in the West Country said that they would have decided as Dr. Cole did had they been faced with the same critical situation. But the court accepted Dr. May's evidence that it was wrong to discontinue the treatment of an infection in a patient in the puerperium until one was sure that the patient was not still at risk from infection, and that organisms on the finger are much more dangerous than organisms elsewhere. A responsible practitioner would make sure that the patient was not at risk until the involution of the uterus was complete.

Damages were awarded against Dr. Cole in the sum of £2,500 with costs, with a stay of execution pending an appeal.

MEDICAL NEWS

British Scientists Share U.S. Award

Two British biochemists, Dr. George J. Popják, M.D., F.R.S., and Dr. J. W. Cornforth, F.R.S., are to share with two Continental scientists an award of $50,000. The Stouffer Prize was established last year by Mr. Vernon Stouffer, a Cleveland businessman, to promote research into reducing heart attacks and strokes. The award to Dr. Popják and Dr. Cornforth is for "their team effort in research into hardening of the arteries." For many years they have worked together on basic chemical studies related to life processes. Both have been members of the scientific staff of the Medical Research Council. In 1962 they were appointed joint directors of a new chemical enzymology unit set up by the Royal Dutch/Shell Group. The scientists with whom they share the award are Dr. V. S. von Euler, of Stockholm, and Dr. Peter Holtz, of Frankfurt. (Photographs by Shell Photographic Unit.)

Dr. G. J. Popják

Dr. J. W. Cornforth

Society of Apothecaries of London

At a meeting of the Court of Assistants of the Society of Apothecaries of London on 14 August Dr. Hugh M. Sinclair was elected Master, Mr. Henry R. Thompson Senior Warden, and Dr. Peter M. F. Bishop Junior Warden.

Allen and Margaret Wilson Memorial Fund

A memorial fund has been launched to commemorate the work of Dr. Allen Wilson and his wife, Dr. Margaret Wilson, who were killed in an accident on the A1 in June.

The objects of the fund are (*a*) to encourage the development of any young person from the parishes of Innerleithen, Traquair, and Walkerburn through recurring prizes of grants; and (*b*) in alternate years to make an award to a country family doctor for original or important work.

Cheques should be made out to the Allen and Margaret Wilson Memorial Fund and sent to Dr. E. V. Kuenssberg, 15 Warriston Crescent, Edinburgh 3, or to the Manager, Bank of Scotland, Innerleithen, Peeblesshire.

Cannabis Synthesis

Two teams of chemists report the synthesis and isolation of biologically active constituents of hashish in the current issue of the *Journal of the American Chemical Society* (16 August, pp. 4451 and 4452). T. Y. Jen and his colleagues, of Wyeth Laboratories, Philadelphia, report the total synthesis of tetrahydrocannabinols, and a different method of synthesis is reported by R. Mechoulam and his colleagues working in Israel. The latter team refer also to a third method of synthesis carried out by T. Petrzilka in Zurich. The compounds yielded by these latest syntheses differ from those produced by earlier methods in that they are suitable for biological experiments to study the effects of hashish.

Paediatric Surgeons

The British Association of Paediatric Surgeons held its 14th international congress in Bremen from 18 to 21 July. Over 260 surgeons from 39 countries took part. Professor Fritz Rehbein gave the Isabella Forshall lecture on paediatric surgery in Germany. An extensive scientific programme included groups of papers on the measurement of bladder and anal functions and on aspects of the postoperative behaviour of the neonate. Receptions were given by the Prime Minister of Land Bremen and various professional societies. Among the guests at the annual dinner was Sir Frank Roberts, British Ambassador to the Federal Republic of Germany.

On 24 July an honorary degree was conferred on Mr. P. P. Rickham, president of the association, by the faculty of medicine of Göttingen University. Mr. F. H. Roberts was elected president for 1969–70.

Newcastle Curriculum

The Nuffield Department of Industrial Health refers in its fourth quinquennial report to the contribution it is making to the new curriculum adopted by the Newcastle Medical School. At the start, in the first stage, two lectures are given on the importance of industrial geography in determining health and work. In the second stage there is a course of lectures (11 hours) on the occupational hygiene of the industrial environment, also on clinical methods. Students are examined at the end of it orally and in writing. In the third stage the teaching is organized in relation to the physiological systems of the body. Formal teaching is supplemented by factory visits. In addition, students can undertake a piece of research under the special study project scheme. At the end of the third stage Part 1 of the final M.B., B.S. is taken.

Society for Research into Hydrocephalus and Spina Bifida

The Casey Holter Memorial Prize for the best essay reporting original work bearing on the pathogenesis or treatment of spina bifida or infantile hydrocephalus was awarded to Dr. A. J. Barson, of the department of pathology, Manchester University, for his essay on "Spina bifida; the significance of the level and of the extent of the defect to the morphogenesis."

Studentship for Medical Research

The Council of St. John's College, Cambridge, invite applications for a Meres Senior Studentship for Medical Research. See advertisement on page xxxiii.

Exhaust Pollution

In 1965 petrol-driven vehicles in Britain discharged 5m. tons of carbon monoxide into the atmosphere. Diesel engines added a further 80,000 tons. These estimates are given in a report on air pollution from road vehicles prepared by the technical committee of the National Society of Clean Air (3s.). It is difficult, according to the report, to determine the effects on human health of pollutants emitted from motor vehicles—firstly, because there is no specific air pollution disease ; secondly, because it is not possible to isolate the effects of motor-vehicle emissions from those from other sources ; and, thirdly, because some of the pollutants emitted by motor vehicles are emitted from other sources as well. "For these reasons the determination of cause and effect is beset with statistical pitfalls." The report considers that for petrol engines modified carburettors and fuel injection systems offer most hope for reductions in carbon monoxide and hydrocarbons. The way is now open, it says, for a standard European method of testing the emission of carbon monoxide, and it urges the Ministry of Transport to fix limits for its content in exhausts. It also suggests that exhaust gas analysis and carburettor adjustments should be included in annual car tests. Commenting on a forthcoming British Standard on diesel engines, the society criticizes the smoke level adopted and calls for a lower level. "There is no point," it adds, "in setting a standard if the smoke level chosen is appreciably above current practice with many existing vehicle engines." (See leader at p. 570.)

New Journal

The *Journal of Communication Disorders* is published quarterly by the North-Holland Publishing Company (P.O. Box 103, Amsterdam). It is concerned with experimental research, also with clinical and theoretical contributions. The general policy is to accept only articles that add to knowledge. Subscription £5 10s. ($15) a volume, post free.

People in the News

▶ Dr. J. H. F. BROTHERSTON and Dr. JAMES H. WEIR have been made honorary Fellows of the Royal Society of Health in recognition of their contributions to the promotion of health.

▶ LORD COHEN OF BIRKENHEAD is to be the first patron of the Association of Sea and Air Port Health Authorities.

Recent Publications

The First Four Years 1963–1967 : a report by the Institute for Operational Research (56–60 Hallam Street, London W.1, 3s. post free). Activities reviewed include work on organization and management in the hospital service.

Safety in Mines : annual report (illustrated) of the Safety in Mines Research Establishment, H.M.S.O., 7s. 6d. net.

Coming Events

Institute of Cancer Research: Roy Cancer Hospital.—International nucle medicine symposium, 25–27 Septemb Imperial College of Science and Technology also technical exhibition. Applications t Dr. V. R. McCREADY, Royal Marsden Hospital, Sutton, Surrey.

British Club for Surgery of the Hand.—Course in hand surgery, 17 November, London Hospital. See advertisement on p. xxxix.

Societies and Lectures

For attending lectures marked ● a fee is charged or a ticket is required. Applications should be made first to the institution concerned.

Tuesday, 5 September

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Hammersmith Hospital, 3 p.m., Dr. V. Wynn: Metabolic Effects of Oral Contraceptives. (Admission by ticket only, obtainable from Secretary, Institute of Obstetrics and Gynaecology, Chelsea Hospital for Women, London S.W.)●

WEST SUFFOLK HOSPITALS POSTGRADUATE CENTRE.—At Bury St. Edmunds, 1.15 p.m., Dr. S. L. Mitra: Topics on Gastrointestinal Radiology.

Wednesday, 6 September

ROYAL FREE HOSPITAL.—5.15 p.m., Professor J. Goodwin: The Cardiomyopathies.

Friday, 8 September

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. R. Bignall: clinical demonstration.

Marriages

Richardson—Hudson.—On 16 August 1967, at St. Richard's Church, Chichester, Dr. J. A. Richardson to Mrs. Gwendoline Hudson.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON W.C.1. TELEPHONE: 01-387 4499. TELEGRAMS: *Aitiology, London W.C.1.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs.

ADVERTISEMENT AND SUBSCRIPTION ORDERS should be addressed to The Manager at B.M.A. House, London, or at 415 Bourke Street, Melbourne, Victoria, Australia.

MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the British Medical Association, B.M.A. House, London, or to the Scottish Secretary, B.M.A. Scottish Office, Drumsheugh Gardens, Edinburgh.

New Issues of Specialist Journals

Obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London W.C.1.

ANNALS OF THE RHEUMATIC DISEASES

Contents of the September issue are as follows :

Assessment of Drugs in Outpatients with Rheumatoid Arthritis. R. M. Mason, D. E. Barnardo, W. R. Fox, and M. Weatherall.
Ultrastructural Study of Leucocytes and Urates in Gouty Arthritis. J. M. Riddle, G. B. Bluhm, and M. I. Barnhart.
Occurrence of Antibody to Salivary Duct Epithelium and Sjogren's Disease, Rheumatoid Arthritis, and Other Arthritides. R. N. M. MacSween, R. B. Goudie, J. R. Anderson, E. Armstrong, M. A. Murray, D. K. Mason, M. K. Jasani, J. A. Boyle, W. W. Buchanan, and J. Williamson.
Levels of Serum Immunoglobulins in Patients with Rheumatoid Arthritis. R. Marcolongo, F. Frullini, A. Bravi, G. Bianco, and A. Carcassi.
The Hypermobility Syndrome. J. A. Kirk, B. M. Ansell, and E. G. L. Bywaters.
Ultrastructure of Synovial Membrane in Rheumatoid Arthritis. F. N. Ghadially and S. Roy.
Book Reviews.
Obituary
I South-east Asia and Pacific Area Congress, 1968.
Abstracts.

Volume 26, No. 5. Yearly subscription (6 numbers) £4 4s., abroad £4 15s.

BRITISH JOURNAL OF OPHTHALMOLOGY

Contents of the September issue are as follows :

Tonographic Studies in Carotid Occlusive Disease. A. J. Bron, D. L. Knox, and D. Gaasterland.
Effect of Temperature and Humidity in the Schirmer Tear Test. John Williamson and Marjorie Allison.
Choriocapillaris and Lamina Elastica (Vitrea) of the Rat Eye. T. S. Leeson and C. R. Leeson.
Ocular Toxoplasmosis among Negro Immigrants in London. J. R. Chesterton and E. S. Perkins.
Corneal and Conjunctival Xylanthracosis caused by Carbon-gas from Generators. John Spero Kinnas.
Unilateral Microcornea and Enophthalmos with Bilateral Anterior and Posterior Anomalies. D. V. Batra and S. D. Paul.
Ocular Cysticercosis in India. D. K. Sen, R. N. Mathur, and A. Thomas.
Angioma of the Iris. G. T. Willoughby Cashell.
Graticule for Measurement of X-ray Films for Intra-ocular Foreign Body Localization. Nigel Cridland.
Ophthalmological Synopses.
Correspondence.
Reviews.
Notes.
Obituary.

Volume 51, No. 9. Yearly subscription (12 numbers) inland £8 8s., overseas £9. With *Ophthalmic Literature* and Index (7 numbers) inland £15, overseas £16.

GUT

Contents of the August issue are as follows :

The Epidemiology of Gastrointestinal Cancer. M. J. S. Langman.
Antral Activity and Symptom Periodicity in Duodenal Ulceration. L. R. Celestin.
Carbohydrate Metabolism in Duodenal Ulcer Patients. K. D. Buchanan, M. T. McKiddie, A. C. Lindsay, and W. G. Manderson.
Prognosis After Resection of Chronic Regional Ileitis. J. E. Lennard-Jones and George A. Stalder.
Caecal Tuberculosis. A. R. Anscombe, N. C. Keddie, and P. F. Schofield.
Ulcerative Oesophagitis in Association with Ulcerative Colitis. Clive Rosendorff and N. W. T. Grieve.
Modification in the Xylose Absorption Test as an Index of Intestinal Function. H. G. Sammons, D. B. Morgan, A. C. Frazer, R. D. Montgomery, W. M. Philip, and M. J. Phillips.
Force in the Anal Canal and Anal Continence. C. D. Collins, H. L. Duthie, T. Shelley, and G. E. Whittaker.
Geographical Distribution of Gastrointestinal Cancers in India with Special Reference to Causation. S. L. Malhotra.
Diarrhoea Due to Sucrase and Isomaltase Deficiency. I. J. Pink.
Hepatic Artery Aneurysm, Hereditary Haemorrhagic-telangiectasia, and Peptic Ulceration. John R. Condon, Norman C. Tanner, and D. M. Cowper.
Secretory Response of the Human Pancreas to Continuous Intravenous Infusion of Pancreozymin-cholecystokinin (Cecekin). J. G. Banwell, B. E. Northam, and W. T. Cooke.
Exocrine Pancreatic Disease and the Malabsorption Syndrome in Tropical Africa. J. G. Banwell, M. R. S. Hutt, P. J. Leonard, V. Blackman, D. W. Connor, P. D. Marsden, and J. Campbell.
Urinary Isoamylases in the Diagnosis of Chronic Pancreatitis. S. E. Aw, J. R. Hobbs, and I. D. P. Wootton.
Measurement of Tryptic Activity in Intestinal Juice as a Diagnostic Test of Pancreatic Disease. H. Bramwell Cook, J. E. Lennard-Jones, S. M. Sherif, and H. S. Wiggins.
Methods and Techniques :
Simple Method for Estimating Trypsin. H. S. Wiggins.

Volume 8, No. 4. Yearly subscription (6 numbers) £4 4s., abroad £4 15s.

BRITISH MEDICAL JOURNAL

LONDON SATURDAY 9 SEPTEMBER 1967

Pointers

Rubella in Pregnancy: Gammaglobulin given before exposure to infection gave some protection against foetal abnormalities in a series report by Professor J. C. McDonald and Dr. Catherine S. Peckham (p. 633). An investigation on behalf of the Public Health Laboratory Service revealed that a second prophylactic dose of gammaglobulin did not increase maternal protection from infection (p. 638).

Hyaline Membrane Disease: Correcting acidosis by intragastric route resulted in fewer deaths than scalp-vein infusion in clinical trial conducted by Drs. J. M. Abraham and R. J. K. Brown (p. 640). Leader (p. 628).

Differential Diagnosis of Hallucination: Involvement of cerebral cortex by occlusive vascular disease produced formed visual hallucinations in two patients seen by Mr. C. T. Hart (p. 643).

Lactation and the "Pill": Oral contraception initiated in the postpartum period did not cause inhibition of lactation in Dr. Teit Kærn's cases from Copenhagen (p. 644).

Sequential Contraceptives: Leader on this page.

Spontaneous Gangrene: Depression of spontaneous plasma fibrinolytic activity demonstrated by Dr. A. G. G. Turpie and colleagues in three African children affected with symmetrical gangrene of fingers and toes (p. 646).

Treating Urinary Infection: Drs. R. N. Grüneberg and W. Brumfitt found one dose of long-acting sulphonamide as effective as a seven-day course of ampicillin, and side-effects were more troublesome with the latter (p. 649). Leader (p. 629).

Diabetic Retinopathy: Dr. P. R. Hunter and colleagues found no beneficial effect from treatment with the anabolic steroid methandienone (p. 651).

Poisoning in the Home: Digitalis glycosides (pp. 660 and 661). Management of children who accidentally eat antidepressant pills (p. 663).

Clinical Reports: Fibrinolytic activity during sickle-cell crises (p. 653). Thrombus in thoracic aorta causing embolism (p. 655). Renal damage from excessive antacid intake (p. 656). Spinal cord degeneration in spite of vitamin B_{12} treatment (p. 657). Irreducible posterior dislocation of the elbow (p. 659). Monkey parasite infecting humans (p. 659).

Health Centres: Progress at Hythe Medical Centre (p. 672); G.P. reaction (p. 683).

University Students: Morbidity (p. 674).

Bedwetting: New alarm (p. 676).

Home Dialysis: Letter on National Kidney Centre (p. 680); leader (p. 631).

B.M.A. Career Service: Information about opportunities in medicine (*Supplement*, p. 128).

Which Pill?

The doctor prescribing oral contraceptives may well be confused by the large number of products available, and the manufacturers' literature, with its mass of conflicting data, does not always help. Recently the range has been increased by the introduction of sequential formulations in which an oestrogen only is given early in the cycle and a progestogen is added for the last few days. This sequential regimen is claimed to be more physiological and to produce fewer side-effects, but it is reputed to be less efficient. How does it compare ?

World-wide experience has shown that for all population groups combined drugs provide the most efficient method of contraception known. They are virtually 100% effective when taken properly. The possibility of patient error has been reduced by the 21-day regimen and by ingenious packaging which makes it impossible for even the most casual or careless woman who can read to make much of a mistake. Experience with the sequential method, however, suggests that it is not and possibly never can be quite so effective. It depends for its efficacy on inhibition of ovulation, and does not make the cervical secretions hostile to sperms nor the endometrium inadequate for implantation—both of which characterize the action of the combined drugs and provide additional anti-fertility factors which are brought into play if ovulation occurs. The effect of oestrogen on ovulation varies with the dosage—a small dose is stimulating, an intermediate dose delays ovulation, and a large enough dose inhibits it. The dose of oestrogen required for consistent inhibition of ovulation shows individual and population differences. For British women 0.05 mg. of ethinyl oestradiol is an inadequate dose[1] (sequential formulations at this dosage give about 20 pregnancies per 100 woman-years), though it is apparently adequate for Mexican women.[2] With formulations containing 0.075 mg. of ethinyl oestradiol the pregnancy rate falls[3] while the best results have been obtained with 0.1 mg.[4] Other sources of error with sequential therapy stem from the need for the different tablets to be taken at the right time, particularly where placebo tablets are included and where breakthrough bleeding occurs. There is no evidence that missed tablets make pregnancy any more likely with sequential formulations than with the combined drugs.

As the mode of action of oral contraceptives becomes more clear it seems likely that the combined drugs act by inhibiting the peak of luteinizing hormone (L.H.) without affecting follicle stimulating hormone (F.S.H.), whereas when ovulation is inhibited by oestrogen—as in sequential regimens—F.S.H. is suppressed and L.H. probably not affected.[5] When treatment is given with combined drugs containing less progestogen and more oestrogen presumably the mechanism of action changes from suppression of L.H. to that affecting F.S.H. Since F.S.H. is produced early in the cycle, it is possible that day five is not early enough to give oestrogen to suppress ovulation with certainty, and claims have been made that giving oestrogen from day one increases the

© *British Medical Journal*, 1967. All reproduction rights reserved.

efficiency of the sequential method. However, as pregnancies with sequential formulations tend to occur in later cycles as a result of breakthrough ovulation it will be some time before these claims can be substantiated. Meanwhile where maximum efficiency is required the combined drugs should clearly be the choice, for one of the main advantages of oral contraception is the complete freedom from anxiety of unwanted pregnancy.

Most of the common side-effects of oral contraceptives are related to the oestrogen/progestogen balance, and any one or more can occur as the effects of a woman's own menstrual cycle, menopause, or normal pregnancy. These symptoms may therefore be either produced or relieved by medication with oral contraceptives. Any product which is "too progestational" for a particular patient would produce symptoms such as discomfort in the breasts, acne, cramps in the legs and abdomen, depression, or decreased libido, and a change should be made to one which is on balance more oestrogenic—that is, containing a higher dose of oestrogen or a lower dose of progestogen or both. Similarly any one which is too oestrogenic will produce symptoms such as breakthrough bleeding, menorrhagia, oedema, tiredness, troublesome varicose veins, tension and irritability, mucorrhoea, and gastric disturbances, and a change should be made to a more progestogenic product. Claims have been made that sequential preparations give a lower incidence of side-effects. It is true that some women feel better on the variable hormonal milieu offered by sequential medication, but it is equally true that some women who have oestrogenic side-effects on sequential preparations feel much better on a more progestogenic combined oral contraceptive. The spectrum of side-effects with the more strongly oestrogenic products differs from that with the more progestogenic products and it is misleading to compare only side-effects at one end of the spectrum.

While there are advantages in using as low a dose as is compatible with efficiency and good control of the menstrual cycle, the claims that with new products or formulations side-effects are fewer than with existing products should be met with a degree of scepticism. Widespread acceptance and the reduction of anxiety over the use of oral contraceptives among doctors and women alike have resulted in fewer recorded side-effects in recent clinical trials. Such results cannot be compared with the results of earlier trials.

Though in practice many women adjust satisfactorily to any product, it can be useful in choosing a product for a particular patient to assess her hormone balance—whether predominantly oestrogenic or progestogenic—and prescribe accordingly. In this way it should be possible to eliminate her own menstrual troubles without precipitating others.

---

[1] Mears, E., In Proceedings of the Second International Congress on Hormonal Steroids, held in Milan, 1966. Amsterdam.

[2] Martinez-Manatou, J., In *Ovulation*, ed. R. B. Greenblatt, 1966, Philadelphia.

[3] Liggins, G. C., *Fertil. and Steril.*, 1967, **18**, 191.

[4] McBride, W. G., *Med. J. Aust.*, 1966, **1**, 172.

[5] Stevens, V. C., *Postgrad. med. J.*, Dec. 1967. (In press.)

Management of the Idiopathic Respiratory Distress Syndrome

The idiopathic respiratory distress syndrome (hyaline membrane disease) remains one of the major unsolved problems of the neonatal period. Its precise aetiology continues to elude us and its treatment is the subject of controversy. At present treatment is based on the fact that it is a self-limited illness of some days' duration, and the objective is, so far as practicable, to neutralize the physiological and biochemical disturbances in order to keep the infant alive until spontaneous recovery occurs.

The disturbances that affect the baby include a lowered arterial $\mathrm{Po_2}$, a raised $\mathrm{Pco_2}$, and a metabolic acidosis which is secondary to the respiratory failure. In untreated cases hyperkalaemia develops between 12 and 60 hours of age, with electrocardiographic changes. The low arterial $\mathrm{Po_2}$ is due largely to inadequate pulmonary perfusion owing to the shunting of venous blood past the gas-exchanging areas of the lungs.[1] This may be due in part to intrapulmonary shunting, and in part to shunting of blood from right to left through the foramen ovale in the heart as a result of an increased pulmonary vascular resistance, which causes also a poor pulmonary blood flow.[2] The accumulation of CO_2 which results in a raised arterial $\mathrm{Pco_2}$ is related to the fact that in these infants the functional dead space is very large and may, indeed, approach the tidal volume.[3] The severity of these disturbances can vary widely from case to case.

In mild cases with moderate tachypnoea and sternal recession, and when cyanosis can be abolished in 40% oxygen, the prognosis is good. The principal requirements are incubator care, including carefully monitored oxygen concentrations of less than 40% and humidity over 80%, plus antibiotic cover. In the severe cases with great respiratory distress and sternal recession, cyanosis which disappears only in high concentrations of oxygen, and with large departures from normal of blood gas tensions and acid–base balance the mortality rate is about 45% unless more active treatment is given. The first essential is to raise the oxygen concentration in the incubator high enough to abolish cyanosis. Indeed, it is now the practice in several centres to catheterize an umbilical artery and to control the oxygen concentrations by periodic measurements of the $\mathrm{Po_2}$. R. Usher[4 5] was the first to claim a significant reduction in mortality from the administration of glucose and sodium bicarbonate by continuous infusion through a scalp vein. J. H. Hutchison and his co-workers[6] reported a substantial reduction in mortality when larger doses of sodium bicarbonate were given by periodic injection through the umbilical vein, controlled by frequent estimations in the blood of the *p*H, $\mathrm{Pco_2}$, plasma standard bicarbonate, and base excess.

These workers also gave fructose in preference to glucose. Others have preferred the amine buffer THAM (trometamol) to bicarbonate because of its greater alkalinity and ability to lower $\mathrm{Pco_2}$,[7] though Hutchison and his colleagues thought that it had little advantage over sodium bicarbonate and carried greater risks. However, those who believe that death from the respiratory distress syndrome is due primarily to hypoxia, and that the prognosis is influenced more by the $\mathrm{Po_2}$ than by the $\mathrm{Pco_2}$ or blood *p*H, have found it difficult to understand why correction of the acidaemia with alkali or buffer should often appear to be beneficial in severe cases with respiratory failure. Part of the explanation may lie in the recent demonstration by J. M. Gupta and co-workers[8] that there is a considerable and often sustained rise in Po_2 after the injection of THAM into the umbilical vein. This effect must be due to a diminution of right-to-left shunting of blood, presumably the result of a direct effect of THAM or alkali in the lung, with lowering of the pulmonary vascular resistance. The administration of THAM via an umbilical artery instead of the vein had a much less beneficial effect.

This week in the *B.M.J.* Drs. J. M. Abraham and R. J. K. Brown report their results (page 640) of a clinical trial designed to compare intravenous (scalp vein) with intragastric administration of glucose and bicarbonate. Surprisingly, the infants who received their fluids by stomach tube had a somewhat lower mortality rate, though the difference was not statistically significant. It is, however, difficult to assess the possible harm of handling small, oedematous, premature infants in the manner which scalp vein infusions often entail. The use of the umbilical vein for intravenous fluid therapy carries some risk of phlebothrombosis in the portal vein, but this complication seems to be rare, and catheterization of either umbilical vein or artery involves a minimum of handling or exposure of the infant. Thus, while there is some evidence that correction of the metabolic acidosis by infusions of bicarbonate or THAM, and of fructose or glucose, under careful laboratory control does reduce the mortality rate, further studies are required to determine the precise effects of these substances and the best way of giving them.

The paramount importance of the accurately controlled administration of oxygen cannot be overstressed. Theoretically, hyperbaric oxygen should have advantages in the worst cases, but in both Glasgow[9] and Boston[10] it was found disappointing in practice. It cannot, of course, relieve CO_2 retention because of the great increase in functional dead space. Assisted respiration by intermittent positive[11] or negative[12] pressure is being tried in some centres for the treatment of deteriorating patients in whom the arterial Po_2 cannot be maintained at a safe level in 100% oxygen, or when the Pco_2 rises and stays above 70 mm. Hg, and especially when there are apnoeic attacks. It is not yet possible to assess the value of these very complicated and time-consuming techniques, which are by no means free of danger.

While there is room for controversy about the best methods of treatment of the respiratory distress syndrome, it is clear that the best results will be obtainable only in centres that can undertake throughout the twenty-four hours of the day the highly complex laboratory and therapeutic techniques required. They cannot be provided in every maternity unit, and these very ill babies should be transferred to a few special neonatal units which are staffed and equipped for this type of work. The portable incubator has made the transfer of the ill newborn baby a relatively simple matter, and each area should have an "infant flying squad" for this purpose.

---

[1] Chu, J., Clements, J. A., Cotton, E., Klaus, M. H., Sweet, A. Y., Thomas, M. A., and Tooley, W. H., *Pediatrics*, 1965, **35**, 733.

[2] Rudolph, A. M., *et al.*, *ibid.*, 1961, **27**, 551.

[3] Warley, M. A., and Gairdner, D., *Arch. Dis. Childh.*, 1962, **37**, 455.

[4] Usher, R., *Pediatrics*, 1959, **24**, 562.

[5] —— ibid., 1963, **32**, 966.

[6] Hutchison, J. H., Kerr, M. M., Douglas, T. A., Inall, J. A., and Crosbie, J. C., ibid., 1964, **33**, 956.

[7] Troelstra, J. A., Jonxis, J. H. P., Visser, H. K. A., and Van Der Vlugt, J. J., in Nutricia Symposium on the *Adaptation of the Newborn Infant to Extra-Uterine Life*, ed. J. H. P. Jonxis, H. K. A. Visser, and J. A. Troelstra, p. 185, 1964. Springfield, Ill.

[8] Gupta, J. M., Dahlenburg, G. W., and Davis, J. A., *Arch. Dis. Childh.*, 1967, **42**, 416.

[9] Hutchison, J. H., *et al.*, *Lancet*, 1962, **2**, 465.

[10] Cochran, W. D., Levison, H., Muirhead, D. M., Boston, R. W., Wang, C. C. S., and Smith, C. A., *New Engl. J. Med.*, 1965, **272**, 347.

[11] Thomas, D. V., Fletcher, G., Sunshine, P., Schaffer, I. A., and Klaus, M. H., *J. Amer. med. Ass.*, 1965, **193**, 183.

[12] Silverman, W. A., Sinclair, J. C., Gandy, G. M., Finster, M., Bauman, W. A., and Agate, F. J., *Pediatrics*, 1967, **39**, 740.

Single-dose Treatment of Pyelonephritis

In the study reported by Drs. R. N. Grüneberg and W. Brumfitt at page 649 of the *B.M.J.* this week the effect of a single dose of 2 g. of the very long-acting sulphonamide sulphormethoxine (Fanasil) was compared with that of ampicillin given in 500-mg. doses three times a day for seven days. Each treatment was successful in 22 out of 25 patients (88%). The two groups were comparable in age and sex, in frequency of a past history of urinary infection, which was obtained in a majority, and in that all had either an *Escherichia coli* or a *Proteus mirabilis* infection. Such good results could not be expected in infections due to other coliform bacilli (*Pseudomonas, Aerobacter,* and *Proteus* species other than *P. mirabilis*) or *Streptococcus faecalis* when treated with a sulphonamide. Side-effects were experienced by nine patients on ampicillin and by only two on sulphormethoxine, which was thus well tolerated, though, as the authors mention, larger doses have recently been found to produce skin reactions.

It is not claimed that sulphormethoxine gives better results than other sulphonamides. Another recent study[1] is mentioned in which a 90% cure rate was achieved with sulphadimidine. The advantages of sulphormethoxine are convenience, economy, and particularly the assurance that a full week of therapeutic effect will be secured, for patients instructed to take drugs daily sometimes omit to do so as soon as their symptoms are relieved. This is a leading advantage which has always been claimed for long-acting sulphonamides, though for most of them the claim has simply been that it is easier to remember one daily dose than three or four. There is the corresponding drawback that should any sensitivity reaction occur it is bound to be prolonged. This drug cannot, like another new sulphonamide, sulphasymazine, be eliminated more rapidly by alkalinizing the urine,[2] nor can it be surgically swabbed out of an injection depot, a treatment which might seem appropriate for such a severe and prolonged reaction to benzathine penicillin as that reported by H. C. Anderson.[3] Sulphormethoxine has not yet been used long enough to decide whether it shares the liability of other long-acting sulphonamides to produce the Stevens-Johnson syndrome, and Grüneberg and Brumfitt are probably wise in suggesting that it should not be administered to children until more experience with it has been gained.

Of the 50 patients treated 16 given ampicillin and nine given sulphormethoxine had a blood antibody titre against infecting organisms considered to be high enough to indicate renal involvement. This is a point of vital interest, because the effect of this sulphonamide must be exerted mainly in the tissues. Its half-life being about seven days, 1 g. of the dose given would be diluted in at least 10 litres of urine passed during that time, giving a concentration of at most 10 mg. per 100 ml., lower than that present in the blood. In ladies fond of their cups of tea (there is no mention of fluid restriction) the volume of urine passed in a week could have been considerably greater and the concentration of drug consequently lower. Even 10 mg. per 100 ml. seems inadequate for an antibacterial effect, particularly when acting on such large numbers of organisms as occur in infected urine. It therefore seems that these patients, in so far as their recovery was due to the treatment given (presumably some would have recovered spontaneously), owed it to the action of the drug in the tissues and not in the urinary tract. No such distinction need be made for ampicillin, which attains high concentrations in the urine as well as an adequate tissue level.

---

[1] Mond, N. C., Percival, A., Williams, J. D., and Brumfitt, W., *Lancet*, 1965, **1**, 514.

[2] Frisk, A. R., and Hultman, E., *Antimicrobial Agents and Chemotherapy*, 1965, p. 672.

[3] Anderson, H. C., *Lancet*, 1954. **2**, 1157.

The question whether an action in the urine or in the tissues is more important has been argued for years. Clearly a tissue effect must be exerted when the substance of the kidney is affected. On the other hand, innumerable patients have incontestably been cured with mandelic acid or nitrofurantoin, neither of which attains an effective concentration except in the urine. The same is probably true of nalidixic acid. Is it to be concluded that in all these patients the kidney is not involved, and other tissues only superficially? The most difficult thing to explain is the similar proportion of successes claimed for drugs having different sites of action in unselected series of cases. Some act in both tissues and urine, several only in the urine, and here we have in sulphormethoxine one apparently incapable of exerting much effect except in the tissues. Yet it was successful in patients without as well as with evidence of renal disease. There is much in this subject which still remains to be explained, and it is not likely to be so except by the application of new and more searching methods to the study of patients undergoing treatment.

Chlorpromazine Melanosis

A side-effect of prolonged treatment with chlorpromazine is oculo-dermal melanosis.[1-3] In this condition the areas of skin exposed to sunlight become excessively pigmented and develop a violaceous or slaty-grey colour in the more severe cases. In the eye the lens, cornea, conjunctiva, and retina are affected.

The first changes usually occur in the lens. Brown or white granules are deposited under the anterior capsule in the pupillary area, and they may progress to form a disc- or star-shaped opacity. Granules also appear in the deeper layers of the cornea around Descemet's membrane; in some they appear also in the epithelium and anterior stroma. The early lens and corneal changes may be visible only with the slit lamp, but later they can be seen with an ophthalmoscope or the unaided eye. Pigmentation is also seen in the bulbar conjunctiva in the palpebral fissure. While no fundal changes were found in most of the surveys carried out[4-8] a few cases have been reported with clumping of pigment at the periphery of the retina or at the macula.[9-11] Some of these patients would have had more than one of the phenothiazine group of drugs, of which thioridazine in particular is a well-recognized cause of pigmentary choroido-retinopathy, but the rest of the patients had received only chlorpromazine.

These ocular changes have caused visual impairment in only a few cases.[5 9] In most of the surveys carried out no visual defects were found, though this may have been due to a lack of co-operation by the patients.[4-8] Electrodiagnostic tests of retinal function have generally been reported as normal,[5 11] but some cases with retinal changes had reduced potentials.[10] The pathological changes occurring in the skin[2] and conjunctiva[9] have been shown by biopsy to consist of clumps of pigment, with the staining characteristics of melanin, clustered round the blood vessels in the dermis. No other pigment has been found histologically, but reflection spectrophotometry[12] suggests that while in the mild cases the pigment was melanin in the more severe ones there was some other pigment present as well. Electronmicroscopical reports are conflicting. One author found[13] the typical appearance of melanin in the skin with some additional osmiophilic particles in the endothelial cells of the blood vessels of the dermis, while another author[14] found no "natural" melanin in the dermis. Lens changes have been produced in guinea-pigs by the administration of chlorpromazine and irradiation with ultra-violet light; extracts of these lenses together with the cornea showed a high concentration of the drug.[15]

So it would seem probable that both melanin and a drug metabolite are deposited in the skin and eye to cause the observed changes. In several post mortem examinations carried out on patients who died suddenly while on chlorpromazine therapy it was found that all the internal organs were heavily infiltrated with melanin,[16] and it has been suggested that infiltration of the heart may cause irregular rhythm, resulting in death. Tests of renal and hepatic function are often abnormal in patients on chlorpromazine therapy.

The condition has been described mainly among the inmates of mental hospitals because it occurs in patients who have taken large doses of chlorpromazine for long periods. The ocular changes seem to be clearly related to the amount of drug given and also to the daily dose.[17] While early reports suggested that affected patients had taken at least 500 g., later reports showed that melanosis could occur after smaller amounts.[6] Some investigators believe that the side-effects are not common if the daily dose is small, even if more than 500 g. are given.[7 18] The side-effects are almost certainly related to the concentration in the body of chlorpromazine,

[1] Greiner, A. C., and Berry, K., *Canad. med. Ass. J.*, 1964, **90**, 663.
[2] Zelickson, A. S., and Zeller, H. C., *J. Amer. med. Ass.*, 1964, **188**, 394.
[3] Cairns, R. J., Capoore, H. S., and Gregory, I. D. R., *Lancet*, 1965, **1**, 239.
[4] Barsa, J. A., Newton, J. C., and Saunders, J. C., *J. Amer. med. Ass.*, 1965, **193**, 10.
[5] Wetterholm, D. H., Snow, H. L., and Winter, F. C., *Arch. Ophthal.*, 1965, **74**, 55.
[6] Galbraith, J. E. K., Gibson, B. H. L., Crock, G. W., and Pearce, T. A. A., *Med. J. Aust.*, 1966, **1**, 481.
[7] Sarin, L. K., Leopold, I. H., and Winkelman, N. W., jun., *J. Amer. med. Ass.*, 1966, **198**, 213.
[8] Margolis, L. H., and Goble, J. L., ibid., 1965, **193**, 7.
[9] Siddall, J. R., *Arch. Ophthal.*, 1965, **74**, 460.
[10] Henkes, H. E., *Ned. T. Geneesk.*, 1966, **110**, 789.
[11] Mathalone, M. B. R., *Brit. J. Ophthal.*, 1967, **51**, 86.
[12] Satanove, A., *J. Amer. med. Ass.*, 1965, **191**, 263.
[13] Hashimoto, K., Wiener, W., Albert, J., and Nelson, R. G., *J. invest. Derm.*, 1966, **47**, 296.
[14] Zelickson, A .S., *J. Amer. med. Ass.*, 1965, **194**, 670.
[15] McDonald, C. J., Creasey, W. A., and Howard, R. O., *Clin. Res.*, 1966, **14**, 492.
[16] Greiner, A. C., and Nicolson, G. A., *Canad. med. Ass. J.*, 1964, **91**, 627.
[17] DeLong, S. L., Poley, B. J., and McFarlane, J. R., *jun., Arch. Ophthal.*, 1965, **73**, 611.
[18] Valentine, M., and Jardine, P., *Brit. med. J.*, 1966, **2**, 586.
[19] Murphy, K. J., *Med. J. Aust.*, 1966, **2**, 1228.
[20] Cameron, M. E., *Brit. J. Ophthal.*, 1967, **51**, 295.
[21] Ban, T. A., Lehmann, H. E., Gallai, Z., Warnes, H., and Lee, H., *Un. méd. Can.*, 1965, **94**, 305.
[22] Gombos, G. M., and Yarden, P. E., *Amer. J. Psychiat.*, 1967, **123**, 872.
[23] Barnes, G. J., and Cameron, M. E., *Med. J. Aust.*, 1966, **1**, 478.
[24] Greiner, A. C., and Nicolson, G. A., *Dig. Neurol. Psychiat.*, 1965, **33**, 175.
[25] —— —— *Lancet*, 1965, **2**, 1165.
[26] —— —— and Baker, R. A., *Canad. med. Ass. J.*, 1964, **91**, 636.
[27] Gibbard, B. A., and Lehmann, H. E., *Amer. J. Psychiat.*, 1966, **123**, 351.

and one patient with uraemia developed marked pigmentation after 34 days when on a dose of 75 mg. a day.[19] The incidence of ocular changes is variously reported as between 20% and 39%,[6 11] and the frequency seems to depend on the concentration of ultra-violet light[20] as well as the drug dosage. The skin pigmentation is believed to be a phototoxic reaction caused by the chlorpromazine which has been shown experimentally to cause more reaction to ultra-violet light than the other phenothiazine drugs in common use.[21] Acute photosensitivity has been reported in a few cases, with erythema and blistering of the skin.[22] The melanosis was originally thought to be confined to women with amenorrhoea,[1] but later the sex incidence was found to be equal,[11 23] and because of the similarity between this melanosis and endocrine melanodermia it has been suggested that the endocrine system is involved. One theory is that chlorpromazine affects the pituitary gland and increases the production of melanocyte-stimulating factor.[24] Another is that the formation of adrenaline and noradrenaline is blocked, so that excess melanin is produced,[16] but estimations have shown the catecholamines in the urine to be normal.[11] A. C. Greiner and G. A. Nicolson[16] have suggested that the production of melatonin, the pigment-lightening factor in the pineal gland, is inhibited, and in some necropsies the pineal body was found to be atrophic. As an interesting outcome of these investigations the authors also found abnormal pigmentation and pineal atrophy in schizophrenics who had not had chlorpromazine. They therefore suggested that there may be an intrinsic abnormality of the pineal gland in schizophrenia and the blockage of melatonin production causes formation of a hallucinogenic compound.[25] Stopping the drug does not reverse the skin or eye changes.[26] Attempts to reduce the skin pigmentation with D-penicillamine have been encouraging.[26 27] This compound will chelate copper, which is concerned in the synthesis of melanin. Keeping the patients in the dark also reduced the pigmentation.

Thus it seems that these changes will occur when chlorpromazine in high dosage is continued for years, but the amount of visual trouble caused does not at present seem to be very great, so that the benefits of treatment outweigh the disadvantages. The possibility of its causing death by deposition in the internal organs has not yet been fully evaluated.

Closure of Kidney Centre

The difficulties in which the National Kidney Centre in North London now finds itself have to be seen against a background of general scarcity of skilled staff. The decision to close the centre, previously announced,[1] has apparently not been irrevocably taken. For Mr. Murray Medway, one of its founder trustees, states in our correspondence columns this week (page 680) that the centre could continue to function if a replacement for its present director, Dr. S. Shaldon, were found. Dr. Shaldon's resignation takes effect from 1 July 1968.

Dr. Shaldon has stated[2] that he hoped from the outset the centre would be able to co-operate with the N.H.S. dialysis programmes whenever possible, to ensure the advancement of this form of treatment. And he attributes the failure of the venture to "the inability to find a suitable formula to bridge the dogmatic distinction separating medical practice inside and outside the N.H.S."

He and other workers have shown that patients can be trained to dialyse themselves in their own homes with the minimum of help from a relative.[3] Such patients are taught to prepare, check, and sterilize the kidney and other equipment, disconnect the arteriovenous shunt, make the connexion to the kidney, and administer heparin as required. It is claimed that there are actually fewer technical failures of dialysis in the home, presumably because in these circumstances the prescribed routine is scrupulously followed. If the shunt should clot it can be freed of clot by the patient or his relative. All disposable material, dressings, dialysate concentrate, heparin, and the rest can be supplied under contract to the patient, so that when all is going smoothly—and that needs emphasizing—the patient is completely independent of the training centre, and does not require support from it other than occasional advice by telephone. The dialysis equipment has to be maintained in perfect order by the manufacturer.

But what is to happen to such a patient when complications arise, as they are certain to do sooner or later? The arteriovenous shunt will not last indefinitely. The standard of care of the shunt may be very high in the home, but from time to time shunt infections occur, and these may be dangerous, even potentially lethal, infections, which must be promptly and vigorously treated. Patients whose shunts repeatedly clot may need long-term treatment with oral anticoagulants. This will require regular supervision, and may lead to haemorrhagic attacks necessitating admission to hospital.[4] When the shunt fails the venous or arterial end must be dealt with or a complete new shunt inserted. Before undertaking the placement of a new shunt it may be necessary to carry out radiological studies of the vessels of the limb to be used. For these and other eventualities related to the treatment the patient will need to be admitted to hospital, preferably to a centre providing intermittent haemodialysis. Patients receiving dialysis in the home are not immune to ordinary illnesses and will need medical or surgical treatment for these without interruption of their dialysis programme.

It is difficult to envisage a scheme which, without prejudice to other patients undergoing intermittent dialysis completely under the N.H.S., will enable a patient to provide and pay for his own treatment when all is proceeding smoothly, yet become dependent on the N.H.S. when things go wrong. Owing to the dearth of highly skilled staff, centres providing dialysis under the N.H.S. are unlikely in the foreseeable future to have sufficient facilities to undertake treatment at short notice, and often for an indefinite time, of patients originally treated in an independent specialist centre. It has been stressed that hospitals providing dialysis centres must include beds to which their patients can be admitted when necessary. It is unlikely that sufficient beds with their supporting services will be provided to cope with an unknown and fluctuating load of patients from independent centres.

Intermittent dialysis is increasingly being regarded as a staging post on the way to kidney transplantation. The patient with a successful kidney graft is fitter and freer from restrictions than even the most successfully dialysed patient. If transplantation is accepted as the ultimate aim patients being treated by a complete renal unit will be in a better position than those treated from an independent centre. So limited are skilled staff at present that it does not seem possible to maintain a half-way position between private medicine and the N.H.S. where intermittent dialysis is concerned, though it might become so if a complete renal unit was established providing not only training in dialysis but laboratory facilities, a comprehensive aftercare system, private hospital accommodation, and such extra medical and surgical treatment as might be required.

---

[1] *Brit. med. J.*, 1967, 3, 252.
[2] Shaldon, S., ibid., 1967, 3, 241.
[3] Ibid., 1966, 1, 1433.
[4] Wing, A. J., Curtis, J. R., and De Wardener, H. E., ibid., 1967, 3, 143.

Role of the Married Nurse

It is widely believed that in the near future there will be few spinsters over the age of 20, and that hospitals which have in the past been largely staffed by these will have to depend on married women. A recent report[1] by the Dan Mason Research Committee supplies some of the facts about the situation which have hitherto been lacking.

A questionary was sent to a sample of nurses who qualified for the *Register* in 1950 and 1959, and for the Roll in 1950, 1954, and 1959. Only half the forms were returned, but 5,974 completed the questionary, and supplied information on their marital status, whether they were working, and, if so, whether they were nursing. Those who were employed received a longer questionary on their future plans about nursing and what inducements might bring them back to hospital or domiciliary work.

There will be few surprises in this report for those familiar with the problems of maintaining the nurse establishment in hospital, except perhaps that 25% of those who answered were still unmarried, so that spinsters are still not uncommon. Nurses in Britain have a firm belief that the welfare of a young family depends on the presence of the mother, and three-quarters of those who had children under 5 were not working.

The longer a nurse's break of service, the less likely she is to return to hospital, and this is perhaps a consequence of the pace of technical advance. Of those who planned to go back to nursing 83% were under 40 years old, though this group formed only 46% of the total. Nearly a half of the registered nurses and over a third of the enrolled were not in paid employment, but those who were working were nearly all engaged in nursing full- or part-time. Many of the older and married women were working outside hospital, and the expansion of domiciliary and public health work is seen as a way of relieving pressure on hospitals.

The most useful part of the report to hospital administrators should be that on deterrents to recruitment and proposals that would encourage return to nursing. There was general agreement on these in all the groups of nurses questioned. Choice of working hours and flexibility to meet family commitments were always at the top. There is no doubt that if planners are able to spend time and thought on duty rosters it is possible to fit in numbers of part-time and married staff, but it is also true that if unmarried nurses are asked to work an undue proportion of evenings, weekends, and public holidays staff relations are bound to be difficult.

Refresher courses had high priority on all lists, as did the provision of crèches and nurseries. Pay was mentioned only by about a third, but the fact that after a break of service the nurse starts again at the rate of a first-year staff-nurse was a constant grievance, and it ought to be one easy to remedy in a manner fair to everyone. Opportunities for promotion and equality of status were often wanted, and it is evident that married and part-time staff are not always integrated without friction.

One point that office sisters do not always remember is that part-time staff need permanent positions, and that if they get them their satisfaction in the job and their morale rise, so that absenteeism is less. It seems probable that patterns of nursing service in Britain are likely to follow those of the United States, where large numbers of married nurses work. It may therefore be appropriate to end with a quotation from an English nurse working in America: "Eight hours nursing, eight hours with the family, and eight hours sleep works very well."

---

[1] *Marriage and Nursing.* A Survey of Registered and Enrolled Nurses. Published by the Dan Mason Nursing Research Committee of the National Florence Nightingale Memorial Committee, London. 1967.

Allergy to Seminal Fluid

Acute anaphylaxis after sexual intercourse must be extremely rare. B. N. Halpern and his colleagues[1] have recently reported the case of a young woman who developed an anaphylactic response due to the presence of reaginic antibodies in her serum directed against a normal mucoprotein in human seminal fluid. The patient had no previous history of allergy, though she came from a highly "atopic" family—her mother had a long history of asthma and atopic eczema, a twin brother suffered from contact dermatitis, and a younger sister from atopic dermatitis. After her first sexual experience the patient developed generalized urticaria, oedema of the lips, eyelids, tongue, and pharynx, severe asthmatic dyspnoea accompanied by congestion of the mucous membranes, violent pelvic pain with uterine contractions, and general malaise culminating in loss of consciousness. Most of the symptoms recurred after every coitus; they reached a maximum within 15 to 30 minutes and took 24 hours to subside. The reaginic antibodies were of such high titre that seminal fluid diluted to one in a million still elicited a weal and flare reaction in her skin. Prausnitz–Küstner (P–K) reactions could be produced in normal subjects when her serum diluted as much as 1:100 was injected intradermally followed 24 hours later by seminal fluid. Passive anaphylaxis could also be obtained in monkeys. The antibodies did not react with spermatozoa and the patient had no other types of antibodies such as sperm agglutinins[2] or any "blocking" antibodies reacting in complement fixation, precipitation, or tanned red cell agglutination. Desensitization treatment with seminal fluid was tried in an attempt to induce such blocking antibodies, which are said to improve clinical symptoms in reaginic allergies, but it was unsuccessful in this patient. Chromatographic and electrophoretic separations of seminal proteins showed the antigen to be in the most basic fraction and the richest in sialic acid.

It was found that the P–K activity could be removed by precipitation with anti-IgA, and Halpern and his colleagues suggested, therefore, that the reaginic antibodies were in the patient's IgA globulins. The detailed and careful work of K. Ishizaka and his colleagues[3-6] strongly suggests, however, that reagins are in a newly defined class of immunoglobulins named IgE. These globulins have the same light chains as all classes of Ig but have antigenically distinct heavy chains with the unique capacity to adhere to cell surfaces, particularly of the mast cells and basophils which release the pharmacological mediators of anaphylactic hypersensitivity.

---

[1] Halpern, B. N., Kay, T., and Robert, B., *Immunology*, 1967, **12**, 247.
[2] Rumke, P., *Vox Sang*, 1954, **4**, 135.
[3] Ishizaka, K., and Ishizaka, T., *J. Allergy*, 1966, **37**, 169.
[4] —— —— and Lee, E. H., ibid., 1966, **37**, 336.
[5] —— —— ibid., 1966, **38**, 108.
[6] —— —— and Hornbrook, M. M., *J. Immunol.*, 1966, **97**, 75.

Papers and Originals

Gammaglobulin in Prevention of Rubella and Congenital Defect: A Study of 30,000 Pregnancies

J. C. McDONALD,*† M.D.; CATHERINE S. PECKHAM,* M.B., B.S.

WITH THE ASSISTANCE OF JUDITH MUNK

Brit. med. J., 1967, 3, 633–637

Gammaglobulin has been available to doctors in England and Wales since 1954 for the protection of pregnant women exposed to rubella. An analysis of results obtained during the period 1954–61 showed a reduction in the attack rates, but the more important question of whether congenital defects were also prevented could not be examined at that time (McDonald, 1963). Since then the isolation of rubella virus and the development of serological tests for antibody have enabled many aspects of the problem to be investigated with more precision. In a study of the effects of gammaglobulin on artificially induced rubella in volunteers Green *et al.* (1964) showed that serological conversion and viraemia may occur in the absence of clinical manifestations of illness. Brody *et al.* (1965) concluded from a trial among young schoolboys during an epidemic in Alaska that gammaglobulin halved the infection rate as determined serologically and reduced the clinical attack rate to about a quarter. The dosage used in this trial was relatively large—0.25 ml./lb. (0.55 ml./kg.) of body weight, presumably in 16% solution.

None of these findings is of much assistance to the pregnant woman or her doctor since they are compatible with optimistic and pessimistic interpretations. Quite modest doses of gammaglobulin may not only reduce risk of infection and clinical illness in the mother but protect the foetus should these occur; moreover, gammaglobulin might protect the foetus from other teratogenic agents. On the other hand, it has been argued that gammaglobulin may at most obscure the symptoms of rubella and do nothing to prevent viraemia or damage to the foetus, so giving rise to a false sense of security, which is worse than useless. This paper, which is mainly concerned with the outcome of pregnancy in women who have received gammaglobulin, throws some light on these questions.

Background

Between 1954 and the end of 1962 gammaglobulin was issued for 36,577 rubella contacts. The demand at first grew slowly, but an epidemic in 1958 helped to popularize its use, which thereafter was maintained at a higher level. Even so, by the end of 1960 only 9,556 doses had been issued, mostly during times of low prevalence. In 1961 the demand increased and 6,565 doses were issued; this was followed in 1962 by what appeared to be a severe and widespread epidemic (Fry *et al.*, 1962), during which 20,456 doses were distributed. The study reported in this paper is confined to the period 1956–62, during which 35,825 doses were issued.

Dosage and the types of gammaglobulin available underwent changes during the period of study. Until June 1958 the dose supplied was 750 mg., the same as that for measles; it was then increased arbitrarily to 1,500 mg., only to be reduced again to 750 mg. from June to September 1961 because of shortage. From then on 750 mg. remained the standard dose, though 1,500 mg. was supplied when the risk seemed specially high—for example, for home contacts exposed during the first eight weeks of pregnancy. As over 60 laboratories undertook the distribution of gammaglobulin and requests were considered on their merits, these trends give only a general indication of what occurred. Comparisons of the effects of dosage are therefore difficult and must be interpreted with caution.

Until 1961 all the gammaglobulin used was prepared at the Lister Institute and over half (54%) of the material used in the entire period was from that source, but after 1960 supplementation became necessary. In 1961 20% was from France, and in 1962 67% was from Holland and 9% from France. Lister gammaglobulin was prepared by the method of Kekwick and Mackay (1954) whereas the French and Dutch manufacturers used the Cohn *et al.* (1944) method of fractionation.

Methods

Information on whether or not women contracted rubella and on the outcome of pregnancy were obtained by three postal inquiries with standard questionary forms. The first inquiry was sent out with the gammaglobulin requesting the doctor to complete and return the form 28 days after inoculation. This form was returned for 30,764 (86%) of the doses issued during 1956–62. A substantial proportion of the remaining 14% of doses were sent back to the issuing laboratory unused; our record system did not allow for this, and the number so returned is unknown. The second inquiry, made three to nine months after the expected date of delivery, gave information on the pregnancy and the state of the baby at birth. It also confirmed whether or not rubella had occurred within 28 days of the injection or at any time subsequently. Of 30,764 forms sent out, 26,930 (88%) were returned. This form was also sent in respect of 143 women who were given gammaglobulin after the appearance of the rash in the hope of modifying the effects on the foetus; all these forms were completed.

Finally, when the children were at least 2 years of age a third postal inquiry was made about cases in which the foetus had been at greatest risk. This group comprised women known to have had rubella while pregnant, together with those who were in contact in the family during the first 12 weeks of gestation. In this inquiry the doctors were asked specifically about the presence of rubella-type defects—deafness, heart

* Epidemiological Research Laboratory, Colindale, London N.W.9.
† Present address: Department of Epidemiology and Health, McGill University, Montreal 2.

disease, and cataract. The third inquiry was sent in respect of 7,631 surviving children in the group at high risk and a report was received on 5,722 (75%). Most of the failures were due to the fact that the child's family had moved to a new address and could not be traced.

In addition to the three postal inquiries, 229 children whose mothers had rubella in pregnancy were selected from 360 children in this category who were reported alive at the second postnatal inquiry. The basis for selection was their proximity to a number of centres throughout the country to which they were called to be seen by one of us (C. S. P.). A complete physical examination was made with careful auditory and ophthalmic assessment; an electrocardiogram and chest *x*-ray film were taken when indicated. The Stycar test devised by Mary Sheridan (1958) was used for the detection of hearing defect.

Some of the least satisfactory data used in the analysis concerned the stage in pregnancy when the gammaglobulin was given. This question was not asked until the first postnatal inquiry, and by that time the doctor was often unable to supply the date of the last menstrual period. So far as possible the dates in question were estimated from available information and at worst from the date of delivery, but even this was not possible in pregnancies which ended in miscarriage.

Results

Rubella Attack Rate

Of the 30,764 women for whom there was information, 370 (1.2%) developed rubella within 28 days of inoculation and a further 97 (0.3%) at varying intervals thereafter. Table I shows that the attack rate was four times higher when the exposure to infection was in the family rather than elsewhere. Only before 1961 was there any evidence of better results with the higher dose. The attack rates increased about twofold between the early years and 1962. The reason for the increase was the high rate during the epidemic period in the first half of 1962 (Table II). The proportion attacked was highest in those given gammaglobulin immediately after exposure (Table III), but it is quite possible that those treated early were at greater risk. The distribution of intervals between exposure and onset of rubella when prophylaxis failed (see Chart) supports the accuracy of diagnosis in these cases. Unfortunately, it does not follow that when prophylaxis was apparently successful the diagnosis of illness in the primary case was equally accurate. Full analysis did not show any consistent difference between the results obtained with the Lister, Dutch, and French products and they have therefore been pooled. Detailed study showed that the attack rates in older women tended to be slightly higher than in younger women, but once again they may not have been at equal risk.

TABLE I.—*Rubella Attack Rates in Relation to Dose of Gammaglobulin and Type of Contact,* 1956–62

Years	Dose (mg.)	Type of Contact			
		In Family		Outside Family	
		No. at Risk	Attacked within 28 Days of Exposure No. (%)	No. at Risk	Attacked within 28 Days of Exposure No. (%)
1956–60	750	1,695	20 (1·18)	1,744	5 (0·29)
	1,500	2,119	17 (0·80)	2,273	5 (0·22)
1961	750	1,114	13 (1·17)	1,137	3 (0·26)
	1,500	1,516	27 (1·78)	1,821	5 (0·27)
1962	750	7,730	195 (2·52)	6,876	42 (0·61)
	1,500	999	24 (2·40)	1,288	13 (1·01)
1956–62	750	10,539	228 (2·16)	9,757	50 (0·51)
	1,500	4,634	68 (1·47)	5,382	23 (0·43)
All*		15,173	296 (1·95)	15,139	73 (0·48)

* In addition to the 30,312 women shown in this Table, there were 452 others for whom the type of contact or dose was not recorded; one of them developed rubella, making 370 cases in all. A further 97 women developed rubella more than 28 days after exposure.

TABLE II.—*Rubella Attack Rates in Family Contacts by Date of Inoculation,* 1956–62

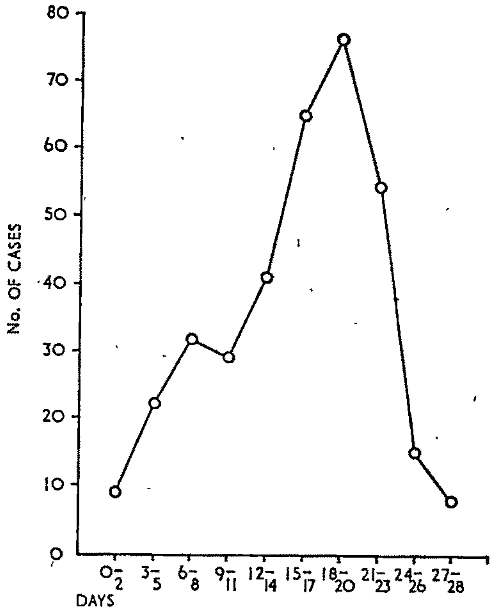
Season	1956–60		1961		1962	
	No. at Risk	Attacked No. (%)	No. at Risk	Attacked No. (%)	No. at Risk	Attacked No. (%)
Jan.–Mar. ..	Not known		409	7 (1·71)	1,598	40 (2·50)
Apr.–June ..			945	15 (1·59)	4,489	146 (3·25)
July–Sept. ..			837	11 (1·31)	2,068	29 (1·40)
Oct.–Dec. ..			441	7 (1·59)	584	4 (0·68)
Whole year(s) ..	3,816	37 (0·97%)	2,632	40 (1·52)	8,739	219 (2·51)

The figures in this Table do not agree entirely with those in Table I because information was not complete in all cases.

TABLE III.—*Rubella Attack Rates in Family Contacts in Relation to Time Between Exposure and Inoculation*

Year	No. at Risk	Exposure to Inoculation (Days)					
		0–4		5–12		13+ and Not Known	
		No. at Risk	Attacked No. (%)	No. at Risk	Attacked No. (%)	No. at Risk	Attacked No. (%)
1956–60	3,816	2,414	34 (1·4)	923	3 (0·3)	479	0
1961	2,632	1,713	31 (1·8)	577	5 (0·9)	342	4 (1·2)
1962	8,739	5,271	158 (3·0)	2,040	46 (2·2)	1,428	15 (1·0)
1956–62	15,187	9,398	223 (2·4)	3,540	54 (1·5)	2,249	19 (0·8)

The figures in this Table do not agree entirely with those in Table I because information was not complete in all cases.



Frequency distribution of intervals from exposure to onset of rubella in 351 cases (97 intervals of more than 28 days and 19 of uncertain length not shown).

Women with Rubella

Only 70% of the 610 women who had rubella in pregnancy came to term. In 16% pregnancy was terminated and the remainder either miscarried or were thought subsequently not to have been pregnant (Table IV). It may be seen in Table V that 13% of the children, live-born or stillborn, were reported to have congenital defects, and in the light of the additional findings in the sample of children visited 18% is probably a better estimate. This high figure was largely accounted for by deafness and heart defects, both characteristic of rubella. There were no cases of cataract, but in only 57 (13%) of 424 pregnancies known to have gone to term was the rubella in the first eight weeks of gestation.

The congenital defects present in this series are listed in Table VI according to the stage in pregnancy that rubella occurred and the stage of the inquiry at which they were ascertained. Most of the heart disease but little deafness was discovered at the first postnatal inquiry. The detailed examinations made during the visits after the second postnatal inquiry almost doubled the estimated percentage of deafness, but the additional cases were not severe and no other congenital defects were discovered at this time. About a quarter of the children whose mothers had rubella in the first 12 weeks had heart or hearing defects ; the rate fell to about 10% during the next four weeks and to about 5% after the sixteenth week. It is difficult to state these risks precisely because of the changing denominators at the first and second postnatal inquiries and visit. The outcome was more favourable in pregnancies in which rubella developed in spite of gammaglobulin than in those in which it was given after onset—4.8% compared with 2.2% for stillbirths and 12.4% compared with 8.2% for rubella-type defects—but these differences have little statistical significance (P>0.2 for both).

TABLE IV.—*Foetal Survival in Women with Rubella in Pregnancy,* 1956–62

	No of Cases of Rubella	Untraced at First Postnatal Inquiry	Not Pregnant	Surgical Abortion	Miscarriage	Total Births (Live and Still)	Stillbirths	Stillbirth Rate
Failures of prophylaxis	467	7	33	81	31	319	7	2·2%
Mother treated with gammaglobulin for rubella	143	0	3	17	18	105	5	4·8%
All cases	610	7 (1%)	36 (6%)	98 (16%)	49 (8%)	424 (70%)	12	2·8%

Except for stillbirth rates, percentages are calculated as a proportion of the number of cases of rubella; the figures for births include twins.

Women without Rubella

Information was obtained on the outcome of pregnancy in all but 13% of the 30,297 women who were in contact with rubella but escaped the illness. This information is summarized in Tables VII and VIII. Six per cent. aborted, 3% were thought subsequently not to have been pregnant, and the remainder gave birth to 23,931 children of which 381 (1.6%) were stillborn and 2.6% were stated to have congenital defects at the first postnatal inquiry. Despite a greater risk from rubella the stillbirth and defect rates in the family contact group were lower, if anything, than in the group with contact outside the family. Using information from the second postnatal inquiry, we estimated that the defect rate at this stage for children whose mothers had been exposed to rubella in the first 12 weeks of pregnancy was 3.6%. Of this total rate only 3.0 per thousand had hearing defects and 3.8 per thousand congenital heart disease.

TABLE V.—*Defects in Children of Women With Rubella in Pregnancy,* 1956–62

	No. of Live Births or Stillbirths at First Postnatal Inquiry	Live Births Untraced at Second Postnatal Inquiry	Children with Rubella-type Defects				Other Children with Defects	Total Children with Defects
			Deafness	Heart	Cataract	Any		
Failures of prophylaxis ..	319	33	19 (6·0%)	9 (2·8%)	0	26 (8·2%)	13 (4·1%)	39 (12·2%)
Mother treated for rubella	105	19	10 (9·5%)	4 (3·8%)	0	13 (12·4%)	4 (3·8%)*	17 (16·2%)
All cases	424	52	29 (6·8%)	13 (3·1%)	0	39 (9·2%)	17 (4·0%)	56 (13·2%)
Additional findings in sample of 229 children visited after 2nd postnatal inquiry			13 (5·7%)†	0	0	10 (4·4%)	0	10 (4·4%)
Estimated rates, using information from visits			12·5%	3·1%	0	13·6%	4·0%	17·6%

* One of these children had microphthalmia and retinopathy. † Three of these children were already known to have heart defects.

TABLE VI.—*Details of Defects in Children of Mothers with Rubella in Pregnancy,* 1956–62

Week of Pregnancy	Defect	First Post-natal Inquiry	Second Post-natal Inquiry	Visit	No. of Children with	
					Rubella Defects	Other Defects
0–8		(57)	(49)	(28)		
	Heart	1			1	
	,, ...	1	2		3	
	,, and deafness		1	2	}10	
	Heart, deafness, and mental defect ..		1		1	
	Deafness		5		5	
	Bilateral talipes ..		1			1
	Pyloric stenosis ..	1				1 }3
	Glaucoma and spasticity	1				1
9–12		(126)	(103)	(67)		
	Heart	1			1	
	Heart, renal and pyloric stenosis	1			1	
	Deafness	3	13	7	23 }26	
	Mental defect ..		1			
	,, ,, and deafness ..			1	1	
	Vitreous opacities		1			1
	Microphthalmia and retinopathy ..		1			1
	Hydrocephaly ..	1				1 }7
	Spasticity	1				1
	Renal	1	1			2
	Defect of diaphragm	1				1
13–16		(139)	(120)	(78)		
	Heart	3			3	
	,, ...	1			1	
	Heart, nystagmus, and deafness ..		1		}10	
	Deafness		5	1	6	
	Anencephaly ..	1				1
	Scoliosis		1			1 }4
	Ptosis		1			1
	Pyloric stenosis ..	1				1
17+ and N.K.		(102)	(88)	(56)		
	Heart		1		1	
	,, and renal ..		1		1 }4	
	Deafness			2	2	
	Defect of hand ..	1				1 }2
	Pyloric stenosis ..	1				1

Defects are listed according to the stage of the inquiry that they were ascertained. Thus, for example, of the three children shown with heart defects and deafness whose mothers had rubella in the first eight weeks of pregnancy, by the second inquiry a heart defect had been noted in all of them, but only one was thought to have a hearing defect. At the visit the other two children were also found to have hearing defects.

TABLE VII.—*Foetal Survival in Women Who Were in Contact with Rubella in Pregnancy But Did Not Develop the Disease,* 1956–62

	No. of Women Inoculated who Did Not Develop Rubella	Untraced at First Postnatal Inquiry	Not Pregnant	Surgical Abortion	Miscarriage	Total Births	Stillbirths	
							No.	Rate
Family contacts	14,840	1,800	538	17	956	11,678	200	1·7%
Other contacts ..	15,032	1,836	397	5	866	12,055	177	1·5%
Contact not known	425	191	10	2	27	198	4	2·0%
All contacts ..	30,297	3,827 (13%)	945 (3%)	24 —	1,849 (6%)	23,931 (79%)	381	1·6%

Except for stillbirth rates, percentages are calculated as a proportion of the number inoculated; the figures for births include twins.

The possibility that gammaglobulin might protect the foetus from hazards other than rubella was also examined by means of data from the first postnatal inquiry. For embryological reasons the probability of any such effect would be greater the earlier in pregnancy the inoculation was given. In Table IX the outcome is analysed in relation to dose of gammaglobulin

TABLE VIII.—*Defects in Children of Women Who Were in Contact With Rubella But Did Not Develop the Disease,* 1956–62

Type of Contact	No. of Live Births and Stillbirths at First Postnatal Inquiry	Children with Rubella-type Defects				Other Children with Defects	All Children with Defects
		Deafness	Heart	Cataract	Any		
Family	11,678	4 (0·03%)	38 (0·33%)	0	42 (0·36%)	241 (2·1%)	283 (2·4%)
Outside family	12,055	5 (0·04%)	49 (0·41%)	1	55 (0·46%)	276 (2·3%)	331 (2·7%)
Not known	198	0	1	0	1	0	1
All contacts	23,931	9 (0·04%)	88 (0·37%)	1	98 (0·41%)	517 (2·2%)	615 (2·6%)
Family contacts in first 12 weeks of pregnancy	7,505	3 (0·04%)	20 (0·27%)	0	23 (0·30%)	156 (2·1%)	179 (2·4%)
Additional findings on 5,362 children from 2nd postnatal inquiry*		14 (0·26%)	6 (0·11%)	0	20 (0·37%)	43 (0·8%)	63 (1·2%)
Estimated total defect rates for family contacts in first 12 weeks of pregnancy by adding findings from 2nd postnatal inquiry ..		(0·30%)	(0·38%)	0	(0·67%)	(2·9%)	(3·6%)

* The second postnatal inquiry was made in respect of 7,233 surviving children whose mothers had received gammaglobulin during the first 12 weeks of pregnancy.

TABLE IX.—*Foetal Survival and Defects in Women Who Did Not Develop Rubella in Relation to Dose of Gammaglobulin, and Stage of Pregnancy When Given,* 1956–62

Weeks of Injection	Dose (mg.)	Live Births and Stillbirths	Stillbirths		Children with Defect		Rate/1,000 of Children with Defects by System					
			No.	Rate	No.	Rate	Central Nervous	Musculo-skeletal	Cardio-vascular	Digestive and Respiratory	Genito-urinary	Miscel-laneous
First 12	1,500	4,746	51	1·1%	104	2·2%	8·4	6·3	2·3	4·6	2·1	2·3
	750	10,814	155	1·4%	276	2·5%	10·2	5·5	3·8	5·1	1·6	3·9
All	..	15,560	206	1·3%	380	2·4%	9·6	5·8	3·3	5·0	1·7	3·4
After 12	1,500	3,133	54	1·7%	68	2·2%	8·6	4·5	3·5	3·2	1·6	2·6
	750	4,179	72	1·7%	142	3·4%	15·3	7·2	4·3	4·5	2·4	3·6
All	..	7,312	126	1·7%	210	2·9%	12·4	6·0	4·0	4·0	2·1	3·1
Week or dose not known	..	1,059	49	4·6%	28	2·6%	13·2	1·9	6·6	8·5	0	1·9
All	..	23,931	381	1·6%	618	2·6%	10·7	5·7	3·7	4·8	1·8	3·2

and to whether it was given before or after the twelfth week. In terms of age distribution and type of rubella contact the four groups were closely comparable. The stillbirth rates were somewhat lower when gammaglobulin was given early, particularly in the higher dose ($P<0.05$). The defect rates also showed differences ($P<0.1$), but these seemed more closely related to dose than to time, and the pattern was not confined to any particular diagnostic groups. The analysis was carried through to a detailed consideration of over 80 specific defects; but wide variations, presumably due to chance, in even the more numerous categories, made the interpretation impossible. Frequencies for the main types of defect found at the first postnatal inquiry are set out in Table X for comparison with other surveys and as an indication of the level of case-finding achieved in this one.

TABLE X.—*Frequency of Congenital Defects Found At or Soon After Birth in* 23,931 *Live-born or Stillborn Children of Women Who Did Not Develop Rubella,* 1956–62

System	More Frequent Defects	No. (Rate/1,000)	Less Frequent Defects
Central nervous system and senses	Anencephaly .. .. Spina bifida .. .. Hydrocephaly .. Mongolism .. .. Spina bifida occulta .. Mental defect ..	57 (2·4) 54 (2·3) 50 (2·1) 45 (1·9) 15 (0·6) 15 (0·6)	Deafness 9, microcephaly 9, epilepsy 8, blindness 7, cerebral palsy 5, neuromuscular 5, encephalocoele 3, nystagmus 2, coloboma 2, other 9
Musculo-skeletal	Talipes .. .. Polydactyly .. .. Syndactyly .. .. Dislocation of hip ..	48 (2·0) 19 (0·8) 12 (0·5) 10 (0·4)	Exomphalos 9, diaphragmatic or hiatus hernia 8, limb 7, absent digit 7, deficient limb 6, achondroplasia 6, spine 5, chest wall 4, mandible 3, skull 3, other 6
Cardio-vascular	Ventricular septal defect Congenital heart disease (type unspecified) .. Patent ductus arteriosus	33 (1·4) 28 (1·2) 11 (0·5)	Fallot's tetralogy 9, coarctation 7, pulmonary stenosis 6, atrial septal defect 6, transposition 4, septal defect 3, aortic stenosis 3, persistent truncus 2, other 1
Digestive and respiratory	Pyloric stenosis .. Cleft palate .. .. Hare-lip	48 (2·0) 29 (1·0) 20 (0·8)	Small gut 6, rectal atresia 6, oesophageal atresia 5, megacolon 4, lung 4, ano-rectal 3, tracheo-oesophageal fistula 2, other 10
Other	Large haemangioma .. Hypospadias .. .. External ear .. .. Kidney	22 (0·9) 20 (0·8) 16 (0·7) 10 (0·4)	Genital 9, tumour 9, gross foetal 6, fibrocystic disease 6, renal pelvis 5, cretin 3, blood dyscrasia 4, ichthyosis 2, other 12

The figures shown give the number of children with the specified defect whether or not other defects were also present.

Discussion

The two questions which require an answer are: does gammaglobulin reduce the attack rate in pregnant women exposed to rubella and, if so, is her child also protected. An attack rate of 1.95% in over 15,000 women, most of whom had no past history of rubella and who were in close contact with a case in the family, usually their own child, seems a low figure, but it is difficult to estimate accurately what it would have been without gammaglobulin. In an earlier report (McDonald, 1963) based on experience before 1962 the attack rate in family contacts was 1.27%, which compared favourably with a rate of at least 3.7% for untreated women in a survey carried out by the College of General Practitioners during roughly the same period (Watson and McDonald, 1963). In 1962, however, the attack rate rose to 2.5% in treated women and to 3.25% at the height of the epidemic. A family survey might have shown a similar increase in the rates for untreated women, but there is little information on this point.

In a description by Fry *et al.* (1962) of the 1962 epidemic in a large London suburban practice about 5% of all women of child-bearing age were actually seen with rubella, and it was estimated that the true attack rate was probably half as great again. Fry (personal communication, 1966) reported that in 156 families with a case of rubella 250 women aged 17–44 were at risk and 39 (15.6%) developed the disease. The figures are quite similar to those presented by Sever *et al.* (1965) for the 1964 epidemic in the U.S.A. They reported an attack rate of 3.5% in women exposed to rubella and given gammaglobulin (15–20 ml.) compared with 12.8% for unprotected women. The evidence from controlled trials must also be taken into account. Though these have been in children and not wholly consistent (Korns, 1952), results have generally indicated a substantial degree of protection (Landon *et al.*, 1949; Grayston and Watten, 1959; McDonald, 1963; Brody *et al.*, 1965). Altogether it seems very probable that without gammaglobulin the attack rate in pregnant women would have been substantially higher than it was.

The absence of an excess of rubella-type defects in the children of women who escaped rubella is more certain. The estimated rates per thousand for the children of family contacts in the first 12 weeks of pregnancy—deafness 3.0, heart defects 3.8, and cataract 0—seem to be within normal limits. Comparable figures, as yet unpublished, from a large prospective study of some 12,000 pregnancies conducted in Britain during the same period and using fairly similar methods of ascertainment were as follows: deafness 1.2, heart defects 4.5, and cataract 0.1. The rate for deafness was thus higher than in the normal series, but in our inquiry special emphasis was put on its detection. An additional point concerns the proportion of children with congenital heart disease who had a patent ductus arteriosus. This lesion is characteristic of rubella (Campbell, 1961), and in our series of women who contracted rubella 8 out of 13 children with heart disease had this defect. In contrast, in our series of women who escaped rubella there were only 11 cases of patent ductus in 93 cases of heart disease. These and other similar figures set out in Table XI suggest that if apparent rubella virus infections occurred they did no appreciable harm to the child.

TABLE XI.—*Patent Ductus Arteriosus as a Proportion of All Congenital Heart Disease*

Series	Description	Congenital Heart Disease		Patent Ductus Arteriosus	
		Rate/ 1,000 Births	No. of Cases	No. of Cases	% of Total
Current series ..	Rubella in early pregnancy	30·7	13	8	62
Manson *et al.* (1960)	Rubella in early pregnancy	26·4	15	Not stated	
Campbell (1961) ..	Congenital heart disease after maternal rubella		153	89	58
McDonald (1961)	Prospective inquiry in normal women	4·7	15	1	7
Slater *et al.* (1964)	Notified cases from general practice		About 1,282	153	12
McDonald (1966)	Prospective inquiry in normal women	4·5	50	12	24
Current series	Rubella contact in family	4·4	44	3	7
	Rubella contact outside family	4·1	49	8	16

Summary

Reports were obtained on the result of inoculation of 30,764 women with gammaglobulin after exposure to rubella in pregnancy during the years 1956–62. The outcome was ascertained soon after the expected date of delivery in 26,930 (88%) cases, and further inquiries were made on selected samples of surviving children when they were 2 or more years of age.

In 1.95% of family contacts and 0.48% of contacts outside the family clinical signs of rubella developed within 28 days of inoculation. Without gammaglobulin these rates would probably have been substantially higher.

Of 610 women who had rubella in pregnancy only 70% came to term. About a quarter of the children whose mothers had the disease in the first 12 weeks had heart or hearing defects; the proportion fell to about 10% for the next four weeks and then to about 5%. The rates for stillbirth and for rubella-type defects were higher when gammaglobulin had been given *after* the onset of rubella than when the disease developed despite prophylaxis, but these differences could have been by chance ($P>0.2$).

There was no excess of cataract or heart disease and probably no excess of deafness in the children of women who did not develop rubella though exposed to it. Subclinical rubella virus infection either carried little risk for the foetus or did not occur often enough for any adverse effect to be detected.

A lower proportion of children whose mothers received gammaglobulin in the first 12 weeks of pregnancy were stillborn (1.3% compared with 1.7%; $P<0.05$) or had congenital defects (2.4% compared with 2.9%; $P<0.1$) than of those whose mothers were injected after the twelfth week.

We are indebted to many people for their help in this inquiry, in particular to general practitioners throughout the country who dealt patiently with our repeated requests for information, and to Miss Barbara Kinsley and Mrs. G. V. Smith for their work on the analysis. The investigation was carried out in the Public Health Laboratory Service assisted by a grant from the Medical Research Council.

REFERENCES

Bass, M., Davidson, H. B., Foote, F., Muckenfuss, R., and Landon, J. F. (1949). *N.Y. Med.*, 5 No. 23, 21.
Brody, J. A., Sever, J. L., and Schiff, G. M. (1965). *New Engl. J. Med.*, **272**, 127.
Campbell, M. (1961). *Brit. med. J.*, **1**, 691.
Cohn, E. J., Oncley, J. L., Strong, L. E., Hughes, W. L., and Armstrong, S. H. (1944). *J. clin. Invest.*, **23**, 417.
Fry, J., Dillane, J. B., and Fry, L. (1962). *Brit. med. J.*, **2**, 833.
Grayston, J. T., and Watten, R. H. (1959). *New Engl. J. Med.*, **261**, 1145.
Green, R. H., Balsamo, M. R., Giles, J. P., Krugman, S., and Mirick, G. S. (1964). *Trans. Ass. Amer. Phycns*, **77**, 118.
Kekwick, R. A., and Mackay, M. E. (1954). *Spec. Rep. Ser. med. Res. Coun. (Lond.)*, No. 286.
Korns, R. F. (1952). *J. infect. Dis.*, **90**, 183.
Manson, M. M., Logan, W. P. D., and Loy, R. M. (1960). *Rubella and other Virus Infections during Pregnancy.* Ministry of Health Reports on Public Health and Medical Subjects, No. 101. H.M.S.O. London.
McDonald, J. C. (1963). *Brit. med. J.*, **2**, 416.
—— (1966). Unpublished.
Sever, J. L., Nelson, K. B., and Gilkeson, M. R. (1965). *Amer. J. Dis. Child.*, **110**, 395.
Sheridan, M. D. (1958). Manual for the Stycar Hearing Test, distributed by the National Foundation for Education Research in England and Wales, London.
Slater, B. C. S., Watson, G. I., and McDonald, J. C. (1964). *Brit. J. prev. soc. Med.*, **18**, 1.
Watson, G. I., and McDonald, J C. (1963). *Brit. med. J.*, **2**, 419.

Incidence of Rubella Antibodies among Pregnant Women in Six Areas: Prophylactic Effect of Two Doses of Gammaglobulin

Report* to the Public Health Laboratory Service Rubella Working Party

Brit. med. J., 1967, **3**, 638–640

The use of gammaglobulin as a prophylactic in pregnant women exposed to rubella during the first trimester has been accepted practice for over a decade. Several surveys have been made to assess its efficacy, but the results showed little agreement (Lundström, 1965). With the isolation of the rubella virus (Parkman *et al.*, 1962 ; Weller and Neva, 1962) an accurate assessment of the value of gammaglobulin as a prophylactic was to be expected. However, the results of experimental work (Green *et al.*, 1964) indicated that gammaglobulin was not protective, whereas field trials (Brody *et al.*, 1965) suggested that some protection was afforded.

During the past 18 months studies into gammaglobulin prophylaxis in pregnant women exposed to rubella have been conducted in this laboratory. This communication reports some of the results so far obtained in two surveys using different dose schedules and the incidence of rubella antibodies in pregnant women in different areas of England.

Method of Study

In England and Wales general practitioners requiring gammaglobulin obtain their supplies from public health laboratories which serve as distribution centres. During the period of both studies an initial dose of 750–800 mg. of gammaglobulin was supplied for each pregnant woman exposed to rubella in the first 16 weeks of pregnancy. Gammaglobulin of both English and Dutch manufacture was used, and several different batches of each product were distributed.

The first study (Study A) was conducted from April 1965 to March 1966 in the area served by the Manchester Public Health Laboratory. Before giving gammaglobulin to patients exposed to rubella in the resident family (home contact) general practitioners collected a specimen of the patient's blood and sent it to the laboratory by post. Each serum was examined for the presence of rubella-neutralizing antibody within a week of receipt. Approximately six weeks later a second specimen was obtained from all these patients whether initially with or without antibody, and the paired sera were titrated together. As only a small percentage of Manchester women were found to be non-immune and as a single dose of 750 mg. of gammaglobulin did not prevent infection in some of these patients, a second study (Study B) was begun in March 1966. The investigation was extended in order to study a large number of non-immunes and to assess the value of a larger dose of gammaglobulin. This report records the results obtained up to 31 August 1966.

General practitioners receiving supplies of gammaglobulin from six public health laboratories for patients exposed both at home and elsewhere (other contracts) collected a specimen of whole blood from their patients and sent these specimens direct to the Manchester laboratory by post. Where possible a throat swab was collected for virus isolation from the suspected case of rubella and posted to the laboratory. The sera were examined for rubella-neutralizing antibody within 48 hours of receipt, the results being available within four days of setting up the test.

If neutralizing antibody was not detected or found to be present at a titre no greater than 1/4 the patient was, for the purposes of this investigation, regarded as non-immune and the local public health laboratory sent a further 1,500 mg. of gammaglobulin to the practitioner to be given to his patient if she was still within 12 days of contact. In home contacts the day of appearance of the rash was taken as the day of contact. Six weeks after the initial dose of gammaglobulin a second specimen of blood was obtained from these patients.

Materials and Methods

Sera.—Blood obtained from the patients was separated and sera were stored at −20° C. and were not inactivated.

Neutralization Tests.—These were performed in the RK.13 continuous line of rabbit kidney cells (Beale *et al.*, 1963). The propagation of the cells and the technique of the neutralization test are described in detail elsewhere (Hutchinson and Thompson, 1965).

Dilutions of sera were prepared in 0.3-ml. amounts to which were added an equal volume of rubella virus suspension ("West Point" strain) diluted to contain 1,000 T.C.D.$_{50}$ per ml. After incubation at 37° C. for one hour an inoculum of 0.2 ml. was added to each of two tubes of RK.13 cells containing 0.8 ml. of medium. Control sera and virus titrations were incorporated in each batch of tests. On receipt, sera were examined for the presence of rubella-neutralizing antibody at serum dilutions of 1/2 and 1/8 only. Titrations were performed with fourfold serum dilutions in the range 1/2 to 1/128. The titre was reported as that dilution of serum inoculated into tubes showing an unequivocal reduction in the number of microfoci, and not, as previously, the dilution of serum in the serum-virus mixture (Hutchinson and Thompson, 1965).

Results

Study A.—Of 429 sera obtained from pregnant women who had home contacts in the Manchester area in 1965–6, only

TABLE I.—*Examination of Paired Sera from Non-immunes*

Study	Amount of Gammaglobulin Given	Total No. Pairs Examined	No. of 2nd* Sera with Neutralizing Antibody	% Infected
		Home Contacts		
A	750 mg.	20 } 30	6 (4) } 8	30 } 26·7
B	750 mg. only	10	2 (1)	20
B	750 + 1,500 mg.	29	9 (4)	31
		"Other" Contacts		
B	750 mg. only	18	—	—
B	750 + 1,500 mg.	51	1 (1)	1·96

* Figures in parentheses indicate cases of clinical rubella.

---

* The Public Health Laboratory Service consultants assisting in the investigations were Dr. B. W. Barton (Derby), Dr. W. L. Hooper (Stafford), Dr. Hélène J. Mair and Dr. N. S. Mair (Leicester), Dr. J. H. McCoy (Hull), Dr. Pauline M. Poole (Chester), and Dr. J. O'H. Tobin (Manchester). The tests were carried out at the Manchester laboratory by Mrs. Eileen Smith, Mr. K. M. Thompson, and Dr. D. N. Hutchinson. The report was prepared by Dr. D. N. Hutchinson.

21 (4.9%) did not possess rubella-neutralizing antibody. A second serum was obtained from 20 of these 21 negatives and the results of examination of these 20 pairs are given in Table I. Six of these patients had developed neutralizing antibody by the time the second specimen was collected. Four of the patients were known to have had clinical rubella, and rubella virus was isolated from the throat in each case.

Study B.—The results of the examination of 1,326 sera obtained from all contacts of rubella in the areas served by the six public health laboratories are shown in Table II. The proportion of non-immunes varied from 21% to 6.3%. The results obtained on examination of pairs of sera from 39 non-immune home contacts and 69 other non-immune contacts are shown in Table I. Six of the 12 women who had developed neutralizing antibody in the second specimen were reported as having had clinical rubella. Rubella virus was isolated from the throat of the two patients from whom specimens were received. Sixteen patients were reported as having a neutralizing antibody titre of 1/4 in the first serum specimen. Titration of paired sera from the patients showed that one pair contained no antibody, five pairs had a titre of 1/8, and the other 10 pairs remained unchanged at a titre of 1/4. In non-immune family contacts the mean number of days between contact and the first dose of gammaglobulin was 4.8 days in those receiving one dose and 2.8 days in those receiving two doses. In the non-family contacts the mean was 7.4 days for those receiving one dose and 5.0 days for those receiving two doses.

TABLE II.—*Rubella-neutralizing Antibody Among Pregnant Women Exposed to Rubella in Sera from Areas Served by Six Public Health Laboratories*

Public Health Laboratory	No. of Sera Examined	Negative*		Contact History*					
				Family			Other		
				Total	Negative		Total	Negative	
		No.	%		No.	%		No.	%
Chester ..	84	11	13·1	28	2	7·1	53	9	17·0
Derby ..	267	34	12·7	81	7	8·6	163	26	15·9
Hull ..	115	11	9·6	57	5	8·8	58	6	10·3
Leicester ..	143	24	16·8	43	9	20·9	94	15	16·0
Manchester	593	38	6·4	237	15	6·3	335	23	6·9
Stafford ..	124	16	12·9	42	3	7·1	78	12	15·4
Total	1,326	134	10·1	488	41	8·4	781	91	11·7

* Excludes those patients with a titre of 1/4 or where the contact history was not known.

Discussion

Workers in America (Sever *et al.*, 1965b) Canada (Givan *et al.*, 1965) and Sweden (A. Svedmyr, personal communication, 1966) have reported that 80 to 90% of women of child-bearing age possess rubella-neutralizing antibody. Dudgeon *et al.* (1964), in this country, found rubella-neutralizing antibody in 82% of cord bloods obtained from a London hospital. In the areas served by the six laboratories we have found a marked variation in the number of immunes, the proportion ranging from 80 to 94%. These differences are possibly associated with the differing size of industrial, urban, and rural populations which these laboratories serve. Our findings are similar to those of Sever *et al.* (1964), who examined sera from several centres in the U.S.A. and found a large difference in the number of immunes between areas and ethnic groups. This variation in different areas makes assessment of field trials into the protective effect of gammaglobulin unreliable, unless the immune state of each area being studied is known.

In five areas the percentage of susceptibles in home contacts was less than that for the other contact group. The total number of patients examined, so far, is too small to attach significance to this finding.

Of 30 non-immune home contacts from both studies who were given only one dose (750–800 mg.) of gammaglobulin, 26.7% showed evidence of infection (Table I). In Study B, 29 home contacts were given an additional dose (1,500 mg.) of gammaglobulin between 8 and 12 days after contact. Of these, 31% were infected. All but one of the patients showing evidence of infection received the initial dose of gammaglobulin within three days of contact. However, the results do not indicate that the giving of a second dose late in the incubation period increases the maternal protection to infection (McDonald, 1963).

The risk of maternal infection would not appear to be very great when the patient and the contact were not living in the same house. Only one of 69 such non-immune contacts (51 given a second dose of gammaglobulin) developed evidence of rubella infection. This patient had repeated contact with several children while transporting them to and from school. Her own child did not develop clinical rubella.

In a review of the protection afforded by gammaglobulin, Lundström (1965) tabulated the results of various surveys and trials and drew attention to the widely different attack rates obtained. Sever *et al.* (1965a), in a preliminary report on the prophylactic value of gammaglobulin given to pregnant women in the first trimester, found a significant reduction in clinical rubella occurring within one month after exposure. It is not yet possible to assess their results as serological data were available for only a small number of cases. McDonald (1963), in this country, found that 1.27% of home contacts who received gammaglobulin still developed clinical rubella. In our studies attack rates of 0.93% (A) and 1.02% (B) were found in all home contacts. However, the true attack rate in susceptible home contacts is at least 30%.

Sixteen batches of gammaglobulin used during these studies were titrated for neutralizing antibody. The titres ranged from 1/32 to 1/256. In our studies too few susceptibles have received material from any one batch to detect a significant difference. Korns (1952) found that only one of three batches of gammaglobulin gave significant protection in field trials. On testing 17 different batches of gammaglobulin, Schiff *et al.* (1963) found an eightfold difference in titres, and they concluded that the variation in the protective value of different lots of gammaglobulin was a reflection of this titre difference. In future trials the titre of rubella-neutralizing antibody in the different batches of gammaglobulin issued should be known and preferably only those with a high titre used.

An attempt was made during study B to prove that the patient was exposed to rubella, as several enteroviruses are known to produce a rubelliform rash (Lerner *et al.*, 1963). A throat swab was obtained from the index cases of home contacts, but this usually necessitated a special visit by the practitioner or a member of the laboratory staff, and was not always possible. Nine specimens collected within four days of the rash were received from children of non-immune home contacts. Rubella virus was isolated from the child of a patient who developed neutralizing antibody. In the other eight instances virus was not isolated and the patients remained non-immune. From other studies in patients with serological proof of rubella infection a virus isolation rate of 90% could be expected from throat swabs transported overnight in the post—a similar result to that obtained by early inoculation of cultures (to be published).

These studies indicate that it is necessary to investigate the prophylactic effect of giving a large dose of gammaglobulin as soon as possible after contact. To do so would be costly, and in future trials some saving would be effected by restricting the use of the large dose to home contacts. If a more rapid test for the detection of rubella antibody was available greater economy could be made. So far, fluorescent antibody techniques (Brown *et al.*, 1964) have not proved readily adaptable to the testing of large numbers of sera; however, a haemagglutination inhibition test for the detection of rubella antibodies may prove suitable for this purpose (Stewart *et al.*, 1967).

This report records only the effect of gammaglobulin on maternal infection, and it is possible that the administration of gammaglobulin, though not preventing maternal rubella, may still reduce the frequency and the severity of foetal abnormalities. It is hoped to study the outcome of the pregnancies in the susceptible patients.

Summary

In six areas of England and Wales the incidence of rubella-neutralizing antibody among pregnant women exposed was found to vary from 80 to 95%.

Two different dose schedules were used and the prophylactic effect of gammaglobulin in pregnant rubella contacts was investigated. The attack rate in home contacts given 750 mg. of gammaglobulin was 26.7%. In similar contacts given an initial dose of 750 mg. followed by a further 1,500 mg. within 12 days of exposure the attack rate was 31%. In non-family contacts only one out of 69 susceptibles developed evidence of rubella infection.

It is a pleasure to record the co-operation of the many general practitioners in the areas served by the six public health laboratories; these investigations would not have been possible without their assistance. This work was supported by a research grant from the Ministry of Health to the P.H.L.S. Rubella Working Party. The members of the Working Party are: Dr. A. D. Macrae (Colindale) (chairman), Dr. D. Reid (Colindale) (secretary), Dr. C. M. P. Bradstreet (Colindale), Dr. S. K. R. Clarke (Bristol), Miss A. M. Field (Colindale), Dr. J. H. Hale (Newcastle upon Tyne), Dr. M. H. Hambling (Leeds), Dr. D. N. Hutchinson (Manchester), Dr. W. F. Lane (Bedford), Dr. C. Miller (Medical Research Council Laboratories, Hampstead), Mr. J. Pope (Colindale), Dr. G. B. B. White (Liverpool), and Dr. J. E. M. Whitehead (Coventry).

REFERENCES

Beale, A. J., Christofinis, G. C., and Furminger, I. G. S. (1963). *Lancet*, **2**, 640.
Brody, J. A., Sever, J. L., and Schiff, G. M. (1965). *New Engl. J. Med.*, **272**, 127.
Brown, G. C., Maassab, H. F., Veronelli, J. A., and Francis, T. J. (1964). *Science*, **145**, 943.
Dudgeon, J. A., Butler, N. R., and Plotkin, S. A. (1964). *Brit. med. J.*, **2**, 155.
Givan, K. F., Rozee, K. R., and Rhodes, A. J. (1965). *Canad. med. Ass. J.*, **92**, 126.
Green, R. H., Balsamo, M. R., Giles, J. P., Krugman, S., and Mirick, G. S. (1964). *Trans. Ass. Amer. Phycns*, **77**, 118.
Hutchinson, D. N., and Thompson, K. M. (1965). *Mth. Bull. Minist. Hlth Lab. Seerv.*, **24**, 385.
Korns, R. F. (1952). *J. infect. Dis.*, **90**, 183.
Lerner, A. M., Klein, J. O., Cherry, J. D., and Finland, M (1963). *New Engl. J. Med.*, **269**, 678.
Lundström, R. (1965). *Arch. ges. Virusforsch.*, **16**, 506.
McDonald, J. C. (1963). *Brit. med. J.*, **2**, 416.
Parkman, P. D., Buescher, E. L., and Artenstein, M. S. (1962). *Proc. Soc. exp. Biol. (N.Y.)*, **111**, 225.
Schiff, G. M., Sever, J. L., and Huebner, R. J. (1963). *Science*, **142**, 58.
Sever, J. L., Nelson, K. B., and Gilkeson, M. R. (1965a). *Amer. J. Dis. Child.*, **110**, 395.
—— Schiff, G. M., Bell, J. A., Kapikian, A. Z., Huebner, R. J., and Traub, R. G. (1965b). *Pediatrics*, **35** 996.
—— —— and Huebner, R. J. (1964). *Obstet. and Gynec.*, **23**, 153.
Stewart, G. L., Parkman, P. D., Hopps, H. E., Douglas, R. D., Hamilton, J. P., and Meyer, H. M. (1967). *New Engl. J. Med.*, **276**, 554.
Weller, T. H., and Neva, F. A. (1962). *Proc. Soc. exp. Biol. (N.Y.)*, **111**, 215.

Comparison of Intragastric and Intravenous Routes of Glucose/Bicarbonate Administration in Respiratory Distress Syndrome

J. M. ABRAHAM,* M.B., B.S., M.R.C.P., M.R.C.P.ED., M.R.C.P.GLASG., D.C.H.; R. J. K. BROWN,† M.B., F.R.C.P., D.C.H.

Brit. med. J., 1967, **3**, 640–642

After the reports of Usher (1959, 1961), who suggested that the use of glucose/sodium bicarbonate solutions had led to a significant reduction in the mortality from the respiratory distress syndrome, his form of treatment was given a preliminary trial in the neonatal ward at the Queen Elizabeth Hospital for Children during 1961 and 1962. Among 61 infants treated within 24 hours of birth with *intravenous* therapy according to his suggested dosage there were 18 deaths, a mortality of 29.5%. Usher emphasized the need to start the infusion early, preferably within three hours, if it was to have any demonstrable effect on the survival rate. Our experience confirmed this, for among 10 babies whose treatment was delayed for over 24 hours there were nine deaths. If these babies had been included in our preliminary trial there would have been 27 deaths out of a total of 71 babies and the mortality increased to 38%. It would, however, give a fairer estimate of the mortality if the 10 cases in which treatment had been delayed for 24 hours or more were excluded. However, even the figure of 38% is significantly lower than the average 60% mortality in most previously reported series where bicarbonate had not been administered.

Unfortunately, in this hospital there were not enough controls to provide statistical proof that the treatment was of value, though there had been 32 babies who had received oxygen and increased humidity but no bicarbonate, and among these there were 17 deaths, a mortality of 53%. The results are given in Table I, alongside some results reported from Glasgow (Hutchison *et al.*, 1962).

TABLE I.—*Comparison of the Mortality Rates from R.D.S. With and Without Treatment With Intravenous Glucose/Sodium Bicarbonate Infusion in Two Centres*

Source	Q.E.H.C. (1961–2). Glucose/$NaHCO_3$ by I.V. Infusion				Glasgow (1962). Glucose and $NaHCO_3$ by "Titration"		Glasgow. O_2 and Humidified Air			
	I All Cases		II Omitting Cases Treated After 24 Hours				1960		1961	
	No.	%	No.	%	No.	%	No.	%	No.	%
Deaths	27*	38	18	29·5	11	41	48	66	38	64
Survivals ..	44	62	43	70·5	16	59	25	34	21	36
Total ..	71		61		27		73		59	

* Nine of these deaths occurred among 10 cases that did not start therapy until 24 hours or more had elapsed, thus causing the mortality to be increased by nearly 10% more than need be.

Differences between percentage mortality rates in the two Glasgow series (results for 1960 and 1961 combined) $P < 0{\cdot}02$ (this is "significant").

The Glasgow figures are quoted from Hutchison *et al.* (1962).

---

* Lately Medical Registrar, Queen Elizabeth Hospital for Children, London E.2.

† Consultant Paediatrician, Queen Elizabeth Hospital for Children, London E.2.

Though lacking strict statistical proof, the results of our preliminary trial engendered a firm conviction that prompt treatment directed against a metabolic acidosis by means of infusions of glucose and sodium bicarbonate could reduce the mortality of the respiratory distress syndrome. With experience the team concerned in the management of these cases became skilled in setting up scalp-vein infusions. In spite of this, difficulties were often encountered which entailed too much handling of very ill infants. Once an intravenous infusion containing glucose has been started there is the risk of "hypoglycaemic shock" if the drip should stop. To avoid this the needle must be reinserted into another vein within an hour, often into an already oedematous scalp. For these reasons it did not seem feasible to use this treatment in the maternity units unless a simpler method of infusion could be used. Because of the dangers of phlebothrombosis it was thought inadvisable to use the umbilical vein.

It was decided, therefore, to carry out a trial in which alternate infants were given the solution intravenously and intragastrically.

Material and Method

Babies were referred from maternity units in affiliated hospitals, mostly within a few hours of delivery, on developing clinical signs of respiratory distress (R.D.S.). They were transported in portable incubators in oxygen (about 25% concentration at the nostril) without increased humidity and before any treatment was initiated. If on arrival they were thought to conform clinically to hyaline membrane disease (H.M.D.) they were allocated alternately to one of two ways of glucose/sodium bicarbonate administration, the one parenterally through a scalp-vein needle (I.V.), the other by gavage (I.G.). Otherwise management was identical for both groups, by the same staff.

The babies were nursed in humidified incubators, and oxygen was administered in a concentration which was thought by the ward sister to be sufficient to control their cyanosis. The usual percentage ranged between 40 and 60% at the nostril. The dosage of sodium bicarbonate in 10% dextrose solution (65 ml./kg./day) was regulated according to serial *p*H estimations of heel capillary blood (Usher, 1961). The solution was given as a slow continuous drip through a polyvynyl stomach tube. Insulin was never used. Antibiotics (penicillin 150,000 units and streptomycin 50 mg. b.d.) and on many occasions a synthetic pressor amine, mephentermine sulphate (1.25 mg. two-hourly when the patient was severely distressed), were administered. Severity of respiratory distress was judged clinically by the respiratory rate, the degree of cyanosis, and the Silverman retraction score (Silverman and Andersen, 1956). With the last, those scoring up to 5 were regarded as mild, 5–7 as moderate, and 8–10 as severe cases. The chest was radiographed on the first morning after admission. A radiograph showing an air bronchogram, a diffuse reticulogranular pattern, or both, was regarded as positive for hyaline membrane disease.

Results

Table II shows the scope of the trial. Of 120 patients who were provisionally given the diagnosis of hyaline membrane disease and started on the alternate treaments 21 were excluded, either because there was no confirmatory biochemical and radiological evidence of the disease and subsequent progress showed nothing more than minimal intercostal recession, or because an alternative diagnosis became obvious later. In retrospect it was apparent that sufficient care had not been taken to obviate bias in the selection of treatment for babies who happened to arrive on the ward simultaneously. Though these included four sets of twins, it was reluctantly decided that they should be excluded from the trial. Babies who were more than 24 hours old on arrival were also excluded, because the preliminary trial had shown that treatment did not influence the survival rate in this group (see Table I). Finally, it was necessary to exclude all those babies for whom the treatment had subsequently been changed for one reason or another.

TABLE II.—*Scope of Trial and Reasons for Exclusion of 73 Cases Referred Initially With Signs of Respiratory Distress*

Period of trial: May 1964–November 1965 (excluding June and July 1965 owing to temporary change of staff)				16 months
No. of cases referred as R.D.S...				152
Excluded:				
(1) Not H.M.D. on initial clinical examination ..			32	
(2) Not H.M.D. on retrospective analysis	15*	6†	21	
Symptoms insufficient for diagnosis of H.M.D. ..	8	3		
Pneumonia	4	1		
Urethral valve: severe metabolic acidosis	1	—		
Neonatal hypoglycaemia ..	—	1		
Congenital heart disease ..	1	—		
Cerebral irritation	1	1‡		
(3) Clinically H.M.D. but omitted for following reasons			20	
Twins (4 × 2)		8		
Arrived simultaneously (2 × 2) ..		4		
Change of treatment I.G. to I.V. ..		5		
Over 24 hours old on admission ..		3		73
No. of cases remaining in the trial				79

* Intragastric. † Intravenous. ‡ Died with intraventricular haemorrhage.

Of the remaining 79 cases 36 were in the "intragastric group" and 43 in the "intravenous group," with 8 and 17 deaths respectively (Table III). Of the 20 cases which finally came to necropsy 18 showed typical hyaline membranes, a reflection of the accuracy of the initial diagnosis.

TABLE III.—*Comparison of Mortality Rates of Two Groups of Alternate Intragastric and Intravenous Administration of Glucose and Sodium Bicarbonate Mixture, and Time When Milk Feeds Begun in Survivors*

	Total No.	Deaths	Time When Milk Feeds Begun
Intragastric	36	8 (22·2%)	67·9 (26–140) hours
Intravenous	43	17 (39·5%)	64·9 (22–115) ,,

Difference between mortality rates = 17·3%. S.E. of difference = 10 5 : 2 (S.E.) = 21. On χ^2 analysis, P = 0·10.

It was hoped that by alternate allocation the two groups would match. However, it will be seen that, though the mean values in many instances are comparable (Table IV), the distribution of some important criteria is not (see Chart). Even allowing for this the difference between the mortality rates is not statistically significant (P=0.10).

TABLE IV.—*Analysis of Clinical and Biochemical Data of 79 Subjects Included in Trial and the Necropsy Findings in 20 Cases*

	Whole Group		Deaths	
	I.G.	I.V.	I.G.	I.V.
Number	36	43	8	17
Birth weight (g.) mean ..	2,000	1,988	1,623	1,786
Gestation (weeks) mean ..	34·2	33·7	33·2	33·1
Sex: Male	22	35	4	13
Sex: Female	14	8	4	4
Delivery: Vaginal ..	26	36	7	15
Delivery: Caesarean ..	10	7	1	2
*p*H (heel capillary blood) mean	7·15	7·14	7·04	7·09
P_{CO_2} (heel capillary blood) (mm. Hg) mean	72·6	66·2	99·3	76
Severity on admission: Mild ..	14	12	1	3
Severity on admission: Moderate ..	14	21	5	11
Severity on admission: Severe ..	8	10	2	3
Chest *x*-ray: Positive ..	14	12	2	5
Chest *x*-ray: Negative ..	7	3	—	—
Chest *x*-ray: Not done ..	15	28	6	12
Treatment: Age started (hours) mean	7·7	7·6	10·6	9
Age at death (hours) mean ..			30·4	33·5
Necropsy: Number ..			6 (2 m., 4 f.)	14 (11 m., 3 f.)
Hyaline membrane			5	13
Pneumonia			1	2
Pulmonary haemorrhage			—	2
Atelectasis			6	12
Intraventricular haemorrhage			1 (female)	6 (1 female)

Discussion

The results of this trial are capable of different interpretations. If one is sceptical of the value of this type of treatment it could be argued that it has done nothing to help these infants, and the difference between the survival rates in the two groups is entirely due to chance. Indeed, it could be suggested that infusing relatively large amounts of fluid and sodium bicarbonate into distressed premature babies is even positively harmful, but less so when the intragastric route is used, because of poor absorption from the alimentary tract, and hence the lower mortality in this group. Neither of these explanations is really acceptable. It is reasonable to expect that careful correction of a metabolic acidosis will benefit a sick infant as it does when acidosis results from other causes such as severe gastroenteritis.

WEIGHT (g.)		INITIAL pH OF HEEL CAPILLARY BLOOD	
>2500	△△△△ ●○○○○○○	>7·3-	△
2251-2500	▲▲△△△△△△△ ○○○○○○	7·2-7·3	▲▲▲△△△△△△△△△ ●○○○○○○○○○○
2001-2250	▲▲▲△△△△△ ○○○○○○	7·1-7·2	▲▲▲▲▲△△△△△△△△△△△△△△ ●●○○○○○○○○○○○○○○○
1751-2000	▲▲△△△△ ●○○○○○	7·0-7·1	▲▲▲▲ ●○○○
1501-1750	▲▲▲▲▲▲△△△△ ●●○	<7·0	▲▲▲△△ ●●●●
<1500	▲▲▲▲△△ ●●●●○○○○		

Intravenous. SURVIVAL △ DEATH ▲ Intragastric. SURVIVAL ○ DEATH ●

Distribution of birth weight and initial *p*H in the two groups.

The published results of several trials have all shown an appreciable reduction in the mortality from the respiratory distress syndrome when intravenous infusions of glucose/sodium bicarbonate have been administered (Usher, 1959, 1961, 1963 ; Hutchison *et al.*, 1962), and the preliminary trial of intravenous therapy in this hospital showed a definite improvement over other forms of therapy which had been used previously. Thus there is no good evidence that these infusions are harmful. The evidence of positive benefit is not quite so convincing, because it is to be expected that intensive care in special units will by itself result in an improved survival rate, but many people have been convinced of this by Usher's (1963) controlled trial.

If it is assumed that the infusion of glucose/sodium bicarbonate solutions is beneficial the results of the present trial show that it is just as effective when given by the intragastric route. In all the cases given intragastric therapy there was biochemical evidence that the bicarbonate was well absorbed and was able to correct the *p*H just as effectively as the intravenous bicarbonate (Table V). Though the mortality in the intravenous group is much greater than in the intragastric group, statistical analysis shows that this difference could have occurred by chance. However, it is remarkable that the intragastric group seems to fare better in consideration of nearly all criteria, and it may be that the greater degree of handling necessary for intravenous therapy is an important factor.

Absorption from the neonatal gut is facilitated by the presence of a well-developed mucosa, though its rate in the first few hours is uncertain. There has been evidence of good absorption of sodium bicarbonate from the gut of babies in this trial, not only from the satisfactory correction of an existing metabolic acidosis, but also from the considerable rise in the total bicarbonate in several cases.

TABLE V.—*Comparison of Biochemical Changes Produced by Intragastric and Intravenous Therapy*

	Baby V. Intravenous		Baby T. Intragastric	
	1	2	1	2
*p*H	7·12	7·39	7·04	7·31
P_{CO_2}	72·2	57	106	85
Base excess	−14·2	+6·3	−17·7	+9·7
Buffer base	41·1	55·8	38·9	59·0
Standard bicarbonate.. ..	15·1	29·3	13·6	31·7
Actual bicarbonate	23·8	33·0	28	41·0
Total CO_2	26·0	35·0	31	43·6

In each case, column 1 represents initial findings. Column 2 represents the findings after less than 24 hours' sodium bicarbonate therapy.

Administration of these infusions by the gastric route has obvious merits, and now that it has been shown that the results are as good as those obtained by intravenous therapy, if not better, it can be firmly recommended as the route of first choice. Rarely, resort has to be made to the intravenous route because of vomiting.

Summary

A clinical trial was carried out to compare the relative values of the intravenous and the intragastric routes for infusion of solutions of glucose and sodium bicarbonate in the management of babies with the respiratory distress syndrome. Somewhat surprisingly those babies who received their infusions intragastrically had a lower mortality rate. Though the difference between the mortality rates was not statistically significant, there is reason to believe that the intragastric route of administration should be preferred.

We are indebted to Sister B. S. Beech, who was in charge of the unit throughout the period of trial and played a helpful and active part in the management of the babies, and to Dr. S. H. Ng, who carried out a great deal of work involved in the preliminary trial. We are also grateful to Dr. R. H. Dobbs and Dr. A. D. M. Jackson for allowing us to include patients under their care, to Dr. B. Levin for the biochemical investigations, and Dr. N. E. France for the morbid anatomy and histology.

REFERENCES

Hutchison, J. H., *et al.* (1962). *Lancet*, 2, 465.
Silverman, W. A., and Andersen, D. H. (1956). *Pediatrics*, 17, 1.
Usher, R. (1959). Ibid., 24, 562.
—— (1961). *Pediat. Clin. N. Amer.*, 8, 525.
—— (1963). *Pediatrics*, 32, 966.

Formed Visual Hallucinations: a Symptom of Cranial Arteritis

C. T. HART,* M.B., B.S., F.R.C.S.

Brit. med. J., 1967, 3, 643–644

Two cases of cranial arteritis are described in which the presence of formed visual hallucinations has been a significant factor in their clinical presentation and course. The purpose of this paper is to draw attention to this symptom—not previously reported—and to suggest a possible aetiology in view of the known pathology of cranial arteritis. It is now well recognized that the disease process, a panarteritis, may involve not only the superficial temporal branches and other divisions of the external carotid but also the internal carotid tree, and the subclavian, coronary, renal, mesenteric, pulmonary, and peripheral vasculature. A full consideration of the pathology, incidence, and symptoms of cranial arteritis will not be dealt with in the present report, since these are well described in previous publications (Horton, Magath, and Brown, 1932; Parsons-Smith, 1959; Simmons and Cogan, 1962).

Case 1

A 79-year-old woman presented in the ophthalmic department on 17 March 1966 with deterioration of vision in the left eye of two weeks' duration. Clinical examination revealed atrophy of the left disc; arterial attenuation, no haemorrhages or exudates. The right disc showed early blurring of the nasal margin. Visual acuity: right, 6/18; left, counting fingers. B.P. was 180/80. Skull *x*-ray examination showed nothing abnormal. E.S.R. was 101 mm./hr.

Further questioning revealed a history of severe headaches associated with tenderness over the temples. She had been seen one month earlier at a dental hospital because of severe pain on chewing. Subsequently she referred to formed visual hallucinations of a most unpleasant nature which had been present for approximately two weeks before her ophthalmic attendance.

Prednisolone 30 mg. brought an immediate improvement in her general condition, and the visual hallucinations disappeared. Treatment was gradually reduced to nil on 25 July, when the E.S.R. was steady at 5 mm./hr. and she was symptom-free.

On 13 November she returned complaining of malaise and a recurrence of disturbing visual hallucinations. Visual acuity: right, 6/18; left, counting fingers. Central field right showed marked inferotemporal field loss with some generalized constriction. The right disc was now thought to be atrophic. B.P. was 160/70; serum vitamin B_{12}, 307 μg./100 ml.; and E.S.R. 82 mm./hr. Applanation pressures right and left, 20 mm.

A temporal artery biopsy was not thought necessary in view of the previous response to treatment, as regards both symptoms and the diminution in the E.S.R. Prednisolone 30 mg./day orally was begun with immediate loss of the formed hallucinations, which up to the time of writing had not recurred on a continued dosage of 5 mg. of prednisolone b.d.

Formed visual hallucinations preceded both emergency ophthalmic attendances. For two weeks before the first visit the patient experienced images of menacing people and flapping brightly coloured curtains which promptly disappeared as soon as systemic corticosteroid therapy was begun. The second visit after four months without corticosteroids was preceded by hallucinations of two days' duration; these took the form of doors which opened out towards her, the doors in fact being quite real; also the patient "saw" a crowd of small children round her whenever she turned her head to either side; treatment with corticosteroids abolished these hallucinations, which have not since returned. Improvement in visual acuity did not occur.

Case 2

A 73-year-old woman was admitted as a medical emergency on 19 February 1963 with bilateral severe visual loss and a diagnosis of possible intracranial space-occupying lesion. One week before admission she presented in the ophthalmic department with sudden loss of vision in the right eye of four days' duration. Papilloedema of the right disc was noticed at this first attendance. A blood pressure of 176/118 was found and she was referred for medical opinion, a hypertensive cause being suspected. The same day sudden loss of visual acuity in the left eye was experienced. On her admission to the ward a past history of three months' occipital headaches, bilateral earache, and jaw ache was obtained.

The clinical findings were as follows. Visual acuity: right, counting fingers; left, counting fingers; fields limited to superotemporal quadrants on confrontation; bilateral papilloedema, no haemorrhages or exudates; B.P. 170/76.

Investigations: E.S.R. 20 mm./hr. Serum cholesterol 310 mg./100 ml. Serum electrophoresis normal. Skull and chest *x*-ray pictures normal.

A diagnosis of cranial arteritis was made and temporal artery biopsy obtained which was reported on as follows: "There is an inflammatory reaction with giant cells in the vessel wall and the elastic tissue is partially disrupted: A 'kink' noted on naked-eye examination of the vessel shows filling of the lumen by organized thrombus which is beginning to recanalize."

The patient began treatment with 60 mg. of prednisolone a day. No improvement in visual acuity occurred. She has now terminated corticosteroid therapy. At no time has the E.S.R. exceeded a level of 20 mm./hr.

Formed visual hallucinations began three months after ocular involvement and have continued for four years. Originally these consisted of three distinct forms: (*a*) three blue and white meat dishes arranged vertically; (*b*) bunches of brightly coloured flowers situated on either shoulder, which swayed as she turned her head; and (*c*) black men outside the window. The first form of hallucination (*a*) persists, though the frequency of appearance has markedly decreased.

On examination on 23 March 1967 she was noted to have visual acuity: right, hand movements; left, hand movements; bilateral atrophic discs; applanation pressures right and left, 18 mm.

Discussion

The incidence of intracranial complications of cranial arteritis would appear to be small, judging from the lack of published evidence to the contrary. Meadows (1954) described the cases of two patients with dementia and one with progressive failure of memory for two years preceding the onset of blindness. Symptoms of vertigo, tinnitus, and loss of hearing have been described (Font, 1960) as occurring in this condition, the cause being presumed to be occlusive involvement of the internal auditory artery. Parsons-Smith (1959) described a series of 50 cases, four of which showed field loss (the type of field loss is not specified) due to cerebral lesions consistent with cranial arteritis.

The symptom of formed visual hallucinations experienced by the above two patients is assumed to be due to involvement of the cerebral cortex, particularly the temporal lobes, by this same occlusive vascular condition.

The onset and duration of the symptom vary greatly in the two cases. Case 1 demonstrated it as a premonitory symptom, associated initially with loss of unilateral vision and subsequently substantial loss of field in the unaffected eye, relieved by the administration of systemic corticosteroids: the hallucinations were a very temporary effect of cortical ischaemia relieved by prednisolone. In Case 2 the hallucinations occurred after an interval of two months, following severe bilateral loss of visual acuity, with no relief from corticosteroid therapy; in this particular case it must be assumed that the occlusive process has been permanent. The time of onset of this symptom after ocular involvement is of interest since it corroborates previous descriptions in that the generalized effect of cranial arteritis may follow ocular involvement by an interval of one to six months.

---

* Department of Ophthalmology, University of Sheffield.

The rarity of visual hallucinations in the blind has been noted by Freeman and Williams (1953) and it should be stressed at this stage that the formed hallucinations experienced by these two patients in no way resemble the psychic disturbances of postoperative cataract patients in which the imagery promptly disappears on uncovering the eyes. Walsh (1957) is of the opinion that formed visual hallucinations are due to involvement of the temporal lobe, and cites both experimental and clinical evidence to substantiate this point. A differing view is held by Weinberger and Grant (1940), who believe that no such strict localization exists within the cerebral hemispheres, such hallucinations representing psychological phenomena involving the total integrative activity of the mind, the formed imagery depending on consititutional factors, not on cortical psychic organization. In his summary, Walsh prefers to accept the localization of such phenomena to the temporal lobe, founded on the available experimental and clinical evidence. Both patients whose cases have been described show marked complacency to their respective visual symptoms, and it is postulated that this euphoria may also be connected with the intracranial occlusive episodes of cranial arteritis.

Summary

Two cases of cranial arteritis, both manifesting formed visual hallucinations as a disturbing symptom, are described. The mode of presentation differed; in one case this symptom preceded the onset of unilateral loss of visual acuity and subsequently gave warning of impending visual loss in the other eye, whereas in the second case this symptom followed the occurrence of bilateral loss of vision. The subject of visual hallucinations and their possible relation to the known intracranial vascular pathology of this disorder are discussed.

I wish to thank Mr. A. Stanworth, Dr. A. W. D. Leishman, and Dr. T. W. May for permission to publish these cases.

REFERENCES

Freeman, W., and Williams, J. M. (1953). *Arch. Neurol. Psychiat. (Chic.)*, 70, 630.
Font, J. H. (1960). *J. Amer. med. Ass.*, 174, 853.
Horton, B. T., Magath, T. B., and Brown, G. E. (1932). *Proc. Mayo Clin.*, 7, 700.
Meadows, S. P. (1954). *Trans. ophthal. Soc U.K.*, 74, 13.
Parsons-Smith, G. (1959). *Brit. J. Opthal.*, 43, 204.
Simmons, R. J., and Cogan, D. G. (1962). *Arch. Ophthal.*, 68, 8.
Walsh, F. B. (1957). *Clinical Neuro-Ophthalmology*, 2nd ed., p. 72. Baltimore.
Weinberger, L. M., and Grant, F. C. (1940). *Arch. Ophthal.*, 23, 166.

Effect of an Oral Contraceptive Immediately Post Partum on Initiation of Lactation

TEIT KÆRN,* M.D.

Brit. med. J., 1967, 3, 644–645

Oestrogens are known to suppress lactation, and are often used for this purpose. The oral contraceptives currently available contain oestrogens and progestogens in varying doses. In some the progestin component itself has oestrogenic qualities (Paulsen, 1965), and treatment with this group might be expected to impair lactation to a marked extent. Rice-Wray (1964) reported that in about half of the lactating mothers she studied the milk yield was diminished by oral contraceptives. This seems to be a dose-dependent effect, for Pincus (1965, p. 262) noted that the percentage inhibited decreased from 77 to 15 as the norethynodrel dose was reduced from 20 to 2.5 mg./day. Satterthwaite (1964) thought that a 2.5-mg. dose of norethynodrel did not significantly affect lactation, but in her study there were no controls and the small number of patients makes generalization difficult.

Of oral contraceptive preparations currently available Norinyl-1 (norethisterone 1 mg. and mestranol 0.05 mg.) has the lowest total steroid content. Furthermore, norethisterone is antioestrogenic in some of its effects. In view of Rice-Wray's findings and Pincus's suggestion of a dose-dependent effect it seemed important to test the action of Norinyl-1.

The immediate post-partum period is the most convenient time to advise on contraception, and if the agent can be prescribed at this time follow-up problems are considerably reduced. This aspect is of prime importance in the developing countries, where the immediate post-partum period may be the only opportunity for contraceptive treatment, and where breast milk may be the infants' only source of protein.

Most studies of the effects of oral contraceptives on lactation have not been controlled, and since many factors influence lactation this reduces their value.

Methods

All mothers delivered in the obstetrics unit of St. Joseph's Hospital, Copenhagen, during the period July–September 1966 entered the trial, with the exception of (1) mothers who it was decided, before or immediately after delivery, should not attempt to breast-feed, and (2) mothers who gave birth to infants weighing less than 2,000 g.

A total of 451 women took part in the trial. Tablets were supplied by Syntex Pharmaceuticals Limited, England, in small containers marked only with a code number and containing 21 tablets. The code was not disclosed in Denmark until the trial had been completed, but it was known that some of the tablets were Norinyl-1 and others were inert placebo tablets. Each woman included in the trial received one tablet daily from the day after the birth of her child until discharge from hospital on the eighth day.

The relevant details of each case were recorded on a form which included the mother's previous history of breast-feeding, the code number of the tablets taken, and the baby's birth weight. A trained nurse accurately recorded on a decimal balance in the lying-in ward the weight of the babies on the second, fifth, and eighth days. The nursing staff were asked to assess the influence of the tablets on the onset of lactation. They recorded observations on the ease and adequacy of lactation, the state of the breast and nipples, and whether the patient was fully breast-feeding, complementary feeding, or completely artificially feeding.

---

* Chief Physician, Maternity Department, Saint Joseph's Hospital, Copenhagen.

Ten patients from each group were asked to continue their pills at home for a further two weeks and on completion to return to the hospital a questionary concerning the progress of lactation.

During the latter part of the trial observations were made with respect to the quantity of uterine haemorrhage, the type of lochia, after-pains, and the rate of involution of the uterus. These were not quantitated, however, and their assessment was purely clinical.

Results

Breast-feeding was discontinued in 33 infants. The reasons are given in Table I, from which it can be seen that the incidence of illness in infants of both groups is almost equal.

Of the 33 infants discharged from hospital on complementary feeds, 26 were from the remaining 212 women receiving the active Norinyl-1 tablets and seven were from the 218 women who were receiving the placebo tablets (Table II).

TABLE I.—*Infants Removed From the Trial and Sent Home on Artificial Feeding*

	233 Taking Norinyl-1		218 Taking Placebo	
	Primips 107	Multips 126	Primips 115	Multips 103
Illness in mother	0	1	0	1
Previous absence of lactation	0	2	0	0
„ breast operation ..	1	0	0	0
Inverted nipples	0	1	1	0
Illness in infant	8	5	6	4
Twins	3	0	0	0
	12	9	7	5

TABLE II.—*Incidence of Complementary Feeding by Parity and Tablet Received*

	Norinyl-1 (212)		Placebo (206)	
	Primips	Multips	Primips	Multips
Fully breast-feeding ..	83	103	103	96
Complementary feeding ..	12	14	5	2
	95	117	108	98

Of the 117 multiparous women who received Norinyl-1 tablets 14 needed to use complementary feeds, and of the 98 who received placebo tablets only two required complementary feeds. This difference was found to be significant at the 1% level ($\chi^2=7.6185$ on 1 degree of freedom). Of the 95 primiparae receiving active Norinyl-1 tablets 12 had to use a complement, while of the 108 who received the placebo only five had to give a complement. The difference is found to be significant at the 5% level, but not at the 1% level ($\chi^2=4.2020$ on 1 degree of freedom). The overall effect when the primiparae and multiparae are grouped together is that Norinyl-1 appears to diminish significantly the quantity of milk produced, as measured by the number of times complementary feeding was found necessary ($\chi^2=11.9114$ on 2 degrees of freedom). Lactation was not inhibited in these patients by Norinyl-1 or placebo tablets, and it was not necessary to resort to full artificial feeding.

The weights of the infants in the two groups have been compared. For this purpose birth weight has not been used, as this was estimated on a spring-balance in the labour room; the difference between the second-day and eighth-day weights has been taken as an estimate of weight change during the first week of life. If we exclude the infants receiving part or total artificial feeding and group together those of primiparous and multiparous mothers, then 186 infants from the Norinyl-1 group and 199 from the placebo group were breast-fed. In the Norinyl-1 group there was an average loss of weight during the first week of 6 g., while in the placebo-treated group there was an average gain of 15 g. The standard error of the difference of these two means is 12 g. Thus the infants who were wholly breast-fed showed no significant change in weight over the first week whether their mothers received Norinyl-1 or placebo tablets ($0.10>P>0.05$). From this trial it was not possible to assess whether a significant weight difference would appear at a later date.

Febrile breast engorgement was not significantly different in the two groups: Norinyl-1, 2 out of 233 cases; and placebo, 5 out of 218 cases. Feeding difficulties (psychological and mechanical) were encountered in approximately equal numbers in both groups, which amounted to 7%.

Discussion

This trial was concerned only with the effect of Norinyl-1 on the initiation of lactation and was confined to observations made in the first week post partum. In no case was the initiation of lactation suppressed by the drug.

A larger number of women in the Norinyl-1 group had to give their babies supplementary feeds than was observed in the placebo group, and this difference was statistically significant: there was a measurable diminution in the quantity of milk. The number of cases of febrile engorgement of the breasts in the Norinyl-1 group tended to be lower than that in the placebo group. Most of the women (88%) could feed their babies without any artificial complement after taking Norinyl-1 from the first day after birth. The woman who is anxious to breast-feed her baby would be best advised not to use Norinyl-1 until her baby is weaned, or at least until lactation is well established.

The follow-up of the 20 patients who continued treatment at home for three weeks was unsatisfactory, as only eight taking Norinyl-1 and eight taking placebo returned their questionaries. Four of the mothers on Norinyl-1 reported that they were still fully breast-feeding and four were having to give complementary feeds. The eight women who were on the placebo were still fully breast-feeding.

As previously mentioned, observations were made on the state of uterine involution in the latter half of the trial. The impressions of the observers were that there was no difference between the women on Norinyl-1 and those on the placebo.

Summary

A total of 451 women were given either Norinyl-1 (norethisterone 1 mg. and mestranol 0.05 mg.) or an inert placebo once daily from the day after birth under double-blind conditions.

In no case was lactation inhibited by the drug. Complementary feeds were given by 12% of the women taking the active tablet and by only 3.5% of those receiving placebo.

There was no significant difference in the change in weight of the infants in the two groups during the first week, though there was a tendency for the treated ones to gain less.

The incidence of febrile breast engorgement appeared to be slightly lower in the group receiving the active drug.

REFERENCES

Paulsen, C. A. (1965). *Metabolism*, **14**, 313.
Pincus, G. (1965). *The Control of Fertility.* New York.
Rice-Wray, E. (1964). *Proceedings of Seventh Conference of the International Planned Parenthood Federation, Singapore*, p. 358, edited by G. W. Cadbury, H. D. Connolly, K. V. Earle, and A. S. Parkes.
Satterthwaite, A. P. (1964). *App. Ther.*, **6**, 410.

Idiopathic Gangrene in African Children

A. G. G. TURPIE,* M.B., M.R.C.P.GLASG.; C. D. FORBES,* M.B., M.R.C.P., M.R.C.P.ED., M.R.C.P.GLASG.
G. P. McNICOL,* M.D., PH.D., M.R.C.P.ED., M.R.C.P.GLASG.

Brit. med. J., 1967, 3, 646–648

Gangrene of the extremities in Africans with apparently healthy arteries is a well-recognized but uncommon clinical syndrome affecting the indigenous population of East Africa (J. R. M. Miller, personal communication, 1966; A. A. Khan, personal communication, 1966). Both sexes and all age groups may be involved, and the condition is not confined to any particular tribal group or localized geographical area.

This communication gives an account of three African children with apparently spontaneous gangrene of the extremities.

According to current concepts it is possible that under physiological circumstances both the coagulation system and the fibrinolytic system may be constantly active to maintain an intact patent vascular tree, the coagulation system laying down a thin layer of fibrin on the vascular endothelium to seal any gaps which may occur, and the fibrinolytic system removing such fibrinous deposits after they have served their haemostatic function. In the coagulation system the inert plasma protein prothrombin is converted by thromboplastin to thrombin, which in turn brings about the conversion of the soluble protein fibrinogen to insoluble fibrin.

A similar basic structure is seen in the fibrinolytic system; plasminogen, an inactive plasma globulin, is converted by activators to plasmin, a proteolytic enzyme which under suitable circumstances digests fibrin, with release of soluble products. Plasminogen activators are present in many tissues, and the evidence suggests that plasminogen activator in the plasma is responsible for physiological fibrinolytic activity in the blood. A urinary activator (urokinase) probably represents, in part at least, excreted plasma activator.

In terms of the postulated dynamic equilibrium between clotting and lysis, thrombotic vascular occlusion, and hence tissue necrosis, might be expected to ensue from either hypercoagulability, with a failure of the fibrinolytic system to respond with increased activity, or from reduced fibrinolytic activity, in the presence of a normal coagulation mechanism (Fig. 1). In such circumstances reduced fibrinolytic activity might be due either to deficiency of the components of the fibrinolytic system or to the presence of inhibitors of fibrinolysis. Accordingly, in the present study particular attention was paid to the coagulation and fibrinolytic mechanisms of the affected children.

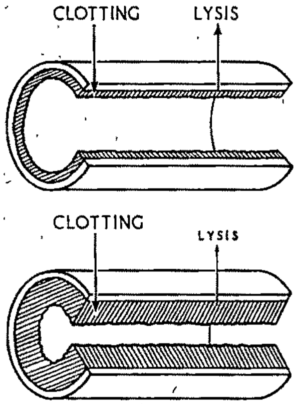


FIG. 1.—Above: the postulated dynamic equilibrium of the clotting and fibrinolytic systems. Below: how reduced fibrinolytic activity with normal clotting might be expected to lead to vascular occlusion.

Materials.—Streptokinase: A. B. Kabi, Stockholm. Urokinase: purified human urokinase was supplied by Abbott Laboratories, Chicago, Illinois. Thrombin: Parke Davis thrombin topical. Thromboplastin: Rabbit-brain thromboplastin. Dade Reagents, Miami, Florida. Casein: Casein of L. Light and Company, Colnbrook, Bucks.

Methods

Plasminogen Assay.—The method of Remmert and Cohen (1949) as modified by Alkjaersig *et al.* (1959) was used. The method is described by McNicol and Douglas (1964).

Fibrinogen Assay.—The plasma fibrinogen levels were measured by the method of Ratnoff and Menzie (1951) as modified by Alkjaersig (1960).

One-stage "Prothrombin" Time.—This was estimated by the method described by Douglas (1962).

Thrombin Clotting-time.—The method described by Fletcher *et al.* (1959) was used.

Thromboplastin Generation Test.—The method described by Biggs and Douglas (1953) was used.

Plasma Recalcification Time.—The method used was that of Biggs and McFarlane (1962).

Urokinase Sensitivity Test.—This was carried out as described by McNicol *et al.* (1963). In this test the lysis time of a plasma clot in the presence of a standard amount of urokinase is measured. Results are presented in arbitrary units, based on a double logarithm plot of lysis times against units of activity, and assigning one unit of activity to a lysis time of 10 minutes. In a patient with normal fibrinogen and plasminogen levels a prolonged lysis time in this urokinase sensitivity test reflects a high level of inhibitor of fibrinolysis.

Euglobulin Lysis Time.—This test was carried out by the method described by Nilsson and Olow (1962). In this test fibrinogen, plasminogen, and plasma plasminogen activators are precipitated from the plasma; antiplasmin is discarded with the supernatant and the precipitate is resuspended; after clotting with thrombin the lysis time is measured. As lysis times are inversely proportional to fibrinolytic activity, results are presented as suggested by Sherry *et al.* (1959) in arbitrary units of activity assigning to a lysis time of 300 minutes, one unit of activity. If plasminogen and fibrinogen levels are normal, variations in euglobulin lysis activity in a population can be regarded as a measure of variation in plasma plasminogen activator levels.

Case 1

A 7-year-old girl was admitted to hospital with an acute febrile illness of one day's duration. Until the onset of the illness the patient had been completely well. There was no history of drug ingestion. Clinical examination revealed a toxic febrile child with a widespread petechial rash. There was bluish discoloration of the tips of the fingers, which felt cold. The mucous membranes were pale but there was no icterus. Generalized non-tender lymphadenopathy and moderate enlargement of liver and spleen were present. The heart was normal and the blood pressure was 135/90 mm. Hg. The peripheral arterial pulses were readily palpable. Digital artery pulsation was present.

---

* Makerere University College, Medical School Extension, Kenyatta National Hospital, Nairobi. On secondment from the University of Glasgow.

Requests for reprints to be sent to Dr. A. G. G. Turpie, Department of Materia Medica and Therapeutics, University Medical Unit, Stobhill General Hospital, Glasgow N.1.

Gangrene of the fingers became evident soon after admission. Despite treatment with low-molecular-weight dextran (Rheomacrodex), corticosteroids, and penicillin, ischaemic changes appeared in the tips of the toes, and the feet later became gangrenous. Dorsalis pedis and posterior tibial pulses remained palpable in both feet. Amputation was recommended at this stage, but permission for operation was refused. Spontaneous sloughing of the gangrenous tissue of the finger-tips occurred (Fig. 2), and a clear line of demarcation developed in the feet.

The patient was discharged from hospital six weeks after the onset of the illness. She was readmitted two months later when the fore parts of the feet had sloughed; bilateral Syme's amputation was carried out. She was discharged well after a further four months in hospital.

The most striking laboratory feature of the acute phase of the illness was autohaemagglutination. This was so pronounced that standard cross-matching of the patient's blood was impossible. Cold agglutination titre was not estimated but marked autoagglutination was noted at room temperature (18.1° C.), and slight agglutinating activity was present at 37° C. The full clinical history and an investigation of this patient have been documented by Othieno-Okanga (1966). The patient's coagulation and fibrinolytic mechanisms were studied during her second admission to hospital some four months after the acute episode of the illness.

Case 2

A female child aged 2 years, with a month's history of a generalized weeping erythematous rash which had been treated unsuccessfully as scabies, was admitted to hospital with the acute onset of necrosis of the tips of her fingers and toes. There was no history of drug ingestion.

Clinical examination revealed an ill child with symmetrical peripheral gangrene of the tips of the fingers and toes. Peripheral pulses, including the digital artery pulsations, were normal. There was no lymphadenopathy and the liver and spleen were not enlarged. Neither auto-agglutination nor cold agglutination was demonstrated. The gangrenous lesions remained apparently uninfected and ultimately sloughed. The patient unexpectedly died after four weeks in hospital.

At necropsy, lobar pneumonia was the only gross lesion demonstrated. Histological examination showed the vascular tree, including small arteries supplying the gangrenous tissue, to be patent. There was, however, organizing thrombus in one vein draining the gangrenous area.

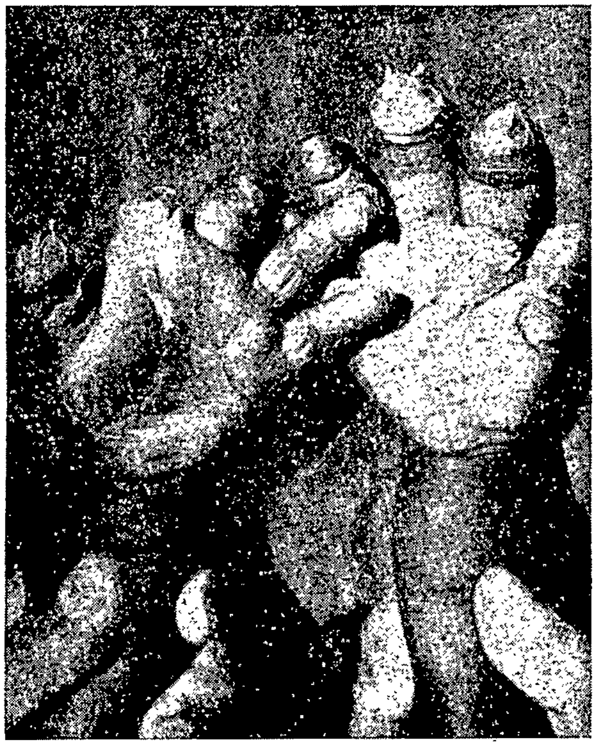


Fig. 2.—Case 1. Necrotic changes in the hands.

Studies of the fibrinolytic and coagulation mechanisms were carried out in the acute phase of the patient's disease.

Case 3

A male child aged 16 months had an illness of insidious onset of some weeks' duration. It was heralded by generalized itching, followed by the development of ulceration of the tips of his fingers. Before admission to hospital necrosis and sloughing of the tip of the little finger of the right hand developed acutely.

Apart from the gangrenous extremities clinical examination was normal. All peripheral pulses, including the digital pulses, were palpable and normal. The red blood cells showed rouleaux formation, but no agglutinins were found in the serum. Studies of the fibrinolytic system and clotting mechanisms were carried out in the acute phase of the illness.

In none of the three cases was there clinical or epidemiological evidence to suggest that they were suffering from ergot poisoning.

Controls

Plasma for control studies was obtained from age-, sex-, and tribe-matched patients from the paediatric and general medical wards who were suffering from a variety of miscellaneous illnesses not known to affect the haemostatic mechanism.

Results

In Fig. 3 recalcification times, thrombin clotting-times, and prothrombin times for the three patients are shown plotted against the mean and standard deviations of the values obtained from the control subjects. The plasma fibrinogen levels in the patients and the controls are shown in Fig. 4.

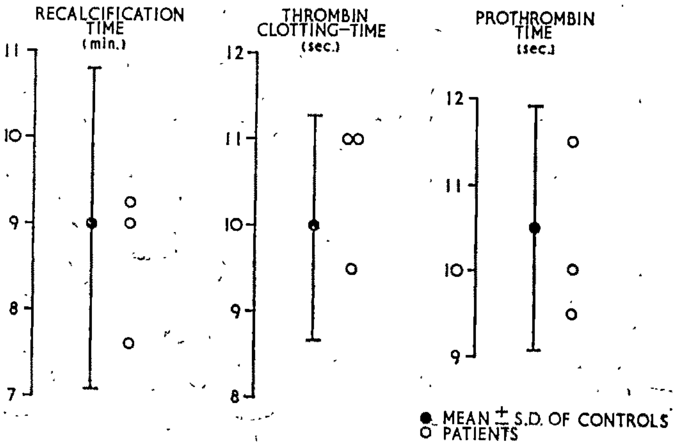


Fig. 3.—Coagulation studies performed in patients compared with the results in control subjects.

In all three patients the thromboplastin generation was normal; one (Case 1), who had purpura, had a platelet count of 72,000/cu.mm.—platelet counts in Cases 2 and 3 were normal. It therefore appears that, apart from the low platelet count in Case 1, the clotting mechanism in all three patients was normal.

Fig. 5 shows that the patients' plasminogen levels are within the range found in the controls. As plasma fibrinolytic activity is known to be low at birth and to increase over the first year or two of life (Samartzis and Cook, 1960), results for euglobulin lysis times in each patient are shown plotted separately, with controls age-matched for each patient (Fig. 6). The data in the controls confirm an increase in fibrinolytic activity with age; and in each case activity in the patient was much depressed compared with that found in the appropriate control population.

The results of the urokinase sensitivity tests from each patient are again shown with the appropriate age-matched controls, and in the controls increased lytic activity in response to urokinase can be seen (Fig. 7). All three patients show greatly reduced response to urokinase as compared with their controls.

Discussion

The results presented show that in the children studied there was a significant depression of spontaneous plasma fibrinolytic activity as compared with age- and sex-matched controls, and there was also a reduction in plasma fibrinolytic activity produced in response to a standard amount of plasminogen activator. In the euglobulin lysis technique, fibrinolytic inhibitors are discarded during preparation of the euglobulin clots, and as plasminogen and fibrinogen levels were normal the results suggest that the plasma from the patients had an abnormally low level of plasminogen activator. The reduced lytic activity in response to urokinase suggests that the patients' plasmas also contained an increased amount of fibrinolytic inhibitor.

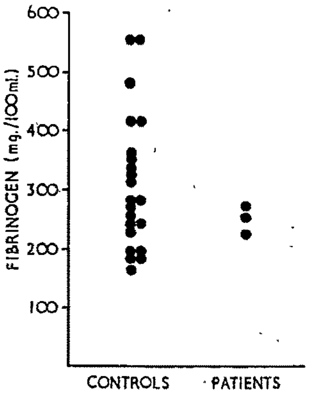


FIG. 4

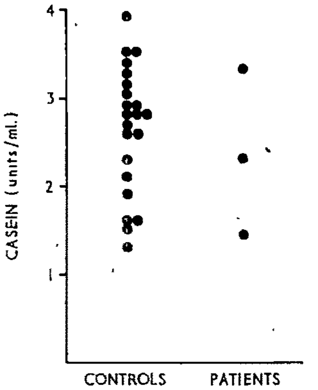


FIG. 5

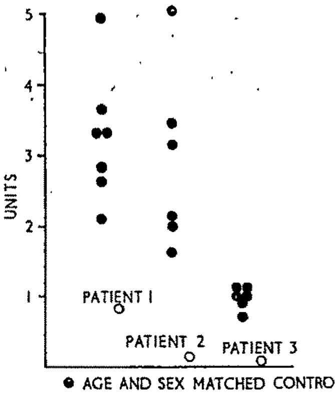


FIG. 6

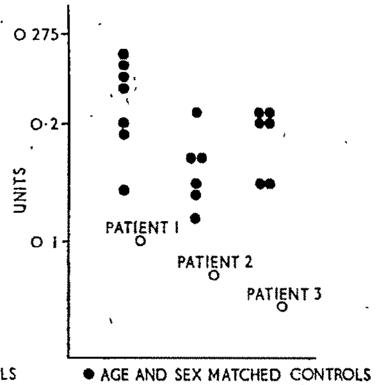


FIG. 7

FIG. 4.—Fibrinogen levels in patients and controls. FIG. 5.—Plasminogen levels in patients and controls. FIG. 6.—Euglobulin lysis times, presented as units of activity (see text), for each patient compared with age-matched controls. FIG. 7.—Urokinase sensitivity tests for each patient compared with the results for age-matched controls. Results are presented in units (see text).

Theoretically, inhibitors of fibrinolytic activity might be expected to act at two levels—inhibition of plasminogen activation and inhibition of formed plasmin. There are at least two antiplasmins in plasma (Norman and Hill, 1958), and platelets also show antiplasmin activity. There is inferential but not conclusive evidence that plasma also possesses anti-activator properties (Paraskevas *et al.*, 1962). The techniques used in the present study do not serve to differentiate between elevated levels of anti-activator and high antiplasmin content. No data are available as regards the basic cause or possible precipitating factors involved in this syndrome. There was no evidence of poisoning or of dysproteinaemia, nor does the condition appear to be genetically determined; an unidentified environmental factor seems the most probable explanation.

Though a causal relation between the abnormalities in fibrinolysis and the gangrene was not established, the association is of considerable theoretical and possibly also therapeutic interest. There are, so far as we can ascertain, only three reports in the literature of an increase in the levels of naturally occurring fibrinolytic inhibitor associated with severe widespread thrombotic disease (Nilsson *et al.*, 1961; Nilsson *et al.*, 1966; Brakman *et al.*, 1966). The finding in the present patients of reduced levels of fibrinolytic activity and increased levels of fibrinolytic inhibitor, in association with tissue necrosis presumably due to thrombotic vascular occlusion, provides support for the concept of a homoeostatic function for the fibrinolytic system in vivo. It would also seem possible that a trial of therapy with fibrinolytic enzymes given early in the evolution of the disease would be worth while.

Summary

Peripheral symmetrical gangrene of unknown origin is a well-recognized but uncommon syndrome affecting all ages and both sexes of the indigenous population of East Africa.

The clotting and fibrinolytic mechanism of three children who suffered from this "disease" were studied. Tests of blood coagulation showed no abnormality in the patients. Of the tests of the fibrinolytic mechanism, plasminogen and fibrinogen assays were normal in each case. The euglobulin lysis time, a measure of overall spontaneous fibrinolytic activity, was grossly prolonged in each case, and the urokinase sensitivity test, a measure of plasma inhibition of fibrinolysis, was markedly reduced.

The results show that in the children studied there was a significant depression of spontaneous plasma fibrinolytic activity due in part to increased levels of fibrinolytic inhibitors.

The significance of these findings is discussed in the light of the postulated dynamic equilibrium between coagulation and fibrinolysis in the maintenance of a patent vascular tree.

We are grateful to Dr. H. P. Ojiambo and Dr. A. A. Khan for permission to study patients under their care, and to Professor S. Alstead and Professor A. S. Douglas for their interest in the work.

Financial assistance was provided by the Kenya Ministry of Health, East African Medical Research Council, Ministry of Overseas Development, Merck Sharp and Dohme Research Laboratories, Hoechst (East Africa) Ltd., Organon Laboratories Limited, G. D. Searle & Co. Ltd., Boehringer Ingelheim Ltd., Pfizer Tropical Research Laboratory, The Pfizer Corporation, I.C.I. Pharmaceutical Division, and Ciba Laboratories Ltd. Reagents were provided by A. B. Kabi.

REFERENCES

Alkjaersig, N. (1960). In *Conference on Thrombolytic Agents*, edited by H. R. Roberts and D. Geraty, p. 316. Chapel Hill.
—— Fletcher, A. P., and Sherry, S. (1959). *J. clin. Invest.*, **38**, 1086.
Biggs, R., and Douglas, A. S. (1953). *J. clin. Path.*, **6**, 23.
—— and MacFarlane, R. G. (1962). *Human Blood Coagulation and its Disorders*, 3rd ed. Oxford.
Brakman, P., Mohler, E. R., Astrup, T. (1966). *Scand. J. Haemat.*, **3**, 389.
Douglas, A. S. (1962). *Anticoagulant Therapy.* Oxford.
Fletcher, A. P., Alkjaersig, N., and Sherry, S. (1959). *J. clin. Invest.*, **38**, 1096.
McNicol, G. P., and Douglas, A. S. (1964). *Recent Advances in Clinical Pathology*, Series 4; edited by S. C. Dyke, p. 187. London.
—— Gale, S. B., and Douglas, A. S. (1963). *Brit. med. J.*, **1**, 909.
Nilsson, I. M., Krook, H., Sternby, N.-H., Söderberg, E., and Söderström, N. (1961). *Acta med. scand.*, **169**, 323.
—— Nilehn, J.-E., Coonberg, S., Norvén, G. (1966). Ibid., **180**, 65.
—— and Olow, B. (1962). *Acta chir. scand.*, **123**, 247.
Norman, P. S., and Hill, B. M. (1958). *J. exp. Med.*, **108**, 639.
Othieno-Okanga, J. B. (1966). *East Afr. med. J.*, **43**, 440.
Paraskevas, M., Nilsson, I. M., and Martinssón, G. (1962). *Scand. J. clin. Lab. Invest.*, **14**, 138.
Ratnoff, O. D., Menzie, C. (1951). *J. Lab. clin. Med.*, **37**, 316.
Remmert, L. F., and Cohen, P. P. (1949). *J. biol. Chem.*, **181**, 431.
Samartzis, E. A., and Cook. C. D. (1960). *Acta paediat. (Uppsala)*, **49**, 724.
Sherry, S., Lindemeyer, R. I., Fletcher, A. P., and Alkjaersig, N. (1959). *J. clin. Invest.*, **38**, 810

Single-dose Treatment of Acute Urinary Tract Infection: a Controlled Trial

R. N. GRÜNEBERG,* M.B., B.S.; W. BRUMFITT,† M.D., PH.D., M.R.C.P., M.C.PATH.

Brit. med. J., 1967, 3, 649–651

Patients with acute urinary tract infection are usually seen and treated by their family doctor, and the majority either do not stay away from work or return to work as soon as the symptoms are relieved. Though a seven-day course of treatment with a number of antimicrobial agents will eradicate most infections, the relief of symptoms and return to normal activities results in some patients not completing the full course. This leads to a number of infections persisting in an asymptomatic form.

Sulphormethoxine (Fanasil) is a sulphonamide with a half-life in the body of about 150–200 hours (Haegi, 1966), and if therefore a seven-day course is required a single-dose treatment is feasible.

We have carried out a trial to compare this treatment with a seven-day course of ampicillin, which is established as an effective treatment of primary urinary tract infection.

Materials and Methods

Examination of Urine.—Midstream specimens of urine were collected by the clean-catch technique after cleansing with a swab moistened in sterile water. Quantitative bacterial and white cell counts were carried out. The sole criterion of infection was a count of 100,000 bacteria or more per ml. of urine. Organisms were identified by conventional methods, and the O antigen of *Escherichia coli* strains was identified by means of specific antisera.

Serum Antibodies.—Antibodies in the patient's serum against infecting organisms were estimated as previously described (Percival, Brumfitt, and de Louvois, 1964). A titre of 1:320 or more was taken to indicate renal involvement whether localizing symptoms were present or not.

Antibiotic Sensitivities.—These were carried out on para-aminobenzoic-acid (P.A.B.)-free sensitivity agar (Oxoid) with discs containing either 200 μg. of sulphormethoxine or 25 μg. of ampicillin. The plates were lightly inoculated with a wire loop from a single colony of the organism to be tested, the density of the inoculum and activity of the disc being controlled by inoculating the plate in a similar way with *Staphylococcus aureus* (Oxford strain N.C.T.C. 6571). Subsequently the minimal inhibitory concentration was estimated in tubes by the serial dilution method, using a final bacterial density of about 200 organisms per ml. For sulphonamide P.A.B.-free medium was used.

Patients

One hundred and four patients who visited their family doctor with symptoms of urinary tract infection were referred immediately to us for investigation and treatment. Each patient was seen by the same observer (R. N. G.), a full history was taken according to a standard questionary, and the patient was then examined clinically. A specimen of urine was collected and a blood specimen taken for measurement of the serum antibody level against the O antigen of the infecting organism.

If typical symptoms of urinary tract infection were present and no treatment had already been given the patient was admitted to the trial. Treatment was decided by the selection of a random number and the patient was given either a single dose of 2 g. of sulphormethoxine or 500 mg. of ampicillin eight-hourly for seven days.

Follow-up was carried out two and six weeks after the first visit. Patients were again asked about symptoms, a midstream specimen of urine was collected, and blood was taken for antibody determination.

Treatment was judged to have been successful if both follow-up specimens of urine were sterile, and to have failed where the organism originally isolated persisted.

Results

Treatment was given to 104 patients who had typical symptoms, but examination of the urine showed that only 50 of these had significant bacteriuria; therefore assessment of the relative chemotherapeutic value of sulphormethoxine and ampicillin was confined to the latter group of patients.

TABLE I.—*Comparison of Clinical and Laboratory Findings in the Two Groups*

	Sulphormethoxine	Ampicillin
Patients treated	25	25
Females	24	21
Average age	38·0	45·3
Previous history of urinary infection ..	18	17
Loin pain	5	5
Infections due to *E. coli*	20	17
Infections due to *Proteus mirabilis* ..	4	6
Infections with urine W.B.C. > 10/cu. mm.	22	23
Serum antibody titre ≥1/320	5	10
Serum antibody titre ≥1/640	4	6

Table II shows that cure rates were the same with sulphormethoxine and ampicillin, both substances being successful in 22 (88%) of the 25 patients in each group. The three patients who failed to respond to ampicillin all had very high serum antibody titres against the infecting organism, which suggested extensive renal tissue involvement. In two of the three ampicillin failures the organism responsible for the infection was sensitive to sulphormethoxine, as judged by in-vitro testing. These two patients were treated with sulphormethoxine and one was cured.

TABLE II.—*Results of Treatment*

Treatment	No. Treated	Cured (6-week Follow-up)
Ampicillin	25	22 (88%)
Sulphormethoxine	25	22 (88%)

The three patients who were not cured by sulphormethoxine were given a seven-day course of ampicillin and one was cured. The other two subsequently failed to respond to several courses of other antimicrobial substances.

---

* Research Registrar, Edgware General Hospital, Edgware, Middlesex.

† Pathologist, Edgware General Hospital; Senior Lecturer, St. Mary's Hospital Medical School, London W.2.

Requests for reprints to Dr. W. Brumfitt, Edgware General Hospital, Edgware, Middlesex.

The three patients who failed to respond to both sulphormethoxine and ampicillin were later investigated radiologically and all were found to have urinary tract abnormalities.

The side-effects were assessed on all patients treated, regardless of whether or not they were subsequently found to have bacteriological evidence of urinary tract infection.

The 104 patients received 109 courses of treatment (three sulphormethoxine failures were given ampicillin and two ampicillin failures were given sulphormethoxine). Sulphormethoxine was given to 53 patients and two developed side-effects, whereas nine of the 56 given ampicillin developed side-effects (Table III). The difference is statistically significant ($0.05>P>0.02$). Side-effects with sulphormethoxine were minimal: one patient felt nauseated for one hour after taking the tablets, and the other had a rash for a similar period. With ampicillin side-effects were more troublesome. One patient had diarrhoea and pruritus ani for four weeks, and five others had diarrhoea for two weeks or more.

TABLE III.—*Side-effects*

Treatment	No. of Courses Given	No. of Patients with Side-effects
Ampicillin	56	9 (16·1%)
Sulphormethoxine	53	2 (3·8%)

Rashes occurred in five patients and were maximal on the arms and trunk and non-pruritic. The rashes did not intensify when treatment was continued, and no urticarial rash characteristic of classical penicillin hypersensitivity was seen. Details of the actual side-effects are given in Table IV. They were equally distributed between patients who had true urinary infection and those who had typical symptoms without infected urine.

TABLE IV.—*Details of Side-effects Observed*

	Ampicillin*	Sulphormethoxine
Diarrhoea	6	—
Nausea	—	1
Rash	5	1
Pruritus	2	—
Other	2	—

* Four of the 9 patients with side-effects showed more than one feature.

Interestingly, three patients who had typical symptoms but no infection when treatment was started were found to be infected at follow-up. One of these patients was subsequently found to have a urinary tract abnormality, and the other two infections were due to organisms resistant to the antibacterial substance used.

Discussion

In a previous study carried out in general practice we found that a seven-day course of sulphadimidine cured 90% of patients with acute urinary tract infection (Mond, Percival, Williams, and Brumfitt, 1965), and in the present investigation 22 out of 25 patients were cured by the long-acting sulphonamide, sulphormethoxine, given in a single dose of 2 g. Ampicillin in conventional dosage cured the same number of patients with similar infections (Tables I and II).

The side-effects of ampicillin were more frequent than those due to sulphormethoxine, but it should be stressed that many of these would be accepted by patients confined to their home. However, effective treatment of patients with less severe clinical forms of urinary infection enabled them to resume normal activities, and under these circumstances side-effects were sometimes troublesome. For example, one patient who returned to work in a factory was unable to continue because of diarrhoea. Patients with side-effects also tend to discontinue the treatment.

The rashes which occurred after ampicillin have been ascribed to hypersensitivity (*British Medical Journal,* 1964), but the evidence for this is uncertain. The rashes were not urticarial and there were none of the other signs usually associated with penicillin hypersensitivity. Furthermore, in such patients skin tests can subsequently be shown to be negative (Stewart, personal communication).

With sulphormethoxine only a single dose was necessary, and therefore there was no danger of the patient forgetting or deliberately omitting to take the treatment. Side-effects were minimal, and many patients remarked favourably on the simplicity of treatment—particularly those who had previously been treated with other courses.

Previous studies have shown that where minimal inhibitory concentrations of sulphonamide are below 50 μg./ml. eradication of urinary infection can be expected, while minimal inhibitory concentrations in excess of 200 μg./ml. usually mean that the infection will prove to be resistant to sulphonamides. We found that 82% of organisms were sensitive to 50 μg. of sulphormethoxine per ml. or less, and these results agreed exactly with those found with sulphadimidine. It was also found that 87% of the organisms were sensitive to 5 μg. of ampicillin per ml. or less.

In the present study failure to respond to treatment was due to resistance of the infecting organism or to the presence of urinary tract abnormalities, and the three patients with sensitive organisms who failed to respond to both sulphormethoxine and ampicillin were all found to have such abnormalities when investigated radiologically.

There has recently been much discussion about the association of long-acting sulphonamides and the Stevens–Johnson syndrome (Carroll, Bryan, and Robinson, 1966 ; Harris, Wise, and Beveridge, 1966 ; Seneca, 1966). The syndrome may have a special association with sulphamethoxypyridazine, and it is said to be especially apt to occur in children (Harris *et al.,* 1966). Sulphonamides in general, together with a variety of other substances, have been associated with the Stevens–Johnson syndrome, but over the past five years we have observed several thousand patients treated with sulphadimidine and the long-acting compound sulphamethoxydiazine but have seen no example of the condition. Clearly a new compound must be used cautiously, and in view of the claim that the Stevens–Johnson syndrome is more likely to occur in children it would be best to avoid sulphormethoxine in paediatric practice until more experience has been gained in its use.

Recent but as yet unpublished experience on a very large scale during an outbreak of meningococcal meningitis, in which sulphormethoxine was used prophylactically in very high and repeated doses, has shown that the drug can occasionally produce skin reactions. These usually occurred in children, were mild, and followed a benign course. In some cases, however, they were generalized, more severe, and showed features of Lyell's syndrome (I. Lennox-Smith, personal communication).

The evidence that long-acting sulphonamides produce a more sustained hypersensitivity reaction than the short-acting compounds is in our view unimpressive, but of course no patient with a history of sulphonamide sensitivity must receive the compound.

Our findings suggest that for treatment of patients with urethrotrigonitis, such as we have described here, results will be as good as with the other antimicrobials at present available, while the side-effects and inconvenience to the patient are likely to be minimal.

In our view a long-acting compound of this variety is unsuitable for the treatment of patients with fever and evidence of acute pyelonephritis. Also, asymptomatic urinary infections in diabetic patients and pregnant women are more difficult to eradicate than the acute infections seen in general practice (Williams, Brumfitt, Leigh, and Percival, 1965), and the possible place of sulphormethoxine in these conditions remains to be defined.

Summary

Sulphormethoxine is a sulphonamide with a prolonged action, which makes possible the treatment of some varieties of acute urinary tract infection with a single dose of 2 g. In a controlled trial on ambulant patients it was as effective as a seven-day course of ampicillin given in a dose of 500 mg. eight-hourly. The cure rate was 88% with both substances. Side-effects occurred in 3.8% of patients treated with sulphormethoxine and in 16.1% of those who received ampicillin.

Sulphormethoxine is not recommended for acute pyelonephritis.

Dr. Grüneberg was in receipt of a grant from the North-west Metropolitan Regional Board. Dr. I. Lennox-Smith, of Roche Products Ltd., kindly arranged for a supply of sulphormethoxine.

REFERENCES

Brit. med. J., 1964, **1**, 132.

Carroll, O. M., Bryan, P. A., and Robinson, R. J. (1966). *J. Amer. med. Ass.*, **195**, 691.

Haegi, V. (1966). *Schweiz. med. Wschr.*, **96**, 1308.

Harris, M. J., Wise, G., and Beveridge, J. (1966). *Aust. paediat. J.*, **2**, 103.

Mond, N. C., Percival, A., Williams, J. D., and Brumfitt, W. (1965). *Lancet*, **1**, 514.

Percival, A., Brumfitt, W., and de Louvois, J. (1964). Ibid., **2**, 1027.

Seneca, H. (1966). *J. Amer. med. Ass.*, **198**, 975.

Williams, J. D., Brumfitt, W., Leigh, D., and Percival, A. (1965). *Lancet*, **1**, 831.

Controlled Trial of Methandienone in Treatment of Diabetic Retinopathy

P. R. HUNTER,[*] M.A., M.B., M.R.C.P.; SUSAN G. COTTON,[†] M.B., M.R.C.P.; J. H. KELSEY,[‡] M.B., F.R.C.S.
ARNOLD BLOOM,[§] M.D., F.R.C.P.

Brit. med. J., 1967, **3**, 651–653

Retinopathy is a common concomitant of diabetes and is related more to the duration of the diabetic state than to any other factor. Present methods of controlling the diabetic state are unable to prevent the onset or progress of retinopathy. Several studies have claimed that diabetic retinopathy is improved by the administration of anabolic steroids (Dardenne, 1961; Houtsmuller, 1961; Fabrykant *et al.*, 1964). Unfortunately the natural history of diabetic retinopathy is a variable one, and assessment of the value of therapy is correspondingly difficult. Leopold (1964) stated: "Further well controlled studies on the influence of anabolic steroids in diabetic retinopathy are mandatory."

In the present study methandienone (Dianabol) was chosen as an anabolic steroid which was effective when given by mouth, and retinal photography was used for the quantitative assessment of retinopathic changes. Forty-nine diabetic patients were observed, the double-blind method of comparing treated patients with controls being used.

Design of the Trial

Selection of Patients.—Diabetics with retinopathy of all grades of severity (except severe retinitis proliferans) were admitted to the trial provided they had clear media. The trial started in May 1965 and ended in March 1967. Patients below 20 or over 70 years of age and those with any major illness were excluded, as were those who were unlikely to co-operate. The patients came from the diabetic clinics of a teaching and a district hospital.

Treatment and Supervision.—The patients were divided by random numbers into a group receiving oral methandienone 5 mg. twice daily and a group receiving a placebo tablet of the same size and colour, also twice a day. Patients were observed for an average of one year (span 6 to 22 months). They were seen monthly, and the following factors were among those recorded: blood pressure, blood sugar (glucose oxidase method), serum cholesterol (Carr and Drekter, 1956), serum aspartate aminotransferase (Reitmann–Fränkel units). Side-effects and regularity of tablet-taking were also noted.

Visual Acuity and Retinal Photography.—Visual acuity was measured before treatment, Snellen type being used. Thereafter it was assessed six-monthly. Refractive errors were corrected when present. Retinal photographs were taken on Kodachrome 2 film with a Kowa or Zeiss retinal camera. Initially multiple fields were recorded, but eventually a series of standardized fields (nasal, inferior temporal, and superior temporal) were taken of each eye. The objective was to produce three comparable fields per eye at six-monthly intervals.

Assessment of Retinal Photographs

Two assessors were present for all assessments. Standard retinal photographs as defined by Oakley *et al.* (1967) were used for grading the retinopathy. This system comprises the following features.

(1) The patient's photographic fields are graded by direct comparison with a set of standard fields. The grading for a whole fundus represents the average for the individual fields comprising the fundus.

(2) Five diabetic retinal abnormalities are featured:

(*a*) *Microaneurysms and Haemorrhages.*—These include all "dots" and "blots" on the retina, but exclude vitreous haemorrhages. The grading is according to the number of lesions present in the field regardless of their size.

(*b*) *Exudates.*—Hard exudates only, soft ones being ignored. As confluent exudates are common *the area of retina involved*, rather than the number of lesions, is used for grading.

(*c*) *New Vessels.*—All abnormal vascular channels, excepting those forming in relation to previously established fibrous retinitis proliferans. Grading according to the area of field involved.

(*d*) *Venous Irregularities.*—All venous irregularities, including dilatation, segmental irregularities, and "sausaging." Grading according to length of veins involved.

(*e*) *Retinitis Proliferans.*—Any fibrotic lesion in front of the retina, regardless of its vascular associations, and including any detectable diffuse veiling over the retinal surface. Grading according to the area of field involved.

---

[*] Pfizer Research Fellow, Whittington Hospital, London 19.

[†] Medical Registrar, Whittington Hospital, London N.19.

[‡] Consultant Ophthalmological Surgeon, University College Hospital, London W.C.1.

[§] Consultant Physician, Whittington Hospital, London N.19.

Soft exudates may be a specific part of diabetic retinopathy but are not included in this classification.

(3) For each retinopathic feature four standard fields, A, B, C, and D, enable five grades of severity to be determined.

No lesion	Grade 0
Lesion present but less than standard A	Grade 1
Equal to or worse than A but better than B	Grade 2
Equal to or worse than B but better than C	Grade 3
Equal to or worse than C but better than D	Grade 4
Equal to or worse than D	Grade 5

(4) *Scoring System.*—In order to arrive at a quantitative assessment each field was given the appropriate number for each retinopathic feature. The total of the grade numbers was divided by the number of fields to produce an average value for each feature per eye. A change for better or worse was defined as a change in one grade number in two out of three fields, or of two grade numbers in one out of three fields. In the majority of patients finally analysed two complete sets of three fields were available for each eye. Where fields showed slightly different areas non-matching parts were excluded.

Results

Sixty-two patients were admitted to the trial. Two died and 11 were withdrawn because of side-effects, unreliability, or moving out of the area. Of the 49 remaining patients, five could not be included because their photographs were not good enough. In a further 10 patients only one eye was studied for the same reason. The total material available for study therefore constitutes 78 eyes—45 in the placebo group and 33 in the treated group. The two groups were basically similiar in respect of the initial severity of their retinopathy, the methods of treatment of their diabetes, the degree of hyperglycaemia, and the length of observation of their retinopathy.

Haemorrhages.—Patients taking methandienone showed a higher percentage of deterioration than occurred in the control group. Six patients in the treated group deteriorated as against four in the control group (Table I). In those who deteriorated the haemorrhages were more severe in the treated than in the untreated group, since in the treated group (10 eyes) the average grade number rose by 1.7 as against a rise of 1.06 in the control group (5 eyes). It was also noted that the haemorrhages tended to be large and multiple in the treated group. Improvement in haemorrhages occurred in only one patient in the treated group whereas it occurred in four patients in the control group. In 37.7% of controls and 48.8% of treated patients one field in six was not usable, deficiencies which cancel each other out as the error produced was in the same direction.

TABLE I.—*Haemorrhages in Treated and Control Groups*

	Placebo			Methandienone		
	Both Eyes	Only One Eye Available	Percentage of Total Eyes	Both Eyes	Only One Eye Available	Percentage of Total Eyes
Improved	1	3	11·1	0	1	3·0
No change	12	11	77·8	8	6	66·7
Deteriorated	1	3	11·1	4	2	30·3
Total eyes	45			33		

Exudates.—Treatment with methandienone was not associated with any overall beneficial effects on hard exudates. In a total of 15 eyes in the treated group five improved and five deteriorated, compared with the placebo group, in which in a total of 28 eyes four improved and five deteriorated. Though a higher percentage showed an improvement in the treated group, there was also a higher percentage of those who deteriorated. Two patients on methandienone showed significant improvement for exudates in one eye while deteriorating significantly in the other.

Other Lesions.—New vessels were seen in six patients, all of whom were receiving placebo tablets. In two of the six the new vessel lesion became more severe during the trial. Retinitis proliferans developed in two patients, both of whom were receiving placebo tablets. In two other patients also receiving placebos mild retinitis proliferans present at the beginning became more severe during the trial. Venous changes were not analysed because discrepancies between observers' findings made results too inconsistent to be of value.

Visual Acuity.—This was regarded as changing significantly if vision altered by two lines on a Snellen chart. Placebo and treated patients did not appear to differ significantly as regards alterations in their visual acuity. Of 25 treated patients, nine improved and two deteriorated. Of 31 untreated patients nine improved but seven deteriorated. The patient's sex did not have any consistent effect on retinal response to methandienone.

Side-effects.—Frequent questioning established that the patients took their tablets regularly. Of 30 patients on methandienone, three developed oedema, three heart failure, two a persistent rise in diastolic blood pressure, two unsteadiness on the feet and headaches, one acne and voice change, and one increased libido. In the control group (32 patients) one patient developed oedema and another heart failure, while two had a sustained rise of diastolic blood pressure. In both treated and placebo groups one patient died of a coronary thrombosis. It would seem that fluid retention and subjective symptoms occurred more frequently in patients on methandienone. However, it does not seem to have caused hypertension. Serum cholesterol rose on average by 108 mg./100 ml. in the treated group, as against 43 mg./100 ml. in the untreated group. In both groups a small rise in serum transaminases occurred.

Discussion

Visual acuity is the most important of all measurements from the patient's point of view, but is an inadequate guide to retinal changes. A small haemorrhage in the region of the macula may cause a considerable loss of vision while a larger haemorrhage more peripherally may scarcely be noticed. Also, visual acuity is diminished by changes outside the retina in the lens or vitreous.

Assessment of changes in the retina can be attempted by direct ophthalmoscopy, but this clearly does not allow detailed comparison. The use of a binocular ophthalmoscope enables the fundus to be drawn while actually under observation, but this method is very time-consuming and is open to observer bias (Davis, 1965 ; Lee *et al.*, 1966).

The retinal camera offers the best objective method of assessing changes in the retina, but it has several disadvantages. Changes in the lens or the vitreous may make photography impossible, and in some patients, particularly negroes, the pupils dilate too slowly and incompletely. It is impracticable to attempt a complete fundus map and difficult to be sure of getting comparable fields when smaller areas are examined. In this study three fields for each eye were chosen (nasal, inferior temporal, and superior temporal), and these proved adequate in practice. Nevertheless, some cases had to be discarded because the fields in series were not regarded as sufficiently comparable.

When a series of comparable retinal photographs has been obtained, the next problem to be solved is that of standards of comparison. The natural history of retinopathy is a variable one. Each component of diabetic retinal pathology may progress, regress, or remain unaltered. Haemorrhages, exudates, new vessel formation, venous dilatation, all may come and go. In this study, and in studies by other observers (Table II), about one-third of patients in the control group showed changes for better or worse while under observation. Hence there is an absolute need for standards of assessment, and in this respect the standard retinal photographs have proved of practical worth. Five retinopathic abnormalities have been photographed in four standard degrees of severity, and the photographs under study were graded according to these standards. In this way not only was it possible to define deterioration or improvement, it was also possible to devise a simple quantitative assessment of the extent of the changes. With the exception of venous changes, observer errors in assigning grades was slight and results were found to be reproducible.

TABLE II.—*Behaviour of Exudates in Control Groups of Similar Studies (Percentage of Total Eyes)*

	Edinburgh (Cullen 1966)	Bristol (Marmion and Harrold, 1966*)	London (King *et al.*, 1963)	Present Study
Improved ..	16	15	12	14·2
No change ..	56	63	59	68
Deteriorated ..	28	22	29	17·8
Duration (years)	2			1

* Personal communication.

Methandienone was chosen as an agent known to be an effective anabolic steroid given by mouth, and the dosage of 5 mg. twice daily was sufficient to induce an average rise of serum cholesterol of 108 mg./100 ml. as compared with a rise of 43 mg./ 100 ml. in the control group. In an ailment such as diabetes mellitus, which is known to be associated with vascular disease, this cholesterol elevation must be regarded as an unwelcome effect, especially in the long term.

The effects of methandienone on diabetic retinopathy were compared with those of placebo tablets by means of the familiar double-blind technique in which neither patient nor observer was aware of the nature of the tablets used. Assessment of the changes at the end of 18 months seemed to show an increase of haemorrhages in patients taking methandienone, and though this was not statistically significant ($P>0.12$), it made it highly unlikely that even over longer periods any benefits would accrue.

Summary

Changes in retinopathy were assessed in two groups of diabetics, one receiving 10 mg. of methandienone daily and the other a placebo. No beneficial effect was observed in the treated group.

Assessment of changes in retinopathy was made by serial retinal photographs. These were compared with sets of standard photographs. This method of assessment proved effective and reproducible and could be used for future trials.

We acknowledge with gratitude the receipt of a grant from the North-West Metropolitan Regional Hospital Board. We are indebted to Dr. Terry Binns, CIBA Laboratories, Horsham, for his help in designing the trial and providing methandienone (Dianabol) tablets and to Mr. Peter Smith, of the M.R.C. Department of Statistics, for assistance in assessing the results. Finally we are grateful to Professor Sir Max Rosenheim for allowing us to include patients attending University College Hospital.

REFERENCES

Carr, J. J., and Drekter, I. J. (1956). *Clin. Chem.*, 2, 353.
Dardenne, U. (1961). *Acta endocr. (Kbh.)*, Suppl. No. 63, p. 143.
Davis, M. D. (1965). *Arch. Ophthal.*, 74, 741.
Fabrykant, M., Gelfand, M. L., and Rosenberg, A. S. (1964). *Amer. J. med. Sci.*, 248, 304.
Harrold, B. P. (1966). M.D. Thesis, University of London.
Houtsmuller, A. J. (1961). *Acta endocr. (Kbh.)*, Suppl. No. 63, p. 154.
King, R. C., Dobree, J. H., Kok, D'A., Foulds, W. S., and Dangerfield, W. G. (1963). *Brit. J. Ophthal.*, 47, 666.
Lee, P., McMeel, J. W., Schepens, C. L., and Field, R. A. (1966). *Amer. J. Ophthal.*, 62, 207.
Leopold, I. H. (1964). In *Diabetes Mellitus: Diagnosis and Treatment*, edited by T. S. Danowski, p. 165. New York.
Oakley, N. W., Kohner, E., Hill, D. W., Joplin, G. F., and Fraser, R. (1967). *Diabetologia*. In press.

Preliminary Communications

Fibrinolytic Activity in the Clinical Crisis of Sickle-cell Anaemia

Brit. med. J., 1967, 3, 653–654

The natural history of subjects with sickle-cell anaemia is punctuated by recurrent clinical crises. There is rarely any evidence of acute haemolysis in the vast majority of episodes of crisis (Diggs, 1956), and emphasis has been placed on the finding of a variety of thromboembolic manifestations affecting almost every body organ. It is inferred that there is a marked tendency towards spontaneous vascular occlusion in sickle-cell anaemia though the mechanism remains unknown. A generally accepted conclusion is that thrombotic crises arise as a consequence of intravascular agglutination of sickled cells leading to local thrombosis and tissue ischaemia (Allison, 1956). Walters (1958) has suggested, however, that infarction might be precipitated by factors likely to influence the coagulability of the plasma, with subsequent precipitation of a fibrin reticulum within vessels. Abnormalities in coagulation factors have been reported in subjects with sickle-cell anaemia (McKellar and Dacie, 1958; Henstell *et al.*, 1965), but their relation to clinical crisis has not been investigated.

The present study is an attempt to assess whether the fibrinolytic mechanism is impaired in sickle-cell anaemia, both during periods of apparent well-being and during episodes of clinical crisis.

PATIENTS AND METHODS

Children attending the sickle-cell anaemia clinic or admitted to the paediatric wards at Mulago Hospital, Kampala, were studied. All blood samples were obtained between the hours of 11 a.m. and 2 p.m., and a clean venepuncture was carried out with minimum stasis. Dilute blood clot lysis was determined with the technique of Fearnley *et al.* (1957) as modified by Lackner and Goosen (1959). The disintegration of the clot was taken as the end-point in this study, and clots were followed for a maximum of 24 hours. The following groups of patients were studied:

Group A (37).—Hospital inpatients with haemoglobin phenotype AA and with a wide variety of disorders. The duration of their stay in hospital preceding examination ranged from 4 to 42 (mean 9) days.

Group B (77).—Subjects with sickle-cell anaemia attending as outpatients and apparently well.

Group C (7).—Subjects with sickle-cell anaemia attending with mild symptoms attributable to the disease, but not severe enough to necessitate their admission to hospital.

Group D (13).—Subjects with sickle-cell anaemia with symptoms attributable to the disease and severe enough to require their admission to hospital. These children were usually bled within 48 hours of admission.

RESULTS

The distribution of the lysis times obtained in the four groups is shown in the Table. In testing for the significance of differences between any two groups, both the actual lysis time in hours and the logarithmic equivalent were used; differences between groups were equally significant whichever value was employed. The Mann–Whitney U test was used for assessing the significance of differences between the groups (Siegel, 1956).

Distribution of Lysis Time in Hours

Hours	A	B	C	D
1	3	2	1	0
2	6	15	0	1
3	3	19	3	2
4	5	13	3	1
5	2	6	0	0
6	2	7	0	0
7	3	1	0	0
8	2	3	0	0
9	1	3	0	0
10	1	2	0	0
11	2	0	0	1
12	0	0	0	0
13	0	1	0	1
14	1	0	0	0
15	0	1	0	0
16	0	0	0	0
17	2	0	0	0
18	1	0	0	0
19–23	0	0	0	0
24+	3	4	0	7
	37	77	7	13

The most striking finding is that the lysis time in group D—that is, sickle-cell anaemia subjects in clinical crisis admitted to the ward—is far greater than in group A (P=0.008), group B (P=0.008), or group C (P=0.006). There is a suggestion that lysis time in the apparently well sicklers is longer than in those with mild symptoms (P=0.02). Lysis time in the children with haemoglobin phenotype AA is slightly longer than in "well" sicklers (P=0.05) or in sicklers with mild symptoms (P=0.04), but it is very likely that this reflects the effect on fibrinolytic activity of the various illnesses for which these children were admitted to hospital and the medication they were receiving—for example, corticosteroids.

DISCUSSION

Fibrinolytic activity is significantly lower in patients with sickle-cell anaemia in whom symptoms attributable to this disorder were severe enough to necessitate their admission to hospital. If the severe symptoms associated with clinical crisis are due to intravascular thrombosis, it is possible that the fibrinolytic mechanism may be involved in either the development or the maintenance of such vascular occlusion. There is presumed to be a dynamic equilibrium between the deposition of fibrin in vessels and its removal by lysis (Astrup, 1956; Fearnley, 1961); and the marked diminution in fibrinolytic activity during episodes of sickle-cell crisis might either reflect some factor inhibiting normal enzyme activity or may represent the body's response to intravascular thrombosis and tissue damage.

High levels of fibrinogen have been reported in older subjects with sickle-cell anaemia in America, though the finding was thought to be nonspecific. There appeared to be no difference in fibrinogen levels when patients were studied in or out of crisis (Fenichel *et al.*, 1950). This report of raised fibrinogen levels is commented upon because Blix (1961) asserted that clots made of plasma containing a high concentration of fibrinogen are more resistant to lysis than those formed from a lower fibrinogen concentration. However, Bennett *et al.* (1967) believe that the situation is far more complex than this and that changes in plasminogen activator, as assessed by euglobulin clot lysis, do not simply reflect changes in fibrinogen levels.

While it is possible that the subjects in sickle-cell crisis form a special group in whom there is a persistently reduced fibrinolytic activity, we think that this is very unlikely. It is more probable that activity is lowered during or before a severe clinical crisis. Four of the 13 patients studied in clinical crisis were studied again several months later, when they were apparently well. Of three subjects with long lysis times (24 hours) one remained prolonged and two had fallen to 3.9 and 3.3 hours respectively.

Several of the 13 children admitted in clinical crisis had haemoglobin levels below the level of those attending the clinic and not admitted to hospital. It has, however, previously been shown that the degree of anaemia per se does not affect fibrinolytic activity (Shaper *et al.*, 1967).

SUMMARY

Fibrinolytic activity has been shown to be significantly reduced in children with sickle-cell anaemia in clinical crisis as compared with sickle-cell anaemia subjects with no symptoms or with mild symptoms. Further studies are indicated to ascertain whether a disturbance of the fibrinolytic mechanism has a causal relationship to the signs and symptoms of the clinical crisis in sickle-cell anaemia.

We are grateful to Dr. M. C. Pike (Medical Research Council Statistical Research Unit) for his advice and assistance. This work is supported by grants from the Medical Research Council to A. M. and A. G. S. and by the World Health Organization.

A. MAHMOOD, PH.D., M.R.C.P.ED.,
Honorary Clinical Lecturer.
DORIS M. MACINTOSH, M.B., CH.B.,
Research Fellow.
A. G. SHAPER, M.B., M.R.C.P.,
Research Professor in Cardiovascular Diseases.

Departments of Paediatrics and Medicine,
Makerere University College Medical School,
Kampala, Uganda.

REFERENCES

Allison, A. C. (1956). *Trans. roy. Soc. trop. Med. Hyg.*, **50**, 185.
Astrup, T. (1956). *Lancet*, **2**, 565.
Bennett, N. B., Ogston, C. M., and Ogston, D. (1967). *Clin. Sci.*, **32**, 27.
Blix, S. (1961). *Acta med. scand.*, **169**, 495.
Dacie, J. V., (1960). *The Haemolytic Anaemias: Congenital and Acquired*, part 1, 2nd ed. London.
Diggs, L. W. (1956). *Amer. J. clin. Path.*, **26**, 1109.
Fearnley, G. R. (1961). *Lancet*, **1**, 992.
—— Balmforth, G., and Fearnley, E. (1957). *Clin. Sci.*, **16**, 645.
Fenichel, R. L., Watson, J., and Eirich, F. (1950). *J. clin. Invest.*, **29**, 1620.
Henstell, H. H., Kligerman, M., and Irwin, L. E. (1965). *Blood*, **25**, 907.
Lackner, H., and Goosen, C. C. (1959). *Acta haemat. (Basel)*, **22**, 58.
McKellar, M., and Dacie, J. V. (1958). *Brit. J. Haemat.*, **4**, 404.
Shaper, A. G., Kyobe, J., and Mwanje, D. K. (1967). *Amer. J. clin. Path.*, **47**, 344.
Siegel, S. (1956). *Nonparametric Statistics for the Behavioral Sciences*. New York.
Walters, J. H. (1958). *Proc. roy. Soc. Med.*, **51**, 646.

Medical Memoranda

Embolism from Mural Thrombus in the Thoracic Aorta

Brit. med. J., 1967, **3**, 655–656

Mural thrombus in the internal carotid artery is a source of emboli to the retinal and cerebral arteries, causing transient or permanent blindness and hemiplegia (Gunning *et al.*, 1946b); thrombi in subclavian arteries damaged by cervical ribs form emboli which lodge in the digital arteries, inducing ischaemia of the fingers and thickened intima (Gunning *et al.*, 1964a). Emboli from mural thrombi in the popliteal artery have been implicated in gangrene of the great toe (Ross, 1936). Mural thrombi on plaques of nodular arteriosclerosis are common in the abdominal aorta, but the frequency with which they form emboli to the abdominal or leg arteries is unknown, the paucity of published cases suggesting the event is either uncommon or unrecognized.

Gross examples of a phenomenon are important because they are easily recognized and may be the extreme variants of events which are commonly unspectacular or undetectable. It is with this possibility in mind that a case in which mural thrombus in the thoracic aorta formed emboli to the abdominal and leg arteries is reported.

CASE REPORT

An unmarried woman (U.O.H. 363216) aged 67 had for many years noticed slight breathlessness and constricting pain in the centre of the chest when walking. She was admitted to a cottage hospital complaining of pain in the right loin, vomiting, and weakness for nine days. Her temperature was 99.6° F. (37.6° C.) and blood-pressure 190/90 mm. Hg. No abnormalities were found in the abdomen or chest. The urine contained moderate quantities of protein, but the centrifuged deposit showed neither red nor white cells. The blood urea was 53 mg./100 ml. Her pain continued for five days and several examinations failed to establish its cause.

She was transferred to the Radcliffe Infirmary, where examination showed a sinus rhythm of 96/minute. The only pulses in the legs were the femorals; her blood-pressure was 125/80 mm. Hg. Crepitations were present in both lungs, but there were no cardiac murmurs and no abdominal abnormalities. The urine had a specific gravity of 1018, it contained between 300 and 1,000 mg. of protein per litre, and the centrifuged deposit had 8 white cells and several hyaline and granular casts per high-power field. The blood urea was 48 mg./100 ml.; plasma sodium 130, potassium 4.2, chloride 90, and bicarbonate 20 mEq/l. The plasma amylase was 7 units. The haemoglobin was 99%; white cells 20,000/cu. mm.—a neutrophil leucocytosis; the sedimentation rate was 97 mm./hour.

The next day her loin pain increased and she complained of pain in the legs. Examination revealed tenderness in the right hypochrondrium. The following day her legs were cold and white, and bowel sounds were absent. On the third day she sweated profusely, the pulse was 120/minute and the systolic blood-pressure 50 mm. Hg, despite metaraminol and hydrocortisone. Faeculent material was aspirated from the stomach. She died on the seventeenth day of her illness.

Necropsy three days after death showed fresh infarcts of the same age in the spleen, intestines, and kidneys, the right kidney being completely infarcted. The corresponding arteries contained fresh thrombus, the right renal artery being occluded by thrombus which projected into the aortic lumen. The femoral arteries below the inguinal ligament did not contain thrombus; the leg arteries were not examined. A mural thrombus 3 cm. long occluded the first two intercostal arteries on the right side. The larger upper end was 1 cm. wide and 0.5 cm. deep; its surface was ragged and necrotic. The rest of the aorta showed moderate nodular arteriosclerosis, particularly below the renal arteries, where atheromatous ulcers were filled with thrombus. The coronary arteries showed moderately thickened intima, but they were patent. The heart valves were normal, neither the left atrium nor ventricle contained thrombus, and the foramen ovale was closed. The pulmonary veins were normal, the lungs were congested, and there were small pleural effusions.

The aortic mural thrombus was cut in half longitudinally and embedded in two blocks, from which sections were taken at 200-μ intervals. The ragged surface from the upper end was fresh fibrin thrombus surrounding granular platelet areas; its superficial irregularities were filled by a loose fibrin reticulum, leucocytes, and macrophages, which suggested either lysis of thrombus or thrombus lost as emboli. The centre of this fresh thrombus was necrotic. The underlying thrombus was hyaline fibrin on an intimal plaque 3 mm. thick. The large thrombus occluding the right renal artery was identical with the platelet fibrin thrombus from the thoracic aorta; in the remainder of this and the other occluded arteries there were small platelet fibrin thrombi and clotted blood. The infarcts in the spleen, kidneys, and intestines were the same age. There was no evidence of an arteritis.

DISCUSSION

The diagnosis of embolism requires a source for the embolus, distal arteries occluded by this material, and absence of multiple arterial thromboses or arteritis, all of which were found after death but not detected during life in this patient.

Mural thrombus in the internal carotid artery is suggested by reduced pulsation and bruits; it is confirmed by arteriograms, which in arteries of this calibre show irregularities of the arterial wall. In contrast, mural thrombus in the aorta is undetected, either clinically or radiologically, unless it is massive, because the remaining lumen is still large.

Transient occlusion of retinal and cerebral arteries by emboli is usually associated with striking symptoms and signs (Russell, 1963; Gunning *et al.*, 1964b); however, Skovborg and Lauritzen (1965) observed three symptomless retinal emboli in a diabetic patient. In a detailed clinicopathological study of aorto-iliac thrombosis Gunning *et al.* (in preparation) found extensive mural thrombus in these arteries, and on histological grounds suggested that emboli of mural thrombus and atheromatous material were to be expected. The case histories, however, did not reveal progress of ischaemic symptoms corresponding to the progressive thrombosis observed anatomically, nor did they suggest episodes of embolism. They concluded that the legs, unlike the retina, brain, and fingers, were not sensitive indices of arterial occlusion unless the blockages were substantial and lasting. Furthermore, Gunning *et al.*'s study of internal carotid endarterectomy specimens showed fresh mural thrombus if symptoms of retinal and cerebral ischaemia occurred in the seven weeks before endarterectomy, but fresh thrombus was not found in cases with a greater interval between symptoms and surgery. By analogy, fresh thrombus on aortic plaques is a potential source of emboli to the abdominal organs and legs; but to demonstrate such a relationship between mural thrombus and embolism in the lower limb requires extensive histological examination.

Deposits of mural thrombus on the intima of coronary arteries (Duguid, 1946) and aorta (Crawford and Levene, 1952) are organized to plaques identical with nodular arteriosclerosis, and homologous pulmonary thrombo-emboli in animals undergo similar changes (McLetchie, 1952). It is probable that emboli of mural thrombus impacted at arterial bifurcations or occluding small arteries are also incorporated into the arterial wall.

In this patient emboli from mural thrombus in the thoracic aorta occluded many distal arteries and caused death. It is likely that the mural thrombi commonly found in the abdominal aorta also form emboli to the legs, which are undetected clinically. The organization of these emboli would contribute to the intimal thickening universally found in the leg arteries of the elderly.

It is a pleasure to thank Dr. A. M. Cooke for permission to publish this case and Professor Sir George Pickering for his helpful criticism.

D. O. OLIVER, M.B., CH.B., M.R.C.P., M.R.A.C.P.,
The Radcliffe Infirmary,
Oxford.

REFERENCES

Crawford, T., and Levene, C. I. (1952). *J. Path. Bact.*, **64**, 523.
Duguid, J. B. (1946). Ibid., **58**, 207.
Gunning, A. J., Pickering, G. W., Robb-Smith, A. H. T., and Russell, R. W. R. (1964a). *Quart. J. Med.*, **33**, 133.
—— —— —— —— (1964b). Ibid., **33**, 155.
McLetchie, N. G. B. (1952). *Amer. J. Path.*, **28**, 413.
Ross, J. P. (1936). *Proc. roy. Soc. Med.*, **29**, 872.
Russell, R. W. R. (1963). *Lancet*, **2**, 1354.
Skovborg, F., and Lauritzen, E. (1965). Ibid., **2**, 361.

Chronic Milk-alkali Syndrome after Prolonged Excessive Intake of Antacid Tablets

Brit. med. J., 1967, 3, 656–657

Rifkind *et al.* (1960) reported the case of a woman who developed the clinical features of chronic milk-alkali syndrome following prolonged excessive consumption of Rennies tablets. We here report a second case, differing in the absence of generalized osteosclerosis.

CASE REPORT

A 40-year-old woman admitted to hospital for investigation on 13 May 1963 complained of excessive thirst for the previous eight years, and because of this her urine had been tested for sugar on several occasions, with negative results. She said that she had sustained rib fractures in 1960 and 1961, once when turning a mattress and once on sneezing. We were unable to obtain the *x*-ray films taken on these occasions. In July 1962 she first noted spontaneous twitching of the legs and itching of the skin of the trunk and arms. From March 1963 her ankles and feet felt stiff. She then became increasingly tired and found it necessary to give up her secretarial work. Two weeks before admission she had a solitary episode of dysuria, urethral pain, and frequency of micturition lasting for two days. Her appetite remained normal, there was no nausea or vomiting, and her weight was steady.

Further questioning revealed that she had consumed about 24 Rennies tablets daily since 1952. She first took this proprietary antacid to relieve heartburn in her second pregnancy. Heartburn did not recur after the baby was born, but she had acquired a taste for the tablets and continued to take them regularly. Each Rennies tablet contains mag. carb. pond. 78 mg., mag. hydrox. 2.9 mg., mag. oxid. lev. 3.4 mg., calc. carb. 671.6 mg., kaolin. lev. 3.4 mg., calc. phosph. 1.1 mg., and ol. menth. pip. 2.6 mg. The patient was therefore taking some 16 gm. of calcium carbonate daily, in addition to her normal dietary intake. She had also been given tablets containing calcium in 1961, after fracturing a rib, but had taken these for only about two weeks. There was no history of vitamin-D medication. Her average consumption of milk was less than 1 pint (570 ml.) daily.

On examination she did not appear acutely ill. Slight generalized brown pigmentation of the skin and numerous scratch marks on her back were present. There were calcium deposits on the nasal and lateral sides of both corneae, but no subcutaneous soft-tissue swellings or other abnormal physical findings. Her blood-pressure was 125/90 mm. Hg.

Investigations.—Haemoglobin 10.6 g./100 ml.; M.C.V. 92 cubic microns; M.C.H.C. 30.5%; W.B.C. 6,500/c.mm.; E.S.R. (Westergren) 68 mm./hr.; blood urea 261 mg./100 ml.; plasma sodium 136 mEq/l.; potassium 5.8 mEq/l.; chloride 95 mEq/l.; bicarbonate 21 mEq/l.; serum calcium 11.4 mg./100 ml.; phosphate 5.7 mg./100 ml.; alkaline phosphatase 7.9 King-Armstrong units; serum albumin 3.3 g.; serum globulin 3.5 g. A 24-hour urine sample (on 23 May) contained 0.34 g. protein, 94 mg. calcium, and 410 mg. phosphate. Urinary cell excretion (measured over four hours): W.B.C. 8,600,000/hr., R.B.C. 1,000,000/hr. Two mid-stream specimens of urine were cultured; one grew micrococci and the other *Escherichia coli* and *Streptococcus faecalis*. Mantoux test was negative, with 1/1,000 old tuberculin. Chest *x*-ray picture was normal and no evidence of generalized bone disease was seen on radiographs of the lumbar and thoracic spine, hands, or teeth, the lamina dura being intact. Plain *x*-ray films of the abdomen and renal tomograms showed small kidneys (each was 9.5 cm. in length) with diffuse parenchymal calcification. An attempt at renal biopsy was unsuccessful.

In hospital she accepted the advice to stop taking Rennies tablets and was given a low-protein diet with high oral fluid intake. By 24 May the blood urea had fallen to 150 mg./100 ml., and the serum calcium level was 9.6 mg./100 ml. and phosphate 6.8 mg./100 ml. She left hospital on 30 May, and in view of the probable urinary infection was given tetracycline, 250 mg. four times daily, to take at home.

She was readmitted on 6 June complaining of vomiting, thirst, and abdominal pain. She was clinically dehydrated, with blood-pressure 90/70 mm. Hg. The blood urea was 396 mg./100 ml. and plasma bicarbonate 9 mEq/l. She was given intravenous fluids with marked clinical improvement, the blood urea falling to 217 mg./100 ml. The serum calcium was 7.4 mg./100 ml., phosphate 8.7 mg./100 ml. She was discharged home for the second time on 16 June, taking sodium bicarbonate, 2 g. three times daily, to correct acidosis. She was still on this treatment at her most recent review in February 1966. She then looked and felt well apart from slight pruritus, which was less severe than formerly. Dysuria had not recurred. Skin pigmentation persisted, and the blood-pressure was 60/30 mm. Hg in each arm. Further investigations in February 1966 showed haemoglobin 12.4 g./100 ml.; E.S.R. (Westergren) 47 mm./hr.; blood urea 95 mg./100 ml.; plasma sodium 144 mEq/l.; potassium 3.4 mEq/l.; chloride 88 mEq/l.; bicarbonate 33 mEq/l.; serum calcium 9.3 mg./100 ml.; phosphate 4.6 mg./100 ml.; alkaline phosphatase 13 King-Armstrong units/100 ml.; serum albumin 4.5 g./100 ml.; globulin 2.8 g./100 ml. Mid-stream urine contained a trace of protein, a few R.B.C.s but no W.B.C.s, and was sterile on culture. Plain *x*-ray film of the abdomen showed no change in the size of the kidneys or in the degree of nephrocalcinosis compared with the 1963 films.

COMMENT

The term "milk-alkali syndrome" has been used to describe two separate conditions that may complicate treatment of peptic ulcer. Cope (1936) first reported hypercalcaemia, alkalosis, and temporary impairment of renal function, these abnormalities being corrected by stopping alkali therapy. Our case, however, is an example of the chronic form of milk-alkali syndrome in which renal function remains permanently impaired when alkalis are withdrawn. This condition was first described by Burnett *et al.* (1949), who described the occurrence of the following syndrome in six patients with a history of prolonged and excessive intake of milk and absorbable alkalis: hypercalcaemia without hypercalciuria or hypophosphataemia, normal serum alkaline phosphatase, marked chronic renal insufficiency with azotaemia, mild alkalosis, calcinosis manifested especially by an ocular lesion resembling band keratitis, and improvement in clinical state on a lowered intake of milk and absorbable alkali. Two of these patients had renal calcification. By 1963 Punsar and Somer were able to review 33 reported cases of irreversible renal failure due to prolonged excessive intake of absorbable alkali, associated in most but not all instances with excessive milk consumption.

Rifkind *et al.* (1960) reported the only previous British case that we have been able to find with the principal features of the chronic milk-alkali syndrome. Their patient was a woman of 48 who had taken 30 Rennies tablets daily for 10 years without excessive milk intake. Besides uraemia and nephrocalcinosis there were calcium deposits in the corneae and sclerae, aorta, and abdominal lymph nodes and there was generalized osteosclerosis, whereas our patient had radiologically normal bones. Our case, like theirs, had an excessive intake of calcium and absorbable alkali derived from Rennies tablets. In our patient the rapid fall in the serum calcium level with subsequent improvement in the general state of health and fall in blood urea after stopping the Rennies tablets indicates that they were the cause of the hypercalcaemia and nephrocalcinosis. The absence of further deterioration of renal function almost three years after stopping the tablets is noteworthy. Both our patient and that of Rifkind *et al.* took large quantities of Rennies tablets because they had developed a liking for them. It seems improbable that any patient would take so many antacid tablets solely to relieve dyspepsia.

We are grateful to Dr. J. D. N. Nabarro for advice. We wish to thank Dr. H. L. Marriott for permission to report this case.

A. J. CAMERON, M.B., M.R.C.P.,
Late Medical Registrar.
M. P. SPENCE,* M.B., M.R.C.P.,
Late Senior Medical Registrar.
Middlesex Hospital,
London.

* Present address: Hertford County Hospital, Hertford.

REFERENCES

Burnett, C. H., Commons, R. R., Albright, F., and Howard, J. E. (1949). *New Engl. J. Med.*, **240**, 787.
Cope, C. L. (1936). *Clin. Sci.*, **2**, 287.
Punsar, S., and Somer, T. (1963). *Acta med. scand.*, **173**, 435.
Rifkind, B. M., Chazan, B. I., and Aitchison, J. D. (1960). *Brit. med. J.*, **1**, 317.

Pernicious Anaemia and Intestinal Malabsorption: Spinal Cord Degeneration Developing during Vitamin B_{12} Treatment

Brit. med. J., 1967, **3**, 657–658

CASE REPORT

The patient was born in Northamptonshire in 1890 and emigrated to New Zealand at the age of 33. In 1927, when aged 37, she began to pass loose pale stools, about six daily. She complained of audible bowel sounds and of excessive flatus. When first seen by a physician she was aged 59 and considerably underweight. Severe macrocytic anaemia and a megaloblastic sternal marrow were present. Gastric analysis showed achlorhydria. Her pale stools, when dried, contained 32% by weight of fat. A barium enema was normal. Her blood picture quickly returned to normal after the twice-weekly injection of Anahaemin (liver extract) 2 ml. As diarrhoea continued in spite of a low-fat diet, folic acid 10 mg. b.i.d. was added, but was soon discontinued because her diarrhoea increased. Fortnightly injections of Anahaemin were continued, given by her general practitioner.

She was not seen again by a physician until the age of 66. Her blood was then normal, with a packed cell volume of 40%. Her stools were still pale and loose, and contained 36% by weight of fat. Her glucose tolerance curve was flat. A gluten-free diet was started and cortisone acetate 25 mg. was given by mouth twice daily. She improved in health, her diarrhoea diminished, and she was able to take a trip to the United Kingdom.

At the age of 69 she was still in good health, with one stool daily. Liver extract injections were then stopped, and vitamin B_{12} 200 μg., weekly at first and later fortnightly, was prescribed. The gluten-free diet and cortisone were continued.

At the age of 70 she was found on routine examination to have reduced vibration sense in both lower legs. Later in the same year she complained of unsteadiness of gait, and there was some oedema of both legs. Her blood count and serum proteins were normal.

The following year she became increasingly unsteady on her feet, especially when walking in the dark. She complained of weakness of her legs and of tingling burning sensations in both feet and to a lesser extent in her hands. Examination revealed a positive Romberg sign, an ataxic gait, and some impairment in her legs of all sensory modalities, especially vibration and postural sensibility. Both knee and ankle jerks were abnormally brisk and the plantar reflexes were extensor. The clinical picture was that of subacute combined degeneration of the cord with mild peripheral neuritis.

In view of this development the vitamin B_{12} dosage was increased to 200 μg. twice weekly and she was admitted to hospital for reassessment. Repeated peripheral blood counts and a sternal marrow examination were normal. Repeated serum vitamin B_{12} levels were well within the normal range—namely, 460 and 480 $\mu\mu$g./ml. (normal 150–650). Her serum folic acid was 8 mμg./ml. (normal 5–16). Augmented histamine stimulation failed to provoke any gastric secretion of hydrochloric acid. Absorption of cobalt-labelled vitamin B_{12} (Schilling test) was grossly defective. This absorption test was repeated after the administration of

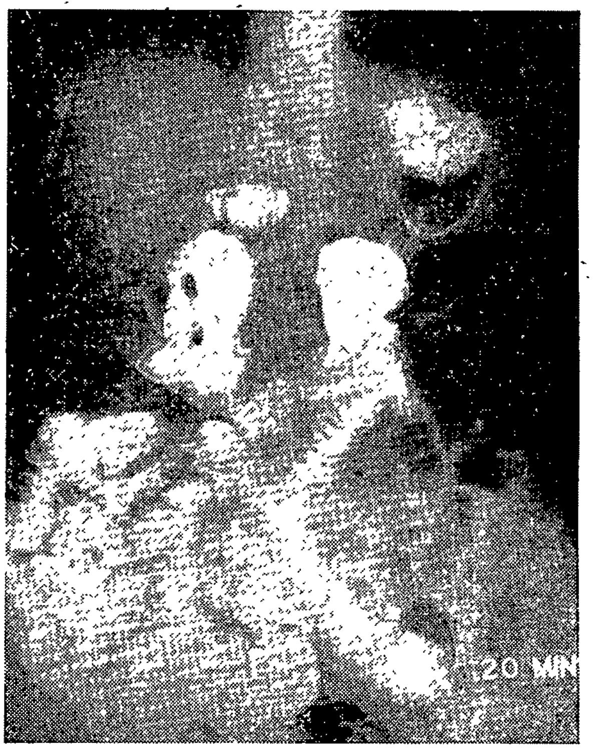


FIG. 1.—Barium-meal examination showing multiple small-bowel diverticula.

intrinsic factor, and though there did seem to be slight improvement this was not thought to be significant. A xylose-absorption test gave an abnormally low result. Her renal function was normal.

A barium-meal examination showed three large diverticula of the duodenum and numerous smaller ones of the proximal jejunum. In the lower jejunum and ileum the barium became flocculated with a typical malabsorption pattern which made demonstration of diverticula impossible in this region.

She was given a prolonged oral course of tetracycline without obvious clinical improvement. Vitamin B_{12} 200 µg. was administered thrice weekly and her serum B_{12} level rose to 1,080 µµg./ml. In addition thiamine hydrochloride 100 mg. was given intramuscularly each day. As there was no obvious improvement in her condition vitamin B_{12} was later discontinued and a change made to Neo-hepatex 2 ml. twice weekly for a period of eight months. There was still no obvious improvement, so the frequency of administration was reduced to once a week and eventually to once a fortnight.

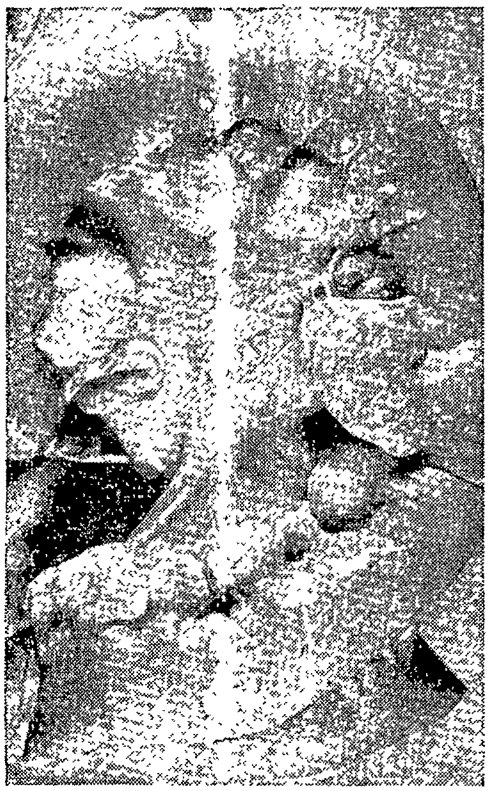


FIG. 2.—Necropsy specimen of small bowel showing diverticulosis.

By this time she was leading a wheel-chair existence because of her ataxia and weakness. Her nervous system signs remained much the same, except that her ankle reflexes were now less brisk than her knee reflexes. She remained in this state, with little progression, during the next four years, and throughout this time she was mentally alert. She then had an attack of persistent vomiting and was admitted to hospital in a state of shock. Her abdomen was distended, and bowel sounds were diminished, though there was an absence of pain or tenderness. Colon bacilli were cultured from her blood. In spite of intensive restorative measures she died. She was then aged 76.

Necropsy Report.—Stomach: thin-walled. Duodenum: three large diverticula of the second part. Jejuno-ileum: numerous large, wide-mouthed, slightly loculated mesenteric diverticula gradually diminishing in number and size to the mid-gut, but still present though smaller, to the terminal ileum ; ulceration of Peyer's patches in lower end of ileum, one of them on the point of perforation. Brain: weight 920 g.; considerable gyral atrophy with focal atrophy of the cerebellum. Spinal cord: general atrophy. Bones: well-marked vertebral osteoporosis.

Microscopical Findings.—Stomach: complete gastric atrophy with reversion to a "colonic" type of mucosa ; muscle also thin. Jejuno-ileum: villous structure preserved. Liver: fatty change associated with peliosis. Brain: no gross neuronal "fall-out" in cortex or brainstem nuclei. Spinal cord: degeneration of dorsal and lateral columns typical of subacute combined degeneration.

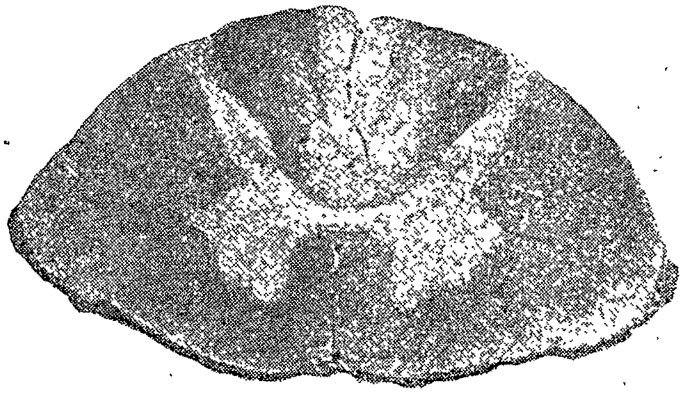


FIG. 3.—Section of spinal cord showing dorsal and lateral tract degeneration.

COMMENT

This unusual case in which symptoms and signs of spinal cord degeneration appeared while the patient was receiving adequate parenteral vitamin B_{12} or liver extract was about to be reported when Ellis, Breuer, Owen, and Laszlo (1966) reported a similar experience. In the present case, however, the clinical findings were supported by post-mortem examination.

This patient undoubtedly suffered from pernicious anaemia. In addition, there was evidence of intestinal malabsorption apparently related to her extensive small-bowel diverticulosis. Subacute combined degeneration progressed in spite of an increase in dosage of vitamin B_{12} and also of a reversion to liver extract. Serum vitamin B_{12} was normal at a time when her condition was progressing and there was no improvement even when her serum B_{12} level was raised to twice normal levels.

It would appear, therefore, that here as in the case reported by Ellis *et al.* (1966) the patient's nervous system was unable to utilize vitamin B_{12}.

I am grateful to the medical superintendent, Christchurch Hospital, Dr. W. I. Paterson, for permission to publish this case and to the director of pathology, Dr. D. T. Stewart, and the assistant radiologist, Dr. R. H. Gibson, for their help.

C. G. RILEY, F.R.C.P., F.R.A.C.P.,
Physician, Christchurch Hospital, Christchurch, New Zealand.

REFERENCE

Ellis, G. J., Breuer, R. I., Owen, E. E., and Laszlo, J. (1966). *Ann. intern. Med.*, 64, 654.

Irreducible Posterior Dislocation of the Elbow

Brit. med. J., 1967, **3**, 659

All published reports on posterior dislocation of the elbow are concerned with old dislocations (Vangorder, 1932 ; Allende and Freytes, 1944), disclocations associated with fracture of the medial epicondyle with displacement into the joint (Roberts, 1934 ; Outland and Hanlon, 1938 ; Patrick, 1946 ; Smith, 1950 ; Purser, 1954), dislocation associated with rupture of the brachial artery (Spear and Janes, 1951 ; Henderson and Robertson, 1952), dislocation complicated by ulnar nerve injury (Outland and Hanlon, 1938), and recurrent dislocations of the elbow (Milch, 1936 ; Reichenheim, 1947 ; Wainwright, 1947 ; Kapel, 1951 ; King, 1953 ; Spring, 1953 ; Osborne and Cotterill, 1966). However, a search of the literature from the English-speaking world has not revealed any reported case where there was failure to reduce an uncomplicated posterior dislocation of the elbow by manipulation under anaesthesia soon after injury. This must be extremely uncommon. This report describes such a case.

CASE REPORT

A girl aged 7 years was seen with an injury to her left elbow after a fall on her outstretched hand. On examination the elbow was deformed and there was no bruising or swelling around that joint. There was no nerve or vascular injury. *X*-ray examination of the elbow showed posterior dislocation without fracture.

Three hours after the injury the elbow was manipulated under general anaesthesia, but the dislocation could not be reduced despite a further attempt later. Even at this stage the elbow did not show any bruising or swelling. Because of the absence of bruising and swelling an old dislocation of the elbow was considered, but the patient was very intelligent and maintained that the left elbow was normal before the fall. Open reduction was undertaken the following day.

Operation.—Initially, the elbow was explored through a medial vertical incision. There was no bruising in the soft tissues. The medial ligament and the medial epicondyle were normal. A posterolateral incision was made and the head of the radius was found dislocated through a small buttonhole tear in the posterolateral capsule of the joint. The proximal ulna was found dislocated posteriorly without any tear in the capsule. On attempting reduction the buttonhole in the capsule tightened around the narrow portion of the neck of the radius and prevented reduction. After enlarging the buttonhole the dislocation was reduced quite easily. The orbicular ligament was found intact.

Postoperative progress was normal and the elbow was immobilized for three weeks. Two months later the elbow movements were satisfactory except for the last few degrees of extension.

COMMENT

It is quite evident in this case that closed reduction failed because the head of the radius had passed through a small tear in the posterolateral capsule and the buttonhole effect tightened around the narrow portion of the neck of the radius. When traction was applied in the line of the deformity the buttonhole tightened and prevented reduction of the dislocation. Once the buttonhole was enlarged the reduction was very easy.

Another interesting feature in this case is that there was no bruising or swelling—a feature sufficient to make one consider the possibility of an old injury. One would expect some bruising and swelling on the medial side of the joint in a recent dislocation of the elbow. In this case the medial ligament would have been stretched and not torn. The torn blood vessels in the buttonhole tear in the capsule did not bleed, probably because the vessels were compressed by the neck of the radius or because displacement was so minimal.

I wish to thank Mr. E. J. Hargadon for permission to publish this case and for his helpful criticism.

A. DEVADOSS, M.B., B.S., F.R.C.S.ED., F.R.C.S.GLASG.,
Park Hospital, Davyhulme, Manchester. Present address: Orthopaedic Unit, Sefton General Hospital, Liverpool 15.

REFERENCES

Allende, G., and Freytes, M. (1944). *J. Bone Jt Surg.*, **26**, 691.
Henderson, R. S., and Robertson, I. M. (1952). Ibid., **34B**, 636.
Kapel, O. (1951). Ibid., **33A**, 707.
King, T. (1953). Ibid., **35B**, 50.
Milch, H. (1936). Ibid., **18**, 777.
Osborne G., and Cotterill, P. (1966). Ibid., **48B**, 340.
Outland, T., and Hanlon, C. R. (1938). Ibid., **20**, 750.
Patrick, J. (1946). Ibid., **28**, 143.
Purser, D. W. (1954). Ibid., **36B**, 247.
Reichenheim, P. P. (1947). *Brit. J. Surg.*, **35**, 201.
Roberts, N. W. (1934). *Lancet*, **2**, 78.
Smith, F. M. (1950). *J. Amer. med. Ass.*, **142**, 396.
Spear, H. C., and Janes, J. M. (1951). *J. Bone Jt Surg.*, **33A**, 889.
Spring, W. E. (1953). Ibid., **35B**, 55.
Vangorder, G. W. (1932). Ibid., **14**, 127.
Wainwright, D. (1947). *Proc. roy. Soc. Med.* (Section of Orthopaedics), **40**, 885.

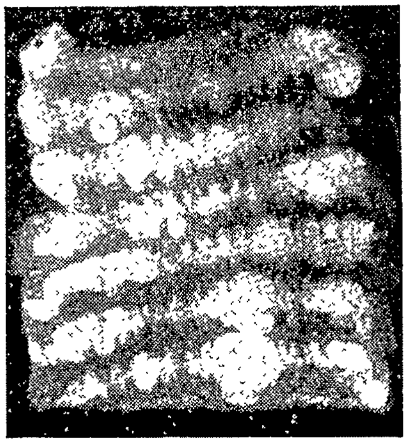
Human Infection with a Tapeworm, Bertiella sp., probably of African origin

Brit. med. J., 1967, **3**, 659–660

Proglottides of a tapeworm were passed intermittently for six months in the faeces of a British boy aged 6 who was otherwise well and had no complaint of bowel disturbance. He had lived in Aden for the previous two years. The proglottides proved to be terminal segments of *Bertiella* sp. Identification to species was not possible. The boy was successfully treated with niclosamide (Yomesan).

Bertiella is normally a parasite of monkeys. On further inquiry it was found that nearly two years previously the boy had spent a fortnight's holiday in Mombasa, East Africa, where he had close contact with monkeys ; these were thought to be of the rhesus type and were tame enough to be fed by hand.

The life history of *Bertiella studeri* (Blanchard, 1891), which is the principal species of the Eastern Hemisphere, was elucidated by Stunkard (1940) ; he fed eggs of the tapeworm experimentally to various free-living mites and later found cysticercoids (the infective stage for the final, definitive host) in the



Segments of *Bertiella* sp. tapeworm. (×5.)

body cavity of some of the mites. Presumably, human infection results from the accidental ingestion of infected mites.

This is the twenty-fifth report of human infection with bertiella. Geographically, these reports are mainly from the Eastern Hemisphere—namely, Mauritius (4), India (8), Sumatra (1), Java (2), Borneo (1), Philippines (1), Singapore (1), East Africa (1). In the Western Hemisphere it has been reported once from Cuba, St. Kitts (West Indies), Brazil, Argentina, and Paraguay. The present case is of interest in that the infection was probably acquired in Africa, whence only one case has previously been recorded (Buckley and Fairley, 1950), and in that from the available evidence the boy had probably harboured the worm for about two years.

The subject of bertiella infection to man has been recently reviewed by D'Alessandro, Beaver, and Pallarés (1963).

We are indebted to Mr. S. Nicholson for the preparation of the specimen and to Dr. M. R. Thomas for the photograph.

C. D. THOMPSON, M.B., B.CH.,
General Practitioner.
C. H. JELLARD, B.M., F.C.PATH., DIP.BACT.,
Director, Public Health Laboratory, Plymouth.
J. J. C. BUCKLEY, D.SC.,
Professor of Helminthology, London School of Hygiene and Tropical Medicine.

REFERENCES

D'Alessandro, B., Beaver, P. C., and Pallares, R. M. (1963). *Amer. J. trop. Med. Hyg.*, **12**, 193.
Blanchard, R. (1891). *Mém. Soc. zool. Fr.*, **4**, 186.
Buckley, J. J. C., and Fairley, N. H. (1950). *Trans. roy. Soc. trop. Med. Hyg.*, **44**, 2.
Stunkard, H. W. (1940). *Amer. J. trop. Med.*, **20**, 305.

Self-poisoning with Digoxin: Successful Treatment with Atropine

Brit. med. J., 1967, **3**, 660–661

Self-poisoning with digitalis is uncommon. Lethal doses are massive (McGuire and Richards, 1936; Bergy *et al.*, 1957; Johnston and Price, 1960), and death is more likely to follow the ingestion of digitoxin than the more rapidly excreted digoxin. Recovery after very large doses of digoxin (Bernstein *et al.*, 1959) and digitoxin (Bergy *et al.*, 1957; Knowles, 1959) has been reported, and it is apparent that survival is more likely when the myocardium is healthy.

CASE REPORT

A housewife aged 52 with a long history of depression started taking digoxin in 1961 for lone atrial fibrillation. At 11 a.m. on 18 October 1965 she took 6.25 mg. of digoxin. On admission to another hospital the pulse rate was 40 a minute and the blood pressure 90/40 mm. Hg; vomiting and diarrhoea decreased after chlorpromazine (100 mg. intramuscularly). On 19 October the pulse rate was 22–25, and she was transferred to the London Chest Hospital.

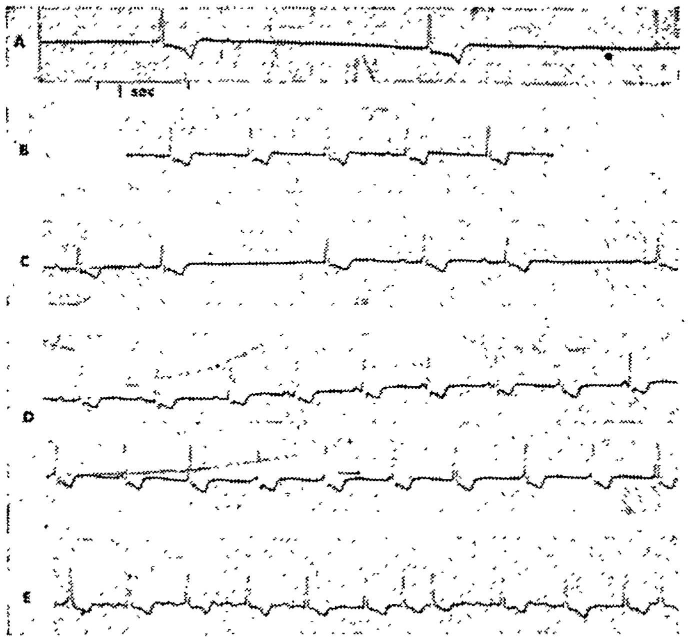
She was drowsy and pale, with cold extremities. The pulse was regular at 15, and the blood pressure 120/60. There was slight hepatomegaly, but no other evidence of congestive cardiac failure. She had profuse cold sweats. An electrocardiogram (see Fig., A) showed no atrial activity; the ventricular rhythm was regular, with normal QRS complexes. Serum potassium was 7.9 mEq/l. and blood urea 61 mg./100 ml.

While preparations were being made to insert an electrode pacemaker catheter it was decided to try the effect of atropine. Atropine (0.6 mg.) was given intravenously; the pulse rose to 60/min. within 20 minutes, but then slowed to 36/min. during the next 20 minutes. Atropine (0.6 mg. intravenously) was repeated, and the rate increased to 72. The electrocardiogram (see Fig., B) showed sinus rhythm, with low-voltage P waves and constant long P–R interval (0.24 sec.). Whenever the heart rate fell below 50, atropine (0.6 mg.) was given intramuscularly; she needed an injection about every five hours for the first 36 hours. During this time the electrocardiogram showed an irregular bradycardia, with variable long P–R interval (0.24–0.30 sec.), and variable P wave morphology (see Fig., C); one tracing after atropine showed atrioventricular dissociation (see Fig., D). On 22 October she reverted to atrial fibrillation, with irregular ventricular response (see Fig., E) and was put back on digoxin.

On admission, she had been anuric for over 24 hours. An intravenous drip (5% dextrose) was started, with added sodium bicarbonate; 20% mannitol was also given (total 300 ml. in 14 hours), and urine flow was re-established within half an hour. After an initial rise to 150 mg./100 ml. the blood urea rapidly fell to normal; the serum potassium also fell, to 4.2 mEq/l., and potassium by mouth was started after 18 hours.

She rapidly became more responsive, but remained seriously depressed, and was discharged for further psychiatric treatment after 10 days.

Liver-function tests initially gave abnormal results (21 October: S.G.O.T. 130 units/ml.; S.G.P.T. more than 160 units/ml. 27 October: sulphobromophthalein excretion test: 47% retention at 25 minutes, and 30% retention at 45 minutes) but later returned to normal.



Serial electrocardiograms (all lead II). A, 19 October, before treatment: sinus arrest; extreme nodal bradycardia. B, 19 October, after intravenous atropine: sinus rhythm; low-voltage P waves; long P–R interval. C, 20 October: wandering pacemaker. D, 20 October, after atropine: two consecutive strips showing atrioventricular dissociation. E, 22 October: atrial fibrillation.

DISCUSSION

The toxic effects of digitalis on the heart have been well reviewed by Burwell and Hendrix (1950), Lown and Levine (1954), Schott (1964), and Dubnow and Burchell (1965). A regular rhythm may occur in the presence of atrial fibrillation as a result of digitalis-induced complete heart block, when the ventricles are controlled by a pacemaker in the main bundle or atrioventricular node below the level of the block; a nodal rhythm may also be associated with atrioventricular dissociation. Sinuatrial block, "wandering pacemaker," and sinus arrest are rare, but were reported by Burwell and Hendrix (1950), and by Bernstein *et al.* (1959) and Knowles (1959) in their cases of massive overdose. In our patient there was atrial asystole with profound slowing due to depression of the nodal pacemaker. Neither ventricular ectopic beats nor paroxysmal atrial tachycardia with block was seen, but may have been prevented by the high serum potassium; Lown and Levine (1954) observed that ectopic beats were rare in digitalis poisoning in patients without heart disease. Hyperkalaemia was probably due to anuria, metabolic acidosis, and the efflux of potassium from the myocardium which occurs with toxic doses of digitalis.

The treatment of digitalis intoxication is based on the withdrawal of digitalis, correction of potassium depletion, and specific measures directed against the arrhythmia (Lown and Levine, 1954; Sodeman, 1965). Sampson *et al.* (1943) abolished digitalis-induced ventricular ectopic beats with potassium salts given by mouth. Procainamide and beta-adrenergic blocking agents (Stock and Dale, 1963; Taylor *et al.*, 1964) have been successfully used for digitalis-induced paroxysmal atrial tachycardia with block and ventricular ectopic beats. Calcium ions potentiate digitalis action, and the chelation of calcium with disodium versenate has been recommended by Gubner and Kallman (1957) and Bernstein *et al.* (1959) in cases of digitalis overdosage.

In our case the blood pressure was well maintained, suggesting that myocardial contractility was not depressed, and that the low cardiac output was due mainly to bradycardia. Atropine was tried as it seemed likely that the extreme bradycardia was due to excessive vagal depression of the nodal pacemaker. It is well known that slowing of the ventricular rate in atrial fibrillation by digitalis is partly mediated by the vagus, though with larger doses the extravagal effect on atrioventricular conduction is more important, so that atropine is relatively ineffective in increasing the ventricular rate (Gold, 1946). In our case, though the dose was massive, the response to atropine was dramatic, but repeated injections were required to maintain a satisfactory heart rate. The nodal rhythm was replaced by a sinus mechanism or wandering pacemaker, and at this stage atropine increased the rate of discharge of both the sinuatrial and the atrioventricular node, with periods of atrioventricular dissociation.

Digitalis is excreted mainly by the kidney (Friedman *et al.*, 1954), small quantities being destroyed in the body or excreted in the bile. Prompt restoration of urine flow was thus very important in clearing digoxin from the body.

Impaired liver function in patients with heart disease may be due to hypotension or cardiac failure (Killip and Payne, 1960; Richman *et al.*, 1961) but may be caused by digitalis itself. Le Winn (1953) found impaired sulphobromophthalein excretion in patients with gynaecomastia, which was attributed to an oestrogenic effect of long-continued digitalis administration in patients with liver damage. In our patient raised transaminases and increased sulphobromophthalein retention probably resulted from reduced hepatic blood flow, but direct injury by digoxin cannot be ruled out.

We are indebted to Dr. H. G. L. Lloyd-Thomas, who referred this patient to us.

F. NAVAB,* M.B., M.R.C.P.
M. HONEY, M.B., M.R.C.P.

London Chest Hospital,
London E.2.

* At present Resident Medical Officer, Westminster Hospital, London S.W.1.

REFERENCES

Bergy, G. G., Fergus, E. B., and Bruce, R. A. (1957). *Ann. intern. Med.*, **46**, 964.
Bernstein, M. S., Neschis, M., and Collini, F. (1959). *New Engl. J. Med.*, **261**, 961.
Burwell, W. B., and Hendrix, J. P. (1950). *Amer. J. Med.*, **8**, 640.
Dubnow, M. H., and Burchell, H. B. (1965). *Ann. intern. Med.*, **62**, 956.
Friedman, M., St. George, S., and Bine, R. (1954). *Medicine (Baltimore)*, **33**, 15.
Gold, H. (1946). *J. Amer. med. Ass.*, **132**, 547.
Gubner, R. S., and Kallman, H. (1957). *Amer. J. med. Sci.*, **234**, 136.
Johnston, D. W., and Price, R. V. (1960). *Tex. St. J. Med.*, **56**, 429.
Killip, T., and Payne, M. A. (1960) *Circulation*, **21**, 646.
Knowles, R. R. (1959). *R.I. med. J.*, **42**, 592.
Le Winn, E. B. (1953). *New Engl. J. Med.*, **248**, 316.
Lown, B., and Levine, S. A. (1954). Ibid., **250**, 771, 819, 866.
McGuire, J., and Richards, C. E. (1936). *Amer. Heart J.*, **12**, 109.
Richman, S. M., Delman, A. J., and Grob, D. (1961). *Amer. J. Med.*, **30**, 211.
Sampson, J. J., Albertson, E. C., and Kondo, B. (1943). *Amer. Heart J.*, **26**, 164.
Schott, A. (1964). *Postgrad. med. J.*, **40**, 628.
Sodeman, W. A. (1965). *New Engl. J. Med.*, **273**, 35, 93.
Stock, J. P. P., and Dale, N. (1963). *Brit. med. J.*, **2**, 1230.
Taylor, R. R., Johnston, C. I., and Jose, A. D. (1964). *New Engl. J. Med.*, **271**, 877.

Self-poisoning with Digitalis Glycosides

Brit. med. J., 1967, **3**, 661–662

Digitalis and its crystalline derivatives are seldom used in suicidal attempts. Moore (1937) reviewed 1,147 cases of attempted suicide; poisons were taken in 692 cases, but only one patient used digitalis. Of 16 previously reported cases of self-poisoning by digitalis (McGuire and Richards, 1936; Tomaszewski and Lapa, 1936; Moore, 1937; Duvoir *et al.*, 1938; Bickel *et al.*, 1951; Vuletic and Ivancic, 1952; Yu, 1954; Bergy *et al.*, 1957; Von Oettingen, 1958; Segre, 1959; Bachmann, 1960; Bernot and Goldberg, 1960; Johnston and Price, 1960; Aubertin *et al.*, 1961; Thomopoulos and Kokkinos, 1965) only three were fatal (McGuire and Richards, 1936; von Oettingen, 1958; Johnston and Price, 1960).

The present report describes two patients who poisoned themselves with digitoxin and digoxin respectively, adding one to this very small number of recorded fatal cases.

CASE 1

A man, aged 59, was brought to the Victoria Infirmary, Glasgow, at 9.30 p.m. on 17 June 1964. Six hours previously he had swallowed 100 tablets (10 mg.) of digitoxin, prescribed for his deceased wife. Since her death he had been depressed and had had epigastric discomfort but no other somatic symptoms. There was no history of cardiac or vascular disease.

He was a small thin man, drowsy but in no way distressed. There were no congestive signs or cyanosis. Blood pressure was 100/70. Cardiac rhythm was totally irregular with a ventricular rate of 44 per minute. The heart was not enlarged; sounds were normal except for a very soft, short systolic murmur localized to the apex. There were no significant abnormalities in other systems. An electrocardiogram taken shortly after admission showed atrial fibrillation and ST–T segment changes in keeping with digitalis effect.

Gastric aspiration yielded no tablets or particles. At 10 p.m. he was given ephedrine 60 mg. and potassium chloride 6 g. by mouth. At 11 p.m. the heart rate was about 50. Atropine sulphate 0.5 mg. was injected subcutaneously. His general condition remained satisfactory until just after midnight, when he suddenly collapsed in coma. He died about 45 minutes later. Electrocardiograms (lead I) were recorded during this period (see Fig.).

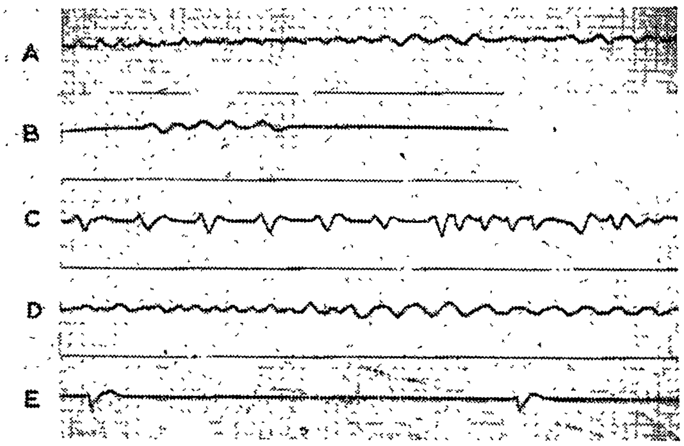
Permission for necropsy was not granted

CASE 2

A man, aged 22, had rheumatic mitral and aortic valve disease with atrial fibrillation. He had been taking digoxin 0.25 mg. twice daily for at least seven years. He had been depressed for several weeks on account of increasing cardiac disability. On the evening of 13

January 1966 he drank some alcohol and swallowed between 16 and 20 tablets (4–5 mg.) of digoxin. He developed headache, giddiness, and nausea but did not have abdominal pain. He was given saline to drink by his family doctor and vomited.

On admission to Stobhill Hospital, Glasgow, early on the morning of 14 January he was fully conscious but depressed. His general condition was good. Blood pressure was 125/65. Cardiac rhythm was totally irregular with a ventricular rate of 60. The heart was considerably enlarged with signs of double mitral and aortic valve lesions. There were no congestive signs. No abnormalities were found in other systems.



CASE 1.—Electrocardiogram (lead I) after collapse. A (at 12.05 a.m.) shows ventricular fibrillation. B (at 12.20 a.m.) shows ventricular fibrillation and periods of cardiac asystole. C and D (continuous) (at 12.30 a.m.) show idioventricular rhythm with a brief episode of ventricular tachycardia followed by ventricular fibrillation. E (at 12.40 a.m.) shows very slow idioventricular rhythm, which led to final cardiac asystole.

Gastric lavage yielded no tablets or particles. Heart rate fell to 40 and rhythm remained irregular. He was given propranolol 10 mg. intravenously without significant effect. After a further slight decrease in heart rate atropine sulphate 0.5 mg. was injected with little effect. Heart rate was 42 eight hours after admission. Subsequent clinical progress was uneventful and bradycardia disappeared within a few days. By 20 January the electrocardiogram showed no clear evidence of digitalis toxicity and the heart rate was 75. On 24 January the previous maintenance dose of digoxin was resumed without ill effect.

DISCUSSION

Treatment of Digitalis Poisoning.—Digitalis has its most toxic effect on the heart, probably related to a shift of potassium from the myocardium (Calhoun and Harrison, 1931). To some extent this may be counteracted by the administration of potassium (Kay, 1955), which was given to Case 1. In animals, digitalis derivatives may cause focal myocardial necrosis (Dearing *et al.*, 1943) possibly owing to vagal stimulation, since atropine can prevent its occurrence (Kyser *et al.*, 1946). Myocardial necrosis ascribed to digitoxin poisoning in man was recorded by Johnston and Price (1960). Atropine was therefore given in both the above cases. Propranolol was given in Case 2 to avert the possible onset of serious arrhythmias. Vaughan Williams and Sekiya (1963) proposed beta sympathetic blockade as an antidote in glycoside intoxication. This measure may be required to maintain sinus rhythm after abolition of digitalis-induced ventricular fibrillation by direct current countershock (Sloman *et al.*, 1965). A combination of all these measures with monitoring in a coronary care unit might prove life-saving in digitalis poisoning, whether suicidal or otherwise.

Digitalis and the Electrocardiogram.—The characteristic effects of digitalis on the electrocardiogram—depression of the S–T segment, shortening of the Q–T interval, and inversion of the T wave (Wood, 1956)—were observed in the electrocardiograms of both cases shortly after admission. In Case 1 digitoxin poisoning presumably caused atrial fibrillation, but in Case 2 it had existed for several years. Digitalis may provoke almost any cardiac arrhythmia. Ventricular tachycardia and fibrillation were observed in Case 1 in addition to very slow idioventricular rhythm (see Fig.). The tracings closely resemble those of patients dying suddenly from myocardial infarction. The heart often shows electrical activity with slowing idioventricular rhythm after apparent clinical death (Stroud and Feil, 1948). This terminal rhythm does not seem to have been reported previously in connexion with digitalis overdosage.

Organic Heart Disease and Self-poisoning with Digitalis.—There have been only three previous reports of successful suicide with digitalis derivatives (McGuire and Richards, 1936 ; von Oettingen, 1958 ; Johnston and Price, 1960). In none of these cases and in few of the documented non-fatal cases was there clear evidence of pre-existing heart disease. This can also be said of the fatal case now reported.

I am grateful to Dr. Ian Murray and Dr. A. S. Rogen for permission to publish these cases and to Dr. T. Semple for helpful advice in the preparation of the paper.

JAMES BUCHANAN, M.D., M.R.C.P.ED., M.R.C.P.GLASG.
Victoria Infirmary, Glasgow.
(Present address: Law Hospital, Carluke, Lanarkshire.)

REFERENCES

Aubertin, E., Lavignolle, A., David-Chausse, F., Le Rebeller, Mme, and Broustet, A. (1961). *J. méd. Bordeaux*, **138**, 398.
Bachmann, M. (1960). *Z. Kreisl.-Forsch.*, **49**, 982.
Bergy, G. G., Fergus, E. B., and Bruce, R. A. (1957). *Ann. intern. Med.*, **46**, 964.
Bernot, A., and Goldberg, B. (1960). *Soc. Méd. milit. franç. Bull.*, **54**, 226.
Bickel, G., Plattner, H., and Edelstein, H. (1951). *Arch. Mal. Cœur*, **44**, 61.
Calhoun, J. A., and Harrison, T. R. (1931). *J. clin. Invest.*, **10**, 139.
Dearing, W. H., Barnes, A. R., and Essex, H. E. (1943). *Amer. Heart J.* **25**, 648.
Duvoir, M., Pollet, L., Desoille, H., and Gaultier, M. (1938). *Bull. Soc. méd. Hôp. Paris*, **54**, 159.
Johnston, D. W., and Price, R. V. (1960). *Texas St. J. Med.*, **56**, 429.
Kay, C. F. (1955). *Circulation*, **12**, 291.
Kyser, F. A., Ginsberg, H., and Gilbert, N. C. (1946). *Amer. Heart J.*, **31**, 451.
McGuire, J., and Richards, C. E. (1936). Ibid., **12**, 109.
Moore, M. (1937). *New Engl. J. Med.*, **217**, 291.
Segre, M. (1959). *Minerva med.-leg.*, **79**, 176.
Sloman, G., Robinson, J. S., and McLean, K. (1965). *Brit. med. J.*, **1**, 895.
Stroud, M. W., and Feil, H. (1948). *Amer. Heart J.*, **35**, 910.
Thomopoulos, D., and Kokkinos, D. (1965). *Brit. med. J.*, **2**, 170.
Tomaszewski, W., and Lapa, W. (1936). *Arch. Mal. Cœur*, **29**, 196.
Vaughan Williams, E. M., and Sekiya, A. (1963). *Lancet*, **1**, 420.
von Oettingen, W. F. (1958). *Poisoning: A Guide to Clinical Diagnosis and Treatment*, 2nd ed. London.
Vuletic, V., and Ivancic, R. (1952). *Arch. Mal. Cœur*, **45**, 853.
Wood, P. (1956). *Diseases of the Heart and Circulation*, 2nd ed. London.
Yu, P. N. G. (1954). Cited by Bergy *et al.* (1957).

Current Practice

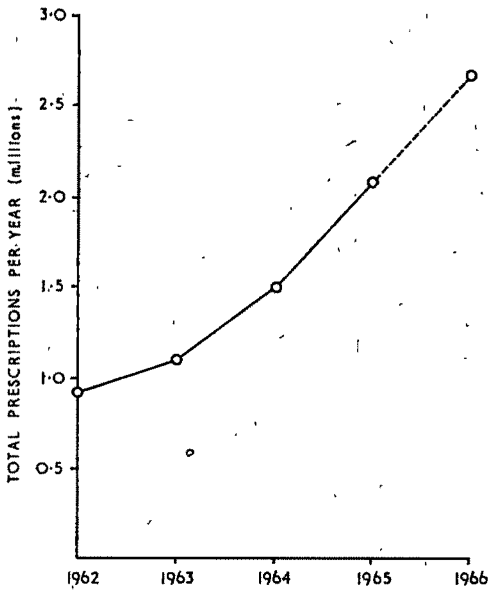
FORENSIC MEDICINE AND TOXICOLOGY

Clinical Effects and Treatment of Imipramine and Amitriptyline Poisoning in Children

C. M. STEEL,*† M.B., CH.B., B.SC. ; J. O'DUFFY,* M.B., B.S., M.R.C.P.ED. ; S. S. BROWN,‡ PH.D., B.SC.

Imipramine and amitriptyline are tricyclic antidepressant compounds whose chemical structure, dosage, pharmacology, and toxicity are so similar that they are commonly considered together (Klerman and Cole, 1965 ; Giarman, 1965 ; Rasmussen, 1965, 1966).

The danger to children of accidental ingestion of these drugs has become increasingly recognized in recent years (Noack, 1960 ; Giles, 1963 ; Sunshine and Yaffe, 1963), and at least 21 such accidents, including five deaths, have been reported. The main features of these reports are summarized in the accompanying Table.



Annual number of N.H.S. prescriptions of imipramine + amitriptyline in Great Britain 1962–6. The 1966 figure is predicted from data for the first six months.

During 1966 seven children were admitted to the medical wards of the Royal Hospital for Sick Children, Edinburgh, with a diagnosis of imipramine or amitriptyline overdosage. Over the preceding two-year period five similar cases were seen, but none was recorded before 1964. This suggests a trend which is entirely in keeping with the prescription rates for these two compounds in Great Britain as shown in the Chart (data supplied by the Ministry of Health). There is therefore reason to believe that from being an alarming but rare event, poisoning of children by these two drugs may become an increasingly common problem.

The purpose of this paper is to record the characteristic features of both mild and severe imipramine or amitriptyline poisoning and to derive a rational scheme of management based on a consideration of the pharmacology of these drugs, on a review of the literature, and on our own experience in practice.

Clinical Features of Mild Poisoning

Ten of our patients (all except Cases 26 and 31) and four of those previously reported (Cases 7, 8, 9, and 10) showed the symptoms of mild poisoning only. Some depression of consciousness was almost invariably seen, while six showed ataxia or a disturbance of posture out of proportion to their drowsiness. A striking feature in five of the children was the extreme agitation with which they responded to any stimulus, or which appeared spontaneously, alternating with periods of drowsiness.

Tachycardia, persisting during sleep, was present in 10 of these children, but none developed arrhythmia or hypotension, and electrocardiograms recorded in Cases 32 and 33 showed sinus tachycardia, with normal complexes. Some degree of pupillary dilatation was noted in four of the patients, while thirst, dizziness, nystagmus, or vomiting was occasionally apparent.

These symptoms tended to develop gradually within one to four hours of ingestion of the drug. Paraldehyde was given to control restlessness in one (Case 8), but all the others recovered spontaneously and completely within 24 hours.

One patient (Case 28) did not develop symptoms of poisoning, and may not in fact have swallowed any drug, though he was found with several tablets in his mouth and surrounded by many more from which he had sucked the sugar coating.

Clinical Features of Severe Poisoning

Severe poisoning is characterized by the development of convulsions and coma ; in addition, severe respiratory depression, cardiac arrhythmias, E.C.G. changes, and profound hypotension may occur. The detailed clinical features are best described by a case report.

Case 31

A previously healthy boy of 5 years 4 months was observed to become grossly ataxic over a period of a few minutes. He seemed to be unaware of his surroundings, and within 15 minutes lapsed into coma and had a generalized tonic-clonic seizure. During the journey to hospital of 45 minutes, almost continuous twitching of the limbs was observed and on arrival he was deeply unconscious. Any form of stimulus, such as the aspiration of pharyngeal secretions, provoked a generalized convulsion lasting some 30 seconds.

---

* University Department of Child Life and Health and Professorial Unit, Royal Hospital for Sick Children, Edinburgh.

† Present address: Department of Medicine, Western General Hospital, Edinburgh.

‡ University Department of Clinical Chemistry, Royal Infirmary, Edinburgh.

On examination there were no localizing signs. Tone and deep tendon reflexes were normal and the plantar responses were flexor. The pupils were dilated equally and responded sluggishly to light (within one hour they became widely dilated and fixed); the fundi appeared normal and there was no meningism. The boy's temperature was normal, his colour good, and respirations were 24/min., regular but shallow. The apex rate was 148/min. and regular. Peripheral pulses were of good volume and the arm blood pressure was 115/70 mm. Hg.

Estimates of blood glucose, plasma calcium, urea, and electrolytes gave normal values, and lumbar puncture yielded clear cerebrospinal fluid under normal pressure with normal glucose and protein concentrations.

After passage of a cuffed endotracheal tube, gastric lavage was performed and the stomach content (which contained no visibly identifiable remnant of tablets) kept for examination.

Paraldehyde (5 ml. intramuscularly) was given to control convulsions, and thereafter he became completely unresponsive even to painful stimuli.

The parents at first insisted that the child could have had access only to a salicylate preparation (Palaprin), but on persistent questioning they recalled that a bottle of grandmother's "nerve tablets" were kept on top of the wardrobe. These were said to be Triptafen tablets, each containing amitriptyline (25 mg.) and perphenazine (2 mg.).

The presence of amitriptyline (though not of perphenazine) in the gastric aspirate was quickly established and a conservative policy of management adopted. Slow intravenous infusion of 5% dextrose in half-strength Ringer's lactate was started. Pulse rate, blood pressure, respiratory rate, pupil size, and conscious level were recorded every 15 minutes and rectal temperature every two hours. Over the next 24 hours the blood pressure fluctuated between 110/70 and 90/60 mm. Hg. Tachycardia persisted, the apex rate reaching 160/min., but no irregularity was detected and the peripheral pulses remained easily palpable.

The level of consciousness rose steadily. Sixteen hours after the estimated time of ingestion of the tablets the endotracheal tube was removed because of gagging, and shortly afterwards the child opened his eyes. His reactions to stimuli then became more vigorous, and by 24 hours he responded to any interference with grossly exaggerated movements of the limbs and signs of great agitation. This was controlled by intramuscular chlorpromazine (25 mg.), a total of four doses being required at intervals of 4, 6, and 13 hours.

No urine was passed spontaneously for the first 24 hours though the bladder became readily palpable above the pubic symphysis. The child's rectal temperature rose to 38.3° C. (101° F.) at 36 hours, but by then there was evidence of a basal pneumonia, which complicated his recovery.

Forty-eight hours from the time of ingestion he recognized his parents and was able to drink from a cup. By 60 hours he was entirely rational with no evidence of neurological deficits, and after a course of antibiotics and physiotherapy he left hospital on the eighth day.

TABLE

Case No.	Author	Age in Years	Drug(s)	Dose (mg.)	Dose (mg./kg. Body Weight)*	Levels (μg./100 g.)	Symptoms and Signs	Treatment	Outcome
1	Noack	2 6/12	Imipramine	2,500	(192)	Liver, 2,700	Coma, continuous convulsions, cyanosis, dilated pupils, cardiac and respiratory arrest	Gastric lavage, artificial respiration, cardiac massage	Died
2	Somuncuoglu	3 4/12	"	375	21·6	—	Vomited, coma, twitching, respiratory depression, cyanosis, tachycardia, sweating, fixed dilated pupils, urine retention, skin rash	Gastric lavage, I.V. calcium	Recovered
2	Arneson	1 7/12	"	1,250	(112)	—	Vomited, coma, continuous convulsions, hypotension, ataxia and athetosis, arrhythmia, E.C.G. changes	Gastric lavage, I.V. barbiturate, artificial respiration, blood and fluids I.V.	"
4	Connelly and Venables	2	"	375	(31)	—	Coma, continuous convulsions, arrhythmia, E.C.G. changes	Paraldehyde	"
5	Alajem *et al.*	1 6/12	"	375	37·5	—	Coma, convulsions, tachycardia, congestive failure, hypotension, small fixed pupils, ataxia, E.C.G. changes	Gastric lavage, barbiturate I.V. and P.R.	"
6	Garrison and Moffitt	1 10/12	"	500	(42)	—	Excitement, coma, convulsions, fixed dilated pupils, hypotension, arrhythmia, E.C.G. changes	Gastric lavage, I.V. barbiturate, forced diuresis, vasopressor agents, assisted ventilation, lanatoside C	"
7	Fendrick	4 6/12	Amitriptyline	75	4·2	—	Ataxia, alternating drowsiness and excitement, propulsive gait, disorientated	Oral fluids and observation	"
8	Giles	2 9/12	Imipramine	?	?	—	Disorientated, vomited, opisthotonos and bizarre movements	Paraldehyde	"
9	"	1 7/12	"	75	(7)	—	Vomited, drowsy, disorientated	Observation	"
10	"	5	Imipramine, ? Thioridazine	75 ?	(4·2)	—	Dizzy, ataxic, semicomatose, hyperreactive to stimuli, tachycardia		"
11	"	1 3/12	Imipramine	100	(9·6)	—	Coma, convulsions, fixed dilated pupils, pyrexia, nystagmus, cyanosis, tachycardia, arrhythmia, hypotension	Oxygen, paraldehyde	"
12	"	1 6/12	"	350	(32)	—	Vomited, excitable, coma, convulsions, tachycardia, hypotension, E.C.G. changes	Paraldehyde	Died
13	Mazur	2 6/12	"	?	?	—	Ataxia, coma, convulsions, cyanosis, fixed dilated pupils, tachycardia, hypotension, agitation, urinary retention	Gastric lavage, oxygen, rectal chloral hydrate, barbiturate I.M., vit. C I.V., I.V. fluids, caffeine, analeptics, adrenaline	Recovered
14	Sunshine and Yaffe	1 3/12	Amitriptyline	1,000	(95)	Serum, 250 Liver, 7,800	Coma, convulsions, cyanosis, fixed dilated pupils, tachycardia, pyrexia, hypotension, E.C.G. changes	Gastric lavage, barbiturate I.V. and I.M., assisted ventilation, vasopressor agents, peritoneal dialysis	Died
15	Jacobziner and Raybin	4	Imipramine	1,000	(63)		Coma, convulsions, respiratory distress, ventricular tachycardia	Gastric lavage, oxygen, barbiturate I.V., paraldehyde, procainamide	Recovered

* Figures in parentheses indicate that calculation is based on average weight for age, where actual weight was not recorded.

(*Continued on next page*)

When discharged from follow-up two months later he was well in all respects, and had resumed normal school activities. He was indeed able to give a full account of having found the tablets, swallowed them all (between 55 and 60), and discarded the empty bottle. His first symptoms had developed some 45 minutes later.

Toxicology

The suggestion of salicylate poisoning in the above case was discounted both on clinical grounds and in view of the fact that side-room testing for plasma salicylate (Brown *et al.*, 1967) yielded negative results. In formally excluding this possibility by spectrophotofluorometric assay of the blood, evidence suggesting the presence of a phenothiazine derivative or a tricyclic antidepressant was found. Concurrently, the appropriate history was obtained. Amitriptyline was then identified and assayed in the gastric aspirate by extraction at alkaline *p*H with heptane, back extraction into acid, and ultra-violet spectroscopy. While the recovery was only 30 mg., it should be emphasized that, in general, gastric washings represent the most suitable clinical material from which to make positive identification of an ingested drug, since metabolic change is minimal and the actual concentration may be higher than in any other available body fluid, particularly if aspiration has been carried out within a short time of ingestion.

The estimation of plasma amitriptyline by a fluorometric method analogous to that used by McBay and Algeri (1963) for imipramine gave a level of 700 µg./100 ml. for the blood sample drawn five hours after ingestion, when absorption would have been virtually complete. This represents a level of about 20 times that obtained in adults on therapeutic doses, and considerably exceeds levels found in the fatal cases of Sunshine and Yaffe (Case 14) and Dingell *et al.* (1964) (Case 18). It is unfortunate that such determinations have been made so rarely in these cases, since the peak blood level represents a valuable measure of the degree of overdosage, in addition to providing confirmation of the identity of the drug in question.

Only 13 mg. of amitriptyline was recovered from the urine passed during the first 48 hours after ingestion. Attempts to establish the presence of perphenazine in this specimen or in gastric aspirate or blood were unsuccessful even when the sensitive and specific method of Ragland *et al.* (1965) was used.

Discussion

From the data in the Table some quantitative assessment of the toxicity of imipramine and amitriptyline to children can be made. The severe symptoms described may be precipitated by the ingestion of less than 10 mg./kg. (Cases 11 and 19), and seem inevitable when the dose exceeds 20 mg./kg. In practical terms the latter figure means, for a 2-year-old, 10 standard tablets of either drug, or one bottle of amitriptyline paediatric elixir (usually prescribed for the treatment of functional nocturnal enuresis).

The smallest fatal dose in a child was 32 mg./kg. (Case 12) and the largest amount taken by one who survived was 112 mg./kg. (Case 3). This variation in susceptibility parallels experi-

Table—*continued*

Case No.	Author	Age in Years	Drug(s)	Dose (mg.)	Dose (mg./kg. Body Weight)*	Levels (µg./100 g.)	Symptoms and Signs	Treatment	Outcome
16	Fruthaler and Snyder	?	„	?			Coma, convulsions, pyrexia, respiratory failure, cardiac arrest	Barbiturate, artificial respiration, open cardiac massage	„
17	„ „	?	„	?			„ „	?	Died
18	Dingell *et al.*	2 6/12	„	750	53·5	Serum, 110 Liver, 2,300	?	Vomiting induced	„
19	Braun *et al.*	2 6/12	„	125	8		Coma, convulsions, cyanosis, respiratory depression, dilated pupils, urinary retention, ataxia, restlessness, hypotension, tachycardia, congestive failure, arrhythmia, E.C.G. changes	Oxygen, forced diuresis, barbiturate I.V., chloral hydrate	Recovered
20	„ „	1 9/12	„	300	25		Ataxia, restlessness, coma, convulsions, respiratory depression, dilated pupils, tachycardia, arrhythmia, hypotension, E.C.G. changes	„ „	„
21	Prout *et al.*	1 11/12	„	600	(50)		Coma, convulsions, cyanosis, respiratory depression, fixed dilated pupils, hypotension, arrhythmia, E.C.G. changes	Gastric lavage, paraldehyde, forced diuresis	„
22	Present series	1 11/12	Amitriptyline	150	13·6		Ataxia, drowsy, hyperexcitable when roused, dilated pupils, tachycardia	Gastric lavage. observation	„
23	„ „	4	Imipramine	200	(12·6)		Very drowsy, dilated pupils, tachycardia	Vomiting induced, gastric lavage, observation	„
24	„ „	1 10/12	Amitriptyline	?	?		Ataxia, drowsiness, tachycardia	Gastric lavage, observation	„
25	„ „	2 4/12	Imipramine	100	6·4		Drowsy, tremor, agitation, tachycardia	„ „ „	„
26	„ „	4 8/12	Imipramine Promazine	750 1,500	40 80		Agitation, coma, convulsions, tachycardia, hypothermia, pupils fixed, not dilated	Gastric lavage, I.V. fluids, observation	„
27	„ „	2 4/12	Imipramine	100	8	—	Drowsy, tachycardia, nystagmus	Gastric lavage, observation	„
28	„ „	1 6/12	Amitriptyline Perphenazine	? ?	? ?	—	Nil	„ „ „	„
29	„ „	3	Amitriptyline	80	5·7	—	Drowsy, tachycardia	„ „ „	„
30	„ „	4 3/12	„	80	4·5	—	Drowsy	„ „ „	„
31	„ „	5 4/12	Amitriptyline Perphenazine	1,400 112	82 6·5	Serum, 700	Ataxia, coma, convulsion, fixed dilated pupils, respiratory depression, tachycardia, agitation, urinary retention	Gastric lavage, paraldehyde I.M., I.V. fluids, chlorpromazine I.M.	„
32	„ „	2 4/12	Imipramine	100	8·3	Serum, 20	Agitation, tachycardia, thirst, dilated pupils	Gastric lavage, observation	„
33	„ „	3 5/12	„	100	6·8	Serum, 10	Tachycardia, thirst, dilated pupils	„ „ „	

* Figures in parentheses indicate that calculation is based on average weight for age, where actual weight was not recorded.

ence in adults, death having been recorded after ingestion of only 625 mg. (9 mg./kg) (Edwards, 1966), but survival after as much as 5.5 g. (80 mg./kg.) (Harthorne *et al.*, 1963).

Of the five deaths among these children, one patient (Case 1) who had ingested 192 mg./kg., was moribund within one hour and failed to respond to vigorous resuscitation. One (Case 18) died three days after ingestion, but no further details are recorded, while the timing of death from cardiac arrest in Case 17 is not reported. Cases 12 and 14 are noteworthy in that both had shown progressive clinical improvement, in terms of conscious level and circulatory status, before sudden collapse and death 12 and 60 hours respectively from the time of ingestion of the drug.

Treatment

On the wide variety of measures which have been used in the management of children or adults poisoned by tricyclic antidepressants, only a minority stand out as being both clinically effective and pharmacologically sound.

Active Therapy

Since there is often some delay in confirming the identity of the drug involved, gastric lavage should be carried out as soon as the child reaches hospital ; the general recommendations of Matthew *et al.* (1966) in relation to gastric lavage in adults are applicable also to paediatric practice. In Case 31 little over 2% of the estimated ingested dose was recovered from the stomach, but when the procedure is carried out very soon after ingestion recovery of some 15% may be achieved (Rasmussen, 1966). If the accident is detected within minutes, induction of vomiting by the parents or the general practitioner may be a useful measure, provided that transfer of the child to hospital is not thereby delayed.

Both peritoneal and extracorporeal dialysis have proved ineffective in the treatment of this type of poisoning (Sunshine and Yaffe, 1963 ; Harthorne *et al.*, 1963). Moreover, our own measurements confirm previous indications that renal excretion of the free drug is so low that forced diuresis is not indicated (Hucker and Porter, 1961 ; Sunshine and Baumler, 1963), though this procedure has been advocated by Prout *et al.* (1965) on the strength of a positive result from a sensitive screening test for the detection of imipramine metabolites in the urine (Forrest *et al.*, 1960). The pharmacological activity of such metabolites is, however, unknown, whereas the *N*-desmethyl derivatives of both imipramine and amitriptyline, which are known to be active, are firmly tissue-bound (Dingell *et al.*, 1964). Beighton and Hardingham (1966) recovered at most 10% of the ingested dose of amitriptyline from the urine of their patient, measurement again being based upon a relatively non-specific test.

Supportive Therapy

Both barbiturates and paraldehyde are effective for controlling convulsions in severe antidepressant poisoning, and the former in particular are recommended by Rasmussen (1965). However, the respiratory depression induced by barbiturates may be potentiated in this situation (Luby and Domino, 1961 ; Arneson, 1960 ; Garrison and Moffitt, 1962 ; Merck, Sharp and Dohme, 1963). This disadvantage does not seem to apply to paraldehyde ; for example, the most severely poisoned of the present series (Case 31), who had a respiratory minute volume of 2.2 litres by direct spirometry on admission—that is, 20% below the ideal basal level, on the criteria of Radford (1955) —required no oxygen or assisted ventilation after 5 ml. of intramuscular paraldehyde.

Circulatory collapse is potentially the most dangerous consequence of imipramine or amitriptyline poisoning. Cairncross and Gershon (1962) and Boissier *et al.* (1965) have shown, in animal experiments, that whereas the initial tachycardia is mediated by an atropine-like vagal blockade larger doses of either drug have direct toxic effects upon the myocardium and conducting tissue. This can result in profound hypotension and a variety of bizarre E.C.G. changes, including A-V block, multifocal extrasystoles, and ventricular tachycardia, together with broadening and distortion of the QRS complex. Corresponding E.C.G. patterns in poisoned children have been described and discussed by Giles (1963) and by Braun *et al.* (1965).

The two unconscious patients in the present series (Cases 26 and 31) developed neither severe hypotension nor any arrhythmia, and electrocardiograms were not recorded ; however, we may have overlooked prolonged ventricular tachycardia (Jacobziner and Raybin, 1963). E.C.G. monitoring should therefore form part of the management of all severely affected patients.

The findings by Cairncross and Gershon (1962) that these severe manifestations of toxicity can be precipitated by an increase in cardiac work load has three important practical implications: (1) That complete control of convulsions is imperative and that sedation and bed rest should be continued for as long as E.C.G. changes are liable to be detected—that is, for three days or more. (2) That the use of hypertensive agents is to be deprecated. In the presence of a healthy vasculature and parasympathetic blockade, vital organs are unlikely to suffer ischaemic damage until the systolic blood pressure has been well below 80 mm. Hg for several hours (Bloch *et al.*, 1966). (3) That large intravenous infusions are dangerous ; this constitutes a further argument against forced diuresis in the treatment of this type of poisoning.

The parasympathomimetic agent pyridostigmine has been shown, both experimentally and clinically, to be of some value in preventing or reversing the cardiotoxic actions of the tricyclic antidepressants (Rasmussen, 1965, 1966), and the same author recommends the use of propranolol for the control of arrhythmias arising in this situation. Cardiac failure in association with ventricular tachycardia was partially relieved by procainamide in Case 15 (Jacobziner and Raybin, 1963), but an analogue, xylocaine, has been shown to have less depressant effect on the myocardium (Harrison *et al.*, 1963) and has become the drug of choice for the suppression of arrhythmias after myocardial infarction (Lown *et al.*, 1967). The adult dose is 25–50 mg. intravenously, followed by continuous intravenous infusion of 1–2 mg./min.

Attempts to stimulate the myocardium with calcium (Somuncuoglu, 1960) or lanatoside C (Garrison and Moffitt, 1962) have not met with demonstrable success, and in the presence of A-V block with ventricular extrasystoles the use of cardiac glycosides would be contraindicated.

The possible influence of the phenothiazines which were alleged to have been taken in combination with imipramine or amitriptyline in Cases 26 and 31 cannot be assessed at present, but the value of phenothiazines in the management of tricyclic antidepressant poisoning warrants further study. There is a complex pharmacological relation between the two classes of compound (Klerman and Cole, 1965), and they have some toxic actions in common (Gordon and McCandless, 1959 ; Irwin and Burlew, 1959). Chlorpromazine has, however, been used in the management of psychotic behaviour occurring as a side-effect of imipramine therapy in adults (Boardman and Fullerton, 1959) and in the treatment of the syndrome associated with the simultaneous ingestion of imipramine and a monoamine oxidase inhibitor (Saunders, 1965). It proved effective in controlling the agitated behaviour in our patient (Case 31), but no superiority has been demonstrated over the paraldehyde or chloral used by others.

Conclusions

A scheme for the management of the severe case of imipramine or amitriptyline poisoning, as derived from the above discussion, may be summarized as follows:

(1) Gastric aspiration and lavage should be carried out as soon as the patient reaches hospital.

(2) Intramuscular paraldehyde should be given as soon as convulsive movements appear.

(3) The patient should be carefully observed, with E.C.G. monitoring, and nursed in surroundings as free as possible from extraneous stimuli.

(4) Oxygen and/or assisted ventilation should be provided as indicated by the clinical state and by blood-gas analysis.

(5) A slow intravenous drip of an isotonic solution, such as dextrose with half-strength Ringer's lactate, should be established.

(6) If arrhythmias or circulatory failure supervene, xylocaine and pyridostigmine (but not hypertensive agents) should be added to the drip.

(7) In the event of cardiac arrest there should be no hesitation in applying full resuscitative measures (see Case 16 of Fruthaler and Snyder, 1963).

(8) While consciousness is being regained, sedation in the form of chlorpromazine, chloral, or paraldehyde should be given.

(9) Relaxation of strict bed rest should be allowed only after a minimum of three days, provided that the E.C.G. is then normal.

Summary

Attention is drawn to the increasing incidence of poisoning due to the ingestion of imipramine and amitriptyline by young children. Twelve non-fatal cases are reported, and compared with 21 others in the literature, including five deaths.

Mildly affected children exhibit drowsiness—sometimes alternating with excitement—tachycardia, ataxia, and sometimes dilated pupils. In more severe cases convulsions and coma rapidly supervene. Arrhythmias and circulatory failure may occur and can prove fatal. These severe symptoms always appear when the ingested dose exceeds 20 mg./kg., though much smaller doses may suffice.

Early gastric lavage is indicated. Peritoneal or extracorporeal dialysis is ineffective and forced diuresis is contraindicated. Treatment of the severe case is symptomatic. Paraldehyde is preferred to barbiturates in controlling convulsions. Xylocaine and pyridostigmine may have a place in the management of arrhythmias, but hypertensive agents are contraindicated.

Careful observation should include E.C.G. monitoring. Sedation is required during recovery, and bed rest should continue for a minimum of three days.

We are grateful for the valuable help in the preparation of this paper given by Professor J. O. Forfar, Dr. Henry Matthew, and Professor L. G. Whitby. Drs. J. W. Farquhar, D. M. Douglas, W. M. McCrae, and H. Simpson offered constructive criticism and encouragement, and gave permission to report cases admitted under their care. Thanks are also due to the staff of the Poisoning Treatment Centre, Edinburgh Royal Infirmary, who co-operated in the management of Case 31; to Mrs. C. Palmer, Ministry of Health Statistician, who provided the data for the Chart; and to Dr. W. Kondradt for assistance with translations.

REFERENCES

Alajem, N., and Albagli, C. (1962). *Amer. J. Dis. Child.*, **103**, 702.
Arneson, G. A. (1961). *Amer. J. Psychiat.*, **117**, 934.
Beighton, P., and Hardingham, M. (1966). *Practitioner*, **197**, 354.
Bloch, J. H., Pierce, C. H., and Lillehei, R. C. (1966). *Ann. Rev. Med.*, **17**, 483.
Boardman, R. H., and Fullerton, A. G. (1959). *Lancet*, **2**, 467.
Boissier, J. R., Simon, P., and Witchitz, S. (1965). *Thérapie*, **20**, 67.
Braun, L., Brodehl, J., Fichsel, H., and Kallfelz, H. C. (1965). *Med. Klin.*, **60**, 1737.
Brown, S. S., Cameron, J. C., and Matthew, H. (1967). *Brit. med. J.*, **2**, 738.
Cairncross, K. D., and Gershon, S. (1962). *Med. J. Aust.*, **2**, 372.
Connelly, J. F., and Venables, A. W. (1961). Ibid., **1**, 108.
Dingell, J. V., Sulser, F., and Gillette, J. R. (1964). *J. Pharmacol. exp. Ther.*, **143**, 14.
Edwards, J. (1966). *Med. J. Aust.*, **1**, 839.
Fendrick, G. M. (1962). *New Engl. J. Med.*, **267**, 1031.
Forrest, I. S., Forrest, F. M., and Mason, H. S. (1960). *Amer. J. Psychiat.*, **116**, 840.
Fruthaler, G. J., and Snyder, C. H. (1962). *Pediat. Clin. N. Amer.*, **9**, 41.
Garrison, H. F., and Moffitt, E. M. (1962). *J. Amer. med. Ass.*, **179**, 456.
Giarman, N. J. (1965). In *Pharmacology in Medicine*, 3rd ed., edited by J. R. Di Palma, p. 365. New York.
Giles, H. McC. (1963). *Brit. med. J.*, **2**, 844.
Gordon, M., and McCandless, R. F. J. (1959). In *Handbook of Toxicology*, vol. 4, edited by R. M. Grebe, p. 14. Philadelphia.
Harrison, D. C., Sprouse, J. H., and Morrow, A. G. (1963). *Circulation*, **28**, 486.
Harthorne, J. W., Marcus, A. M., and Kaye, M. (1963). *New Engl. J. Med.*, **268**, 33.
Hucker, H. B., and Porter, C. C. (1961). *Fed. Proc.*, **20**, 172.
Irwin, S., and Burlew, R. W. (1959). In *Handbook of Toxicology*, vol. 4, edited by R. M. Grebe, p. 51. Philadelphia.
Jacobziner, H., and Raybin, H. W. (1963). *N.Y. St. J. Med.*, **63**, 1394.
Klerman, G. L., and Cole, J. O. (1965). *Pharmacol. Rev.*, **17**, 101.
Lown, B., Fakhro, A. M., Hood, W. B., and Thorn, G. W. (1967). *J. Amer. med. Ass.*, **199**, 188.
Luby, E. D., and Domino, E. (1961). Ibid., **177**, 68.
McBay, A. J., and Algeri, E. J. (1963). In *Progress in Chemical Toxicology*, vol. 1, edited by A. Stolman, p. 87. New York.
Matthew, H., Mackintosh, T. F., Tompsett, S. L., and Cameron, J. C. (1966). *Brit. med. J.*, **1**, 1333.
Mazur, E. (1963). *Pediat. pol.*, **38**, 845.
Merck Sharp and Dohme Ltd. (1963). Pharmaceutical Circular 231600, "Elavil."
Noack, C. H (1960). *Med. J. Aust.*, **2**, 182.
Prout, B. J., Young, J., and Goddard, P. (1965). *Brit. med. J.*, **1**, 972.
Radford, E. P. (1955). *J. appl. Physiol.*, **7**, 451.
Ragland, J. B., Kinross-Wright, V. J., and Ragland, R. S. (1965). *Analyt. Biochem.*, **12**, 60.
Rasmussen, J. (1965) *Lancet*, **2**, 850.
—— (1966). *Proceedings of International Conference of Poison Control Centres, Copenhagen*, p. 11.
Saunders, J. C. (1966). *J. Kans. med. Soc.*, **66**, 471.
Somuncuoglu, S. (1960). *Med. Welt. (Stuttg.)*, **2**, 2509.
Sunshine, I., and Baumler, J. (1963). *Nature (Lond.)*, **199**, 1103.
Sunshine, P., and Yaffe, S. J. (1963). *Amer. J. Dis. Child.*, **106**, 501.

ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Typhoid Immunization after Measles

Q.—*Is it safe to give T.A.B. or T.A.B.T. vaccine to a child aged 5 within five weeks of the onset of an attack of measles?*

A.—Clinical and immunological responses to T.A.B.T. vaccination are not affected by a previous attack of measles, provided the period between the onset of the rash and the time of vaccination is more than four weeks and the patient has clinically recovered from the measles and any complications.

Though immune responses, such as the tuberculin reaction, are temporarily depressed by measles the effect rarely persists for more than four weeks. The marked leucopenia of the prodromal period is even more transient. The leucocyte count returns to normal soon after the rash appears. There is no reason, therefore, why T.A.B.T. should not be administered in the case in question.

Ranges of Forced Expiratory Volume

Q.—*What is the normal range for the forced expiratory volume in one second (F.E.V$_1$.) in adults and in children?*

A.—The normal forced expired volume in adults depends upon the sex, age, and size of the subject. One of the largest series of normal values was measured in 468 normal men by Kory *et al.*,[1] and they produced a nomogram from which the *average* value for the F.E.V.$_1$ can be measured in relation to a subject's age and size. They found that the best measurement of size was height, which was more closely related to the F.E.V.$_1$ than weight or surface area.

In adults the F.E.V.$_1$ decreases by about 0.03 litres per year of age, so that the average F.E.V.$_1$ for a man of 170 cm. tall and aged 20 is about 4.1 litres, whereas in a man of the same height age 60 it is only 2.9 litres. Of course, from such regression relationships of F.E.V.$_1$ in relation to age and size only the average expected value is obtained, but there is a scatter of values about this average depending on the standard deviation. The latter for the adult F.E.V.$_1$ is about 0.5 litre in men and 0.4 litre in women. That means that for a given age and height 95% of normal subjects will have an F.E.V.$_1$ within a range of about half a litre plus or minus of the expected average for that height and age. For example, 95% of women aged 40 and 160 cm. tall would be expected to have an F.E.V.$_1$ of between 2 litres and 3 litres, since the expected average for that age and height in women is 2.5 litres.

There is a good discussion of all this problem of normal values in Cotes's book on lung function.[2] It contains regression graphs for men and for women from which the average F.E.V.$_1$ for a given age and height can be seen and to which average the scatter, expressed as plus and minus standard deviation, can be added.

In children the same principles for obtaining the normal range apply, though here the F.E.V.$_1$ increases with age, since age is itself directly related to an increase in size. Age is a relatively poor standard for comparison of children, since children of the same age often differ in size. It is usual to get the average normal value for boys and for girls only for their height, and to add and subtract the standard deviation from this average to get the normal range. Strang,[3] Cherniack,[4] Murray *et al.*,[5] and Bjure[6] have all reported normal values for children, and Cotes's book again gives graphs for boys and for girls from which normal values can be read. Four graphs (for men, women, boys, and girls) should be used to read the range of normal values for both sexes and all ages. Of course, different graphs would be needed for different races, such as negro subjects as opposed to Caucasian stock.

REFERENCES

[1] Kory, R. C., Callahan, R., Boren, H. G., and Syner, J. C., *Amer. J. Med.*, 1961, 30, 243.
[2] Cotes, J. E., *Lung Function*, 1965. Oxford.
[3] Strang, L. B., *Thorax*, 1959, 14, 305.
[4] Cherniack, R. M., *Canad. med. Ass. J.*, 1962, 87, 80.
[5] Murray, A. B., Cook, C. D., Shaw, J. H., and Shahidi, M. A., *J. Pediat.*, 1963, 62, 186.
[6] Bjure, J., *Acta paediat. (Uppsala)*, 1963, 52, 232.

Predicting Height

Q.—*At what age is a child supposed to be half his eventual adult height, and how accurate is the prediction?*

A.—Children who are growing at the average rate reach half their eventual adult height at 2.25 years if a boy or at 1.6 years if a girl. The normal limits are wide, however, and half adult height could be reached anywhere between 1.5 to 3 years in boys and 1.25 to 2.25 years in girls. The prediction of adult height from length at these early ages is not good, the correlation being of the order 0.7.

Exercise and Blood Calcium

Q.—*Does exercise have any effect on blood calcium and the triglyceride levels?*

A.—Most commonly employed methods measure the total plasma calcium. This level is influenced by meals, so that only fasting levels are valid if comparisons are to be made. Furthermore, it has been shown there is both a day-to-day and a seasonal variation in a given individual which may amount to 0.6–1.4 mg./100 ml.[1] The second factor to be considered is that calcium exists in three states in the blood—as free ions, bound to protein, and a small amount complexed to organic acids. It is possible for variations to occur within these fractions without the change being reflected in the total calcium level.

The plasma calcium accounts for a small proportion of the calcium in the body and a dynamic equilibrium exists between the various compartments, notably the blood and the main reservoir in the skeleton, so that any change in plasma calcium in response to exercise is likely to be short-lived. Isotope studies using Ca-47 have demonstrated that exercise produces an increased calcium turnover.[2] Excretion of calcium is reduced during moderate exercise,[3] and brief but severe exercise produces a temporary rise in total blood calcium.[4]

This was also shown by Radcliff *et al.*,[5] who studied the effect of venous stasis and venous stasis accompanied by exercise of the forearm muscles, and were able to demonstrate statistically that both the exercise and stasis could produce an increase in the plasma calcium level. Clearly, all specimens examined for calcium levels should be drawn from fasting patients, preferably without the application of a venous tourniquet and clenching of the fist to promote filling of the veins.

The plasma triglyceride level is also markedly affected by food intake, and any change in response to exercise must be considered in relation to the fasting level. After a meal containing fat the plasma triglyceride level rises, reaching a maximum after about four hours and reverting to fasting levels in about six hours. Exercise—for example, a route march—results in a four-hour level little different from the fasting level, and the six-hour level may be lower than the fasting level.[6 7] If short-term exercise is carried out in fasting subjects there is a fall to below the initial triglyceride level.[8] In a more prolonged study in middle-aged men Holloszy *et al.*[9] showed that six months of physical conditioning produced a significant reduction in mean fasting triglyceride levels.

REFERENCES

[1] Gronemeyer, W., and Künzel, K. E., *Dtsch. Arch. klin. Med.*, 1950, 196, 585.
[2] Ragan, C., and Briscoe, A. M., *J. clin. Endocr.*, 1964, 24, 385.
[3] Heaton, F. W., and Hodgkinson, A., *Clin. chim. Acta*, 1963, 8, 246.
[4] Lanne, R. de, Barnes, J. R., and Brouha, L., *J. appl. Physiol.*, 1959, 14, 804.
[5] Radcliff F. J., Baume, P. E., and Jones, W. O., *Lancet*, 1962, 2, 1249.
[6] Nikkila, E. A., and Konttinen, A., ibid., 1962, 1, 1151.
[7] Konttinen, A., and Somer, T., *J. appl. Physiol.*, 1963, 18, 991.
[8] Wood, P., Schlierf, G., and Kinsell, L., *Metabolism*, 1965, 14, 1095.
[9] Holloszy, J. O., Skinner, J. S., Toro, G., and Cureton, T. K., *Amer. J. Cardiol.*, 1964, 14, 753.

Notes and Comments

Pain in the Back.—Dr. J. MARKS (Cardiff) writes: Your expert ("Any Questions?" 22 July, p. 223) neglects the fact that we spend a third of our lives in bed. My wife's disabling backache of some years' duration vanished at once on our changing an ordinary bed for an "orthopaedic" model sold commercially. A much milder backache which I had disappeared similarly. The discarded bed seemed to be in quite reasonable condition.

OUR EXPERT replies: It is true that a large proportion of patients with backache are made worse by sleeping on an unsuitable type of bed. The orthopaedic model, however, is expensive, and much the same effect can be obtained by sleeping on fracture boards placed between the mattress and the base. I am, nevertheless, grateful to Dr. Marks for reminding me of this important point.

Book Reviews

Environment and Ophthalmology

Culture, Race, Climate, and Eye Disease. By Ida Mann, C.B.E., M.A.Oxon, D.Sc., M.B., B.S.Lond., F.R.C.S.Eng., F.R.A.C.S. (Pp. 580+xi; illustrated. $21.00.) Springfield, Illinois: Charles C. Thomas. 1966.

In our thoughtful moments we all recognize that half the human population is subsisting on a starvation diet, but it rarely crosses our minds that probably a similar proportion is diseased and we prefer not to think of the morbidity which this entails. In *Culture, Race, Climate and Eye Disease* data on this subject have been collected by several methods: from official hospital records, from certificates of blind registers, from the ophthalmic scientific literature, and from the relatively few planned surveys which comprise the only method likely to give dependable results. The collected facts provoke the author to state in her early chapter on General Considerations, "It will be seen soon how little we really know."

Nevertheless, new ground has been broken in this volume by inspecting ophthalmology from a vantage point which is astronautical in its width of horizon. Essentially a primer because our knowledge is so patchy and incomplete, it nevertheless lays bare a challenge of enormous complexity and size to medical men and modern methods. Some of the questions which may find an answer from such studies are the relationship of heredity and environment in disease, the effects of diet, climate, and culture on disease, and the correlation of ophthalmic disease with microbiological inhabitants of the same area.

This study opens with chapters on the more remote and primitive cultures. The first 100 pages are concerned with islands mainly in the Southern Hemisphere. From these the author passes to the Arctic, to Africa, to Mongolia, to the Indian Peninsula, and approaches the Western World via the Middle East. 160 pages are given over to the complex Western culture, which is rapidly threatening to engulf all others. The final chapter discusses world distribution of certain eye diseases. There is a workable index, and references to the literature are given at the end of each chapter.

There are so many facts in this volume on the incidence of ocular syndromes that it is quite impossible to condense them or even understand their significance at times. As an example it is pointed out that blindness from glaucoma measured in percentage of blind persons ranges from 52 in Iceland to 0.8 in Australia. What does this mean? Nevertheless, the overall message is that blindness from infection and malnutrition is characteristic of the under-privileged section of the human race whereas the dangers of our own progressively richer culture are essentially industrial, genetic, iatrogenic, and geriatric.

STEPHEN MILLER.

Neurology Today

Modern Trends in Neurology, 4. Edited by Denis Williams, C.B.E., M.D., D.Sc., F.R.C.P. (Pp. 293+ix; illustrated. 75s.) London: Butterworth. 1967.

This is the fourth successive volume in the series and the third to appear under the editorship of Dr. Denis Williams. Its predecessors have kept neurologists up to date in scientific and clinical research relevant to their study of human nervous disease, and they have also provided a bird's-eye view of the current neurological landscape for less specialized physicians. Their continuing usefulness as sources of reference has been ensured by the inclusion of authoritative reviews on headache, arachnoiditis, intracranial aneurysm, internal carotid artery occlusion, and polyneuropathy, to mention only a few.

Judged by such standards the reviewer must confess that his first reaction to the present book is one of slight disappointment, and even some suspicion that it might be cited in support of the view occasionally expressed by the neurologist's colleagues in internal medicine that his subject makes an unimpressive showing in the matter of clinical research. Such an assessment of the book would be hardly fair. Dr. Williams is surely right to refresh each new edition with contributions from younger and less established workers in the field, and the comprehensive coverage accorded to some current clinical problems in previous editions, precludes their further presentation without risking considerable repetition.

Nevertheless some sense of regret remains that there is little here to make neurology exciting to the general physician and a good deal that is of limited interest even to the clinical neurologist. The key to this situation lies in the editor's preface, which stresses the contribution of both clinical and experimental neurology to our study of "the integrative function of the brain," the elucidation of normal behaviour, and the clarification of the boundaries between physical structure and psychological activity. This may indeed "anticipate the needs of sophisticated, busy neurologists." On the other hand, it expresses a traditional British view of clinical neurology as a handmaiden of neurophysiology, according to which the patient's illness is interesting mainly for the light it throws on normal function. This is in striking contrast to the modern American neurologist's preoccupation with the epidemiology, aetiology, experimental pathology, and even (save the mark!) the treatment of nervous diseases. It is significant that twelve of Dr. Williams's sixteen contributors work in the metropolis, nearly all in the shadow of Queen Square. More closely integrated with general medicine, British neurology outside London leans towards the more clinical and pragmatic American viewpoint.

For the unsophisticated clinician the book gets off to a heavy start with twenty pages on the ventral tier thalamic nuclei by M. B. Carpenter and thirty-three of scrupulous anatomical observations on lesions produced by stereotactic surgery (Marion Smith), followed by an account of the motor neurone surface as the basis of an interesting theory on the nature of spinal shock (L. S. Illis). In the third chapter A. M. Halliday elaborates his previous studies of myoclonus in an exhaustive review which will be a useful source of reference. This is followed by Malcolm Piercy on the neurological basis of intellectual function, D. A. Pond on the brain-damaged child, Macdonald Critchley on developmental dyslexia, and W. I. McDonald on experimental neuropathy. Dr. J. B. Cook discusses the prognosis of spinal injury, and his chapter is followed by three on various aspects of cerebrovascular disease, one on angiography and a brief account of H. E. Webb's views on the significance of immune reactions in viral infections. Marcia Wilkinson discusses the neurological implications of all the unpleasant things that can happen to the cervical spine, and the editor closes with some observations on the management of myasthenia gravis, which is a reflective rather than a practical guide to procedure—though he comes down heavily in favour of early thymectomy. The chapters on the pathology and surgical treatment of cerebrovascular disease add little to what has already been written: the surgical author regrets the absence of controlled evaluation of carotid surgery but states that it is "very effective" in the treatment of intermittent ischaemic attacks. Wilkinson's chapter on the cervical spine is a useful catalogue, and the section on angiography is also in the nature of a textbook account.

Judgement on the relative merits of the various contributions is bound to depend on personal interests, and the reviewer's pleasure in Cook's account of the socio-economic implications of the aftermath of spinal injuries and Spalding's excellent description of the neglected field of circulatory disorders due to neurological disease reflects his relief that there are still neurologists who can lift their eyes from the neurone. "*Modern Trends 4*" will be bought, read, and discussed by all who are interested in neurology. General physicians who can overcome their feelings of unworthiness that they are not more excited by its first seventy pages will also find many pearls concealed in its text.

HENRY MILLER.

Emphysema Described

The Pathology of Emphysema. By Lynne Reid, F.R.A.C.P., M.R.C.P., F.C.Path. (Pp. 372+ix; illustrated. 70s.) London: Lloyd-Luke. 1967.

It is easy to think one knows about emphysema until one starts thinking and reading about it. The inquirer then finds himself groping in semidarkness through a confusion of terminology, conflicting pathology, confident but contradictory clinical observations, and sparse but exotic experimental work, the whole experience having the qualities of a Danteesque nightmare, from which one hopes to wake and find after all it just isn't true. Indeed, a lot of it probably isn't. Dante, when making his well-publicized descent, took the precaution of engaging as his guide the sage Virgil, who conducted him with remarkable sang-froid around the infernal circles.

The explorer of the no less formidable abyss of emphysema would be well advised to retain Dr. Lynne Reid as dragoman. She pursues a calm and systematic course, coolly recounting the relevant, making reasonable inferences when they are justified, and giving ignorance its due when evidence is insufficient. Much of the work is her own, or that of her immediate colleagues, but she refers to that of many others, and there is an excellent bibliography.

It is right that a study of emphysema, which has to be defined in pathological terms, should start from pathology, but there is very much more than pathology in this book. Dr. Reid has much to say on radiology, which, with Dr. George Simon, she has correlated with pathological findings. There is also a good deal on the clinical and functional manifestations of emphysema. Many of the points are illustrated with relevant case histories. The classification of emphysema, however provisional, seems to make sense and to be a reasonable basis on which to found further work. There is a good section on the pathology of chronic bronchitis, in the study of which the author has been a pioneer, and a useful appendix on the normal anatomy of the lung. The diagrams and illustrations are excellent.

No doubt experts in the field will find one thing or another in this book with which to disagree, but most of us must indeed be grateful for an intelligent and intelligible approach to a difficult and confusing subject.

JOHN CROFTON.

Care of the Cleft Palate

Treatment of Patients with Clefts of Lip, Alveolus and Palate. Symposium, Hamburg, 1964. Edited by Karl Schuchardt. (Pp. 237; illustrated. 84 DM.) Stuttgart: Georg Thieme. 1966.

This volume reports verbatim the second symposium held in Hamburg on the treatment of patients with clefts of lip, alveolus, and palate. Fourteen of those taking part were also contributors to the first symposium ten years earlier. Topics for discussion were introduced by invited speakers, after which three-minute contributions were made by any delegate who wished; in this way it was hoped to avoid set papers which would have been of little value to an expert audience well versed in the principles of the subject matter and to promote instead well-informed discussion of controversial issues. The topics chosen were broadly grouped into three categories: the primary treatment of patients with clefts, the disorders of growth and function after primary operations and their treatment, and documentation.

In the first category topics included the incidence and aetiology of clefts, their morphology, early orthodontic care, and logopedic problems as well as modern surgical procedures. The second category was mainly concerned with secondary corrective procedures and with the disorders of growth which made these necessary. Broadly planned the topics included dental, orthodontic, and E.N.T. aspects, besides considering the surgical contribution to the alleviation of speech defects. The third category produced two valuable discussions on documentation in which R. B. Stark (New York) gave an introductory survey of an embryological basis for a new classification of cleft lip and palate and G. Pfeifer (Hamburg) described the system of documentation worked out for use in Schuchardt's clinic. Contributions by P. Fogh-Andersen (Denmark), B. Vilar-Sancho (Spain), J. Converse (New York), and T. R. Broadbent (Salt Lake City) indicated the need and desire for the establishment of an internationally acceptable classification born of uniform documentation.

This is not a beginner's book. It is a study in depth of the most difficult problems of this most difficult subject; and it succeeds. It is for the surgeon who is intimately concerned with these problems and responsible for the day-to-day care of these deformed children. The reader can enjoy the considered opinions of acknowledged experts both in invited comment and in free discussion, testing his own beliefs and practice against the verbatim reports of their views. In this way it brings him into the discussions as he reads, and offers him the opportunity to modify his own ideas or the justification to continue as before as his judgement dictates. Professor Schuchardt is to be congratulated on convening this symposium, on the scope of its work, and on the method of presentation of the outcome. It is to be hoped that in due time a third similar symposium will be held and that it will be reported in a volume as well set out and illustrated as the present one by Thieme Verlag.

DAVID MATTHEWS.

Biological Control at Many Levels

Regulation and Control in Living Systems. Edited by H. Kalmus. (Pp. 468+viii; illustrated. 90s.) London: John Wiley. 1967.

Dr. Kalmus is reader in biology at University College, London, and his book consists of 16 sections, three of which he has written himself, and one in collaboration, while the other 12 sections are by eleven other authors, a number of them being colleagues at University College. Apart from an introduction and a conclusion the sections are grouped under the three main heads of "Cells and Individuals," "Development and Genetics," and "Groups and Populations."

Under the first head are five papers. "Molecular regulation in the cell," by the botanist D. Lewis, gives a condensed account of how enzyme synthesis may be controlled by special genes called operators and regulators. It was work in this field for which Jacob and Monod were recently awarded a Nobel prize. This account of it, however, is difficult for beginners. "Physiological control systems," by Kalmus and B. R. Wilkins, describes some applications of engineering ideas to human eye movements, to temperature regulation, and to invertebrate eye function and orientation. D. B. Fry reviews "the control of speech and voice," G. Kalmus in "circadian regulation and related responses" gives a very brief account of some diurnal rhythms, and K. Brown-Grant gives a very detailed review of experiments demonstrating the hypothalamic-anterior pituitary control of thyroid, adrenal cortex, and ovary in "regulation and control in the endocrine system."

Under the second head we find an essay by J. S. Wilkie describing eighteenth century work on regeneration in polyps and worms, and brief and all too short accounts of "regulation of plant growth," by P. R. Bell, and "regulation in animal development," bv D. R. Newth. Under the third there is an interesting account by J. B. Free of the self-regulation of the honey bee population in a hive, and the indication by V. C. Wynne-Edwards that animal populations practice birth-limitation, and that very primitive man did likewise, so that modern man is somewhat out of step in his conflict over birth control.

All life being the antithesis of chaos must involve many kinds of control, and the present reviewer is not convinced that the bringing together inside one book of scattered examples of control at all levels of complexity from all over biology is intellectually useful. It certainly makes for cramped pedestrian writing and difficult reading. The value of the book lies in the usefulness of one or two of its review articles.

J. L. CRAMMER.

Forms and Patterns of Childhood Illness

The Psychiatric Disorders of Childhood. By Charles R. Shaw, M.D. (Pp. 442+ix. $11.50.) New York: Appleton-Century Crofts. 1966.

So few books are published on child psychiatry that the appearance of a new one is likely to arouse keen interest, which in this case may be blunted for many by a glance at the table of contents, which does not appear to follow any recognizable system. After opening chapters on heredity, experience, case finding, and diagnosis, the real substance of the book is in the third section on "specific disorders." It is completed by brief sections on treatment and perspective. Thus it is clear that the book is primarily concerned with forms and patterns of illness and not with the living child.

Although much of the writing is illuminated with warmth and humour, Dr. Shaw appears to mistake order and method for science in his very cut-and-dried presentation. For example, he sets out 139 itemized reasons for referral among 500 consecutive patients at the Hawthorn Center, and names 36 functions of the ego. But to give a list of 28 types of "behavior functions affected by heredity," without differentiation between the evidence taken from observations of caged animals, free domesticated animals, wild animals, and human beings, is to act very unscientifically indeed.

The children are presented in static poses to illustrate some "specific disorder" or other. There is no movement, no development, no family life. Claiming that history is unimportant in child psychiatry—"the clinical examination is everything"—Dr. Shaw is consistent when he is prepared to diagnose brain damage in the absence of any history of damaging circumstances; but inconsistent in not also requiring the presence of clinical signs of damage. All that he requires is that the child's behaviour should resemble that of children "in proven cases of brain damage such as post-encephalitic . . . or known severe cerebral anoxia at birth." But he does not indicate how the damage can be "proved" when the children first have to live long enough after their disaster to serve as behaviour models before their brains can become available for histological examination. Where change and development are unrecognized, diagnosis, in Dr. Shaw's own words, may become a "vexing" problem, for whenever the child comes up "with a new symptom-complex . . . he has to be picked out of one pigeon-hole and put into another."

Where there is no individual or family history, social and cultural problems may appear no less confusing. The first essential is to do full justice to the fact that children are growing and developing and live in families. Before this book can contribute something new to thought and practice in the modern field of child psychiatry such factors have to be taken into account.

KENNETH SODDY.

Glasgow History

The Victoria Infirmary of Glasgow. History of a Voluntary Hospital. 1890–1948. By Ian Murray. (Pp. 89; illustrated.) Obtainable from the Board of Management for Glasgow Victoria Hospitals, 24 St. Vincent Place, Glasgow C.1. 1967.

A just tribute is paid to the Glasgow Southern Medical Society by the author of this attractive little book, for he states that "it was due to their continued advocacy that the Victoria Infirmary in large measure owes its inception." The infirmary was opened in 1890 with 84 beds, but it was soon extended, and the stages of its growth are carefully and chronologically recorded in the first ten pages of the book. In 1948 it was handed over to State control as a fine, well-equipped, well-staffed hospital of 500 beds together with Philipshill Auxiliary Hospital.

The main part of the book consists of brief biographies of the chief physicians, surgeons, and specialists who served the infirmary during the period of its existence as a voluntary hospital. Many of the earlier members of the staff had experience as general practitioners before they became consultants. Among the early surgeons Maylard is perhaps the best known as a pioneer in abdominal surgery. Of the specialists at least two gained international reputations—Brown Kelly in laryngology and Albert Alexander Gray in otology. The first pathologist was Thomas Kirkpatrick Monro, who later became regius professor in the university; the author mentions his *Manual of Medicine* but omits to tell of his later well-known compilation *The Physician as a Man of Letters.* The best-known physician attached to the infirmary was that brilliant writer O. H. Mavor, better known as James Bridie. He was a good physician but as a dramatist he won world renown. Dame Louise McIlroy was a Glasgow graduate and was at one time on the staff of the Victoria Infirmary. The present gynaecologist, Sir Hector MacLennan, as the author says, "has brought much lustre to the Victoria."

The last five pages are devoted to an account of the various architects who helped to plan and construct the infirmary—a well-deserved but often overlooked tribute.

ZACHARY COPE.

Introduction to the Operating Theatre

Demonstrations of Operative Surgery. 3rd edition. By Hamilton Bailey, F.R.C.S., F.A.C.S., F.R.S.E. Revised by A. R. Isaac, F.R.C.S.(Ed.). (Pp. 431 + xii; illustrated. 50s.) Edinburgh and London: E. & S. Livingstone. 1967.

This edition, like the previous ones, is described as "a manual for general practitioners, medical students, and nurses," and it retains the original format. The first section is concerned with general principles of operating theatre technique, the second with endoscopic procedures, and the remaining ten sections with accounts of most of the common surgical operations. These last are arranged regionally and are written in the form of demonstrations in the first person. They are all short and clear, and are accompanied by helpful lucid illustrations.

Operative surgery, however, cannot be considered in isolation, and further editions would benefit enormously from a discussion of the role of anaesthesia, blood-transfusion, preoperative and post-operative care, and of the complications which might be encountered during and after operation. Admittedly some of these aspects are mentioned in passing, but in general they are not given the prominence which they deserve.

However, within the strict terms of the title, this book could hardly be bettered for those to whom it is directed, and nurses undergoing theatre training will find it particularly helpful.

R. B. WELBOURN.

Books Received

Review is not precluded by notice here of books recently received.

Doctor Sahib. By Stephen Kerry. (Pp. 204. 30s.) London: Cassell. 1967.

Laboratory Outline in Physiology. 2nd edition. By the Staff of the Department of Physiology, University of Toronto. Edited by R. E. Haist and L. W. Organ. (Pp. 81+iii; illustrated. 48s.) Toronto: University Press. London: Oxford University Press. 1967.

The Development of Modern Surgery. By Frederick F. Cartwright. (Pp. 323+x; illustrated. 50s.) London: Arthur Barker. 1967.

New Aspects of the Mental Health Services. Edited by Hugh Freeman and James Farndale. (Pp. 776+xvi. £9 9s.) Oxford: Pergamon. 1967.

Lecture Notes on Endocrinology. By Ronald F. Fletcher, B.Sc., M.D., M.R.C.P. (Pp. 277 +viii. 25s.) Oxford and Edinburgh: Blackwell. 1967.

Bacteriology and Immunity for Nurses. 2nd edition. By Ronald Hare, M.D. (Pp. 201+ix; illustrated. 21s.) London: Longmans. 1967.

Gray's Anatomy. Descriptive and Applied. 34th edition. Edited by D. V. Davies, D.Sc. (Lond.), M.A.(Cantab.), M.B., B.S., F.R.C.S. With the assistance of R. E. Coupland, M.D., Ph.D., F.R.S.E. (Pp. 1669+xv; illustrated. £8.) London: Longmans. 1967.

Great Ideas in the History of Surgery. 2nd edition. By Leo M. Zimmerman, M.D., and Ilza Veith, M.A., Ph.D. (Pp. 587+xii; illustrated. 24s.) London: Constable. 1967.

Diabetes Mellitus. Lehrbuch für Ärzte und Studierende. 2nd edition. By Professor Konrad Seige. (Pp. 245+xii. £3 0s. 9d.) Leipzig: Georg Thieme. 1967.

Proceedings of the Second International Congress on Hormonal Steroids. Edited by L. Martini, F. Fraschini, and M. Motta. (Pp. 1172+xv; illustrated. $57.00.) Amsterdam: Excerpta Medica. 1967.

The Year Book of Neurology, Psychiatry and Neurosurgery. 1966–1967. Edited by Roland P. MacKay, M.D., Sam Bernard Wortis, M.D., and Oscar Sugar, M.D. (Pp. 757; illustrated. 83s.) London: Lloyd-Luke. 1967.

Hormone Chemistry. By W. R. Butt. (Pp. 397 +xiv; illustrated. 75s.) London: D. Van Nostrand. 1967.

Animal Toxins. Collection of papers presented at the First International Symposium on Animal Toxins, New Jersey, 1966. Edited by Findlay E. Russell and Paul R. Saunders. (Pp. 428+ xiii; illustrated. £6.) Oxford: Pergamon. 1967.

Strontium Metabolism. Proceedings of the International Symposium held at Chapelcross, Glasgow, and Strontian, 1966. Edited by J. M. A. Lenihan, J. F. Loutit, and J. H. Martin. (Pp. 354+xiii. 84s.) London: Academic Press. 1967.

Methods and Achievements in Experimental Pathology. Vol. 2. Investigative Techniques. Edited by E. Bajusz and G. Jasmin. (Pp. 289; illustrated. sFr./DM. 58.) Basel and New York: S. Karger. 1967.

Diagnostica Pneumoradiografica in Medicina Interna. By Luigi Lacrois. (Pp. 350; illustrated. No price given.) Rome: Il Pensiero Scientifico. 1967.

Mental Disorder. A Problem with many Facets. By Man Mohan Singh, M.B., B.S., D.P.M. (Pp. 378. 7s. 6d.) London: Pan. 1967.

Psychiatric Disorders in Obstetrics. By A. A. Baker, M.D., D.P.M. (Pp. 140+viii. 27s. 6d.) Oxford: Blackwell. 1967.

Middle Articles

GENERAL PRACTICE OBSERVED

Hythe Medical Centre—an Appraisal

G. H. WARRICK, M.A., M.R.C.S., L.R.C.P., D.C.H.

Brit. med. J., 1967, **3**, 672–674

The Hythe Medical Centre has been working for two years—too short a time for full assessment. I feel, however, that interest in the health centre concept has developed so rapidly that objective criticism can now be useful. The opinions expressed are my own, and I hope will lead to further discussion and perhaps a truer picture. The centre was described when it was opened (*B.M.J.*, 3 July 1965, p. 42), and not long afterwards your Special Correspondent (*B.M.J.*, 11 December 1965, p. 1425) recorded comparative attitudes to the centre and our group practice centre at Blackfield.

The Centre

The centre is attached to Hythe General Practitioner Hospital and provides accommodation for three general-practitioner firms, visiting consultants, and local authority services, including a school dental unit, child psychiatric clinics, and speech and audiometry clinics. It contains a new casualty department, a small *x*-ray unit, and facilities for electrocardiography. The pathology room is available mainly for consultative advice, for specimen collection, and as a depot. The name "medical" rather than "health" centre seemed to describe its function more aptly. The hospital has 22 beds—11 maternity and 11 general—and a physiotherapy department. The reception and office are managed by an administrative officer appointed by both county and hospital boards, with a staff of 11 part-time secretaries. The records include those of the N.H.S., the consultant sessions, and the school medical service. Health visitors and district nurse-midwives are attached to practices and work from the centre.

History.—Hythe lies between Southampton Water and the New Forest. Southampton is 11 miles (18 km.) away by road. Between Hythe and Fawley is an industrial belt which includes the Fawley Refinery. In 1959 the three larger practices in the area were beginning to think of increasing their surgery accommodation because of the steady rise in the population. As a group of doctors we knew each other well. We shared a general practitioner hospital and had founded our own medical society. Some of us had already sought special help from the county medical officer, who had allowed health visitors to assist in running our baby clinics. It was he who approached us to seek advice in siting a proposed welfare clinic, and then entered with enthusiasm into our common interest in the possibility of a comprehensive health centre. Although Hythe Hospital was already listed for closure under the hospital plan, we insisted that the centre must, so far as was possible, be combined with it. A desire for more accommodation and better diagnostic facilities had broadened to include an ambitious scheme to lower the barriers within the tripartite health service in our part of the country.

Planning.—This seemed incredibly difficult. Our main difficulties were that agreement in policy lagged behind design. Considerable time could have been saved if we had decided on the basic design of surgery accommodation and the various sections of the building before the building itself was discussed. Planning of centres will now be easier with access to existing centre designs. The most depressing delay occurred because ministerial study of the plans took more than 10 months. A great improvement should now accrue from the formation of a ministerial department with special knowledge of health centres. Expert criticism should help to remove faults in design and may even speed building. In retrospect I regret our too ready acceptance of parts of the building which did not then seem to be our direct concern. In fact, every aspect of work in a health centre is in some way important. I am sure, too, that where costs have to be reduced the plans should be discussed by the doctors themselves. We could have suggested several items that might have been omitted without detriment. The most notable feature of planning was a committee representative of all three branches of the Health Service in the area.

The Building

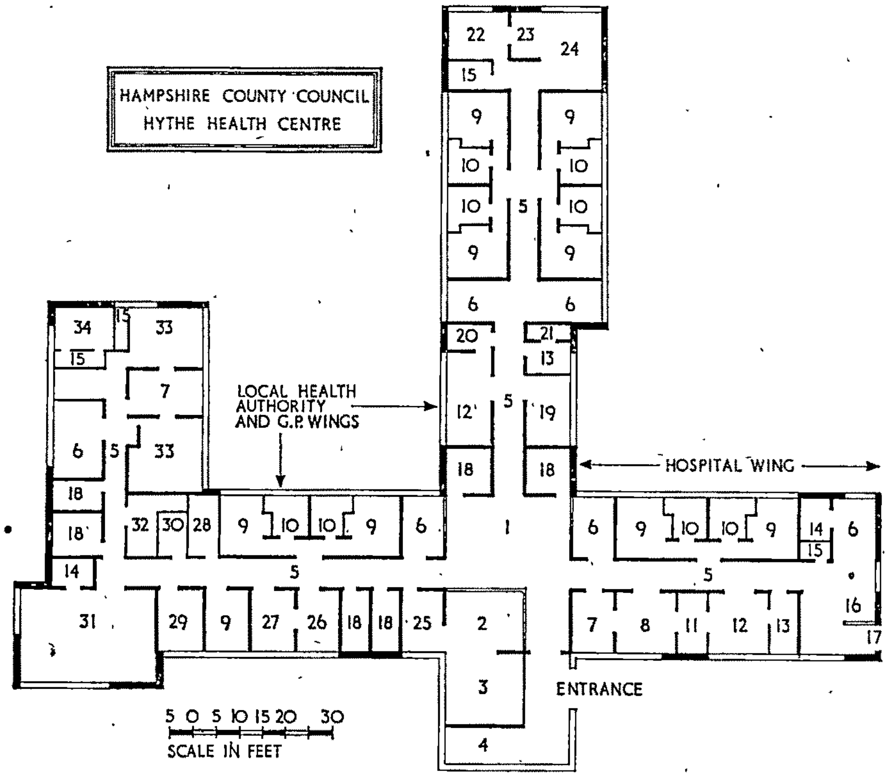
The building is attractive, bright, and pleasant to work in. The three main wings meet at the reception and office area and the main entrance. In criticizing lay-out and shape, I think points may be made in favour of a design based on a "circulation diagram," avoiding the necessity of everyone tending to meet at one point. The single-storey building saves building costs but increases the spread and the distance to be walked. The tile floor covering is attractive and wears well, but I would now be in favour of carpet over concrete, with a lessening of noise.

Each general-practitioner suite comprises two consulting-rooms with two intervening examination rooms. This arrangement is ideal for antenatal and baby clinics, for a midwife or health visitor can then use the second consulting-room. I miss a secretary/nurse close at hand, and a great improvement would be a small practice office for her, with space for the health visitor. Our real failure was in the design of the office and reception area. Doctors' secretaries need more privacy and space, and problems arise from the grouping of several telephones in a constricted area. Our open counter with adjacent office space is about to be screened and secretaries will be given more room. If there is a central office the practice suites must be next door. Two of ours are much too far away.

Adjacent to the centre is an ambulance station, which ensures speedy transfer of patients from the maternity unit or casualty department to the major Southampton hospitals.

Administration

One of the major advantages to the patient is the availability of his or her own doctor, consultant, health visitor, and district nurse-midwife, and diagnostic services under one roof. Appointments can usually be arranged with great ease at the same counter. The charge that in health centres a patient is less able to see his own doctor is unfounded. Where real difficulty does arise is in the impossibility of several secretaries, often interchanging duties, knowing one's practice and the idiosyncrasies of the patients as did the doctor's wife or practice secretary. So far as possible one secretary for each practice copes with the visiting-list, repeat prescriptions, and practice business during the morning surgery. One secretary arranges appointments for the three practices. In my view the real problem in health centres is the maintenance of family practice in which the doctor is not too "distant" and the secretary is able to allay the anxieties of the patient. I think a nursing or paramedical training will become increasingly necessary for a secretary. After all, it is she who decides on priorities.



1. Entrance hall.
2. Reception.
3. Card index.
4. Pram shelter.
5. Corridor.
6. Waiting.
7. Recovery room.
8. Minor operations.
9. Consulting room.
10. Examination.
11. Sluice.
12. Treatment.
13. Nurse.
14. Cloaks.
15. Store.
16. Trolleys.
17. Link to hospital.
18. Toilet.
19. Laboratory and store.
20. Anteroom.
21. Urine test.
22. Health visitor.
23. Kitchenette.
24. Staff common room.
25. Office.
26. Playroom.
27. Interview.
28. Records.
29. L.H.A. medical room.
30. Dark room.
31. Lecture hall.
32. Caretaker and meter room.
33. Dental surgery.
34. Red Cross store.

General Practice in a Health Centre

How has our work altered ? Can we give our patients a a better service ? I find the environment good for medicine and the ease of consultation with specialist and colleagues an advantage. The greatest advance, perhaps, is in the growing use of the medical team as a unit in general practice—the family doctor, the health visitor, and the district nurse-midwife. I am now more conscious of being a personal doctor than before. Can you really be one with an N.H.S. list of two to three thousand and no help ? Close proximity to the hospital ensures that the doctor is quickly available to the labour ward or casualty department. Antenatal clinics can cover both hospital and district cases with help from both hospital midwife and district nurse-midwife. The health visitor broadens the work of the practice and shares its burden.

The casualty department and practice treatment room will soon be combined, with a resultant saving of nursing time. District midwives can deliver short-stay cases in hospital. Perhaps midwives will one day go out from the hospital and work in the district. A mental welfare officer works from the centre. His help to our patients and to ourselves is of great value. A common room is available to everyone. Here one may meet the children's officer, the probation officer, or the parish priest.

In the Hythe area each school has a general-practitioner medical officer. We usually work with a health visitor from another practice, and thus between us know two-thirds of the children seen.

An Integrated Medical Service

At Blackfield, 5 miles (8 km.) away, we have a group practice centre to look after the other half of two of the practices. An automatic exchange links the two centres. A group practice centre certainly has the advantage of speed in building. Here, too, changes in structure or policy can be rapidly implemented. I think that a health centre is the answer when integration with a hospital or with local health authority services on a large scale is envisaged, but otherwise private enterprise is certainly less cumbersome. Twelve doctors work from the two centres, and provide the area with an integrated medical service. A house committee meets at Hythe ; it consists of our hospital matron, administrative officers of hospital and centre, and doctors from each practice. Hythe Medical Society continues to fulfil a most important role in linking us together and enabling us to meet our consultant colleagues professionally and socially. The three practices, however, retain their complete identity and do not share a rota system except for casualty work.

The Future

A health centre should be an ideal place for planning health education, and we have started some schemes here. This centre should also make a good base for general practice research, but so far no plan has been adopted. It is possible that we would need expert advice, with secretarial and financial assistance. Time spent on consultation increases steadily, and it is thought that time could be saved by bringing some patients to us by special transport arrangements.

Plans are advanced towards setting up a high-frequency radio link between the centre, doctors, and midwives. The suggestion has been made that doctors working from health centres should be salaried. We have no wish for this, and seek to retain our independence. Finally I am sure that this centre must remain an experimental venture, and also that there must be pooling of knowledge on the design and administration of health centres to aid their future development in this country.

Summary

An attempt is made at an objective criticism of the Medical Centre at Hythe. Some suggestions are included regarding possible planning for future health centres, particularly in relation to reception and office arrangements.

The main advantages of health centre practice are the availability to the patient of his or her own doctor and easy access to consultant advice and diagnostic aid.

The centre encourages the concept of a medical team in general practice. Together with a neighbouring group practice centre the area now has an integrated medical service.

STUDENT HEALTH

Hospital Admissions among Students during a Three-year Period

GRAHAM GRANT,* M.SC., M.B., B.S.

Brit. med. J., 1967, 3, 674–676

A recent leading article in the *British Medical Journal* (1967) discussed the special arrangements needed for the management of psychological problems among university students. It also contained the following comment about their physical health: "He [the student of 30 years ago] suffered from influenza, the occasional inflamed appendix, and athletic injuries . . . The incidence of these physical maladies has altered little." In other words, students are to be regarded as a comparatively healthy group exempt from serious illness or disability. How true is this?

Reference has been made to the prevalence of chronic illness and to the special problems of handicapped students who, as a result of a more enlightened educational approach, are reaching university in increasing numbers (Grant, 1960). In a report of the Expert Committee on University Health Services (W.H.O., 1966) the suggestion is made that, in fact, a "wide range of acute and chronic medical and surgical disorders is seen." A brief study of the reasons for admission to hospital among students attending the University of Newcastle upon Tyne during a three-year period (September 1963 to August 1966) certainly lends support to this view.

Sources and Nature of Information

Shortly after its inception in 1963 arrangements were made for the university health service to be notified of the admission of students to the main teaching hospital in the area. Initial information about admission to other hospitals was obtained from medical certificates accounting for absence from studies, copies of which were sent to the health service by the university administration. Information came also from tutors and the wardens of halls of residence who were concerned about the implications of absence through illness or injury, which in some instances had occasioned admission to hospital either in the student's home town or elsewhere.

Clinical information was obtained in a number of ways. As the period covered by the inquiry progressed, an increasing number of students were registered with the university health service general practice, and reports about hospital admissions among them were received in the usual way, but in a number of instances follow-up inquiries had to be initiated as a result of information received from one or other of the sources mentioned in the foregoing paragraph. Sufficient diagnostic information was invariably available for purposes of simple classification.

It is inevitable that a survey of this kind should be incomplete. In particular, information about admissions during university vacations is likely to have been defective, though knowledge of admissions during term will have been more reliable.

Results and Discussion

Student numbers (postgraduates included) varied somewhat from year to year during the three years under review, with a mean annual figure of 4,610. Approximately one-quarter of the students were women.

During the three years 213 men were admitted to hospital on 229 occasions for the investigation or treatment of 215 different conditions, and 120 women were admitted on 129 occasions for 124 conditions. Altogether, therefore, 333 students were admitted on 358 occasions for 339 conditions. There was little annual variation in the proportions admitted, and a reasonable interpretation of the findings would be to say that annual admission rates were between 2 and 3% of the total population at risk, with, as might be expected, a somewhat higher proportion of women admitted than men. Analysis of causes of admission into broad categories according to the *International Classification of Diseases* is given in the Table. In some instances diagnostic descriptions have been adapted or modified for the sake of brevity. Because of the small numbers in some of the subgroups, the findings in the sexes have been combined. Much of the Table is self-explanatory, but five of the items call for special comment.

Group V

Mental, psychoneurotic, and personality disorders predominated as a cause of admission. (In fact, 36 men were admitted on 47 occasions and 24 women on 28.) The difficulties of psychiatric diagnosis among late adolescents and young adults are well known, and though the neat classification given in the Table may not be entirely accurate it reflects the spectrum of psychological disorders among students and underlines the importance of adequate facilities for dealing with them. The majority of students are, of course, living away from home, sometimes in flats or bed-sitters, or in other circumstances where it is unreasonable to expect to find anyone prepared to exercise the care and responsibility these cases demand ; and admission to hospital may be essential to the preservation of group morale even when a disturbed student is living in a university residence. Social reasons which would not necessarily be operative in a family setting may therefore contribute towards an inflation of admission rates considerably above the level expected among members of a similar age group in the community at large.

---

* Senior Medical Officer, University of Newcastle upon Tyne Health Service.

It is of interest that, of the 60 students admitted, 24 (40%) were women. Admission for mental breakdown also occurred disproportionately among foreign students. Approximately 8% of the total student population were from overseas. None of the women students admitted with mental illness were expatriates, but seven of the men—that is, one-fifth of the men admitted—came from abroad. The findings as regards women and foreign students in respect of mental illness are in agreement with those reported elsewhere (Kidd, 1965 ; Maclay, 1967).

Three Years' Hospital Admissions. Analysis by "Final" Diagnosis According to International Classification of Disease (Sexes Combined). (Numbers of Cases in Parentheses)*

	Admissions	
	No.	%
(I) *Infectious and Parasitic Diseases* Respiratory tuberculosis (2), tuberculosis (other) (4), hydatid (1), paratyphoid (1), filariasis (2), glandular fever, infectious hepatitis, other virus diseases (10) ..	22	6·2
(II) *Neoplasms* Malignant: Melanoma (1), reticulosarcoma (1), leukaemia (1), Hodgkin's (2). Benign: Including pilonidal sinus (6)—(18)	23	6·4
(III) *Allergic, Endocrine, Metabolic, and Nutritional* ● Asthma (status) (1), thyrotoxicosis (partial thyroidectomy) (1)	2	0·6
(IV) *Diseases of Blood and Blood-forming Organs* Anaemia of unspecified type	1	0·3
(V) *Mental, Psychoneurotic, and Personality Disorders* Schizophrenia, including paranoid reaction (16), manic depressive reaction (2), neurotic depressive reaction (17), anxiety reaction (8), hysterical reaction, including anorexia nervosa (2), obsessive compulsive reaction (1), personality disorder (10), alcoholism (1), drug addiction (1), drug intoxication (2)	75	20·9
(VI) *Diseases of Nervous System and Special Sense Organs* Subarachnoid haemorrhage (1), epilepsy (1), keratitis (1), glaucoma (2), strabismus (1)	6	1·7
(VII) *Diseases of Circulatory System* Malignant hypertension (1), haemorrhoidectomy (4) ..	5	1·4
(VIII) *Diseases of Respiratory System* Acute bronchitis (3), spontaneous pneumothorax (3), bronchiectasis, including lobectomy (2), pneumonia (2), tonsillectomy (9), chronic sinusitis, deflected nasal septum, etc. (7)	27	7·5
(IX) *Diseases of Digestive System* Disorders of occlusion, eruptions, etc., of teeth (chiefly admission for extractions of 3rd molars under endotracheal anaesthesia)	36	10·1
Duodenal ulcer (2), appendicectomy (23), hernia (2), ulcerative colitis (3), refashioning of ileostomy (1), fibrocystic disease (1), observation appendicitis (5), other (5)	43	12·0
(X) *Diseases of Genitourinary System* Infections of kidney (2), hydrocele (3), other (3), phimosis (1), gynaecomastia (2), disorders of menstruation (4), twisted ovarian cyst (1), ovarian cystectomy (1)	18	5·0
(XI) *Deliveries and Complications of Pregnancy, Childbirth, and the Puerperium* Normal delivery (19), caesarean section (1), abortion (6), therapeutic termination (6) .. .. .. (Total: 32—i.e., 24·8% of all female admissions)	32	8·9
(XII) *Diseases of Skin and Cellular Tissue* Erythema nodosum (1), drug eruption (2), infections of skin and subcutaneous tissue (5)	8	2·2
(XIII) *Diseases of Bones and Organs of Movement* Loose body in knee, meniscectomy (7), ruptured intervertebral disc (1), other symptoms referable to back (1)	9	2·5
(XVII) *Accidents, Poisoning, Violence* Accidents causing death (6), found dead (2), injuries involving fractures or dislocations (19), multiple lacerations, contusions, concussion (19) other injuries (5)	51	14·3
Total admissions	358	100·0

* The number of admissions may be greater than the sum of the numbers in parentheses because some individuals were admitted on more than one occasion.

Deaths (12)		
	Accidental	6
	Found dead	2
	Malignant hypertension ..	1
	Neoplasms	3

Group I

Overseas students also contributed disproportionately to the admissions for infectious and parasitic diseases. Apart from conditions obviously of tropical origin—for example, filariasis—five of the six cases of tuberculosis occurred in foreign students, who altogether accounted for one-third of the admissions in this group. These findings demonstrate the need for special screening of overseas students either before or as soon as possible after their arrival.

Group XI

It will be noted that 32 women were admitted for "deliveries and complications of pregnancy and the puerperium," comprising a quarter of the total admissions among women students. The findings relate only to cases admitted to hospital and known to the university health service. It may well be that during the early formative period of the work of the service, while students were developing confidence in it, some preferred to take such problems elsewhere. Moreover, a number of pregnancies which occurred during the last year of the inquiry had not gone to term by the end of it and are consequently excluded. Pregnancy rates based on the figures in the Table would therefore be misleadingly low. Working in a well-established university health department, Finlay (1965, 1966), who has made a special study of the problem, estimates that between 2 and 3% of unmarried women students become pregnant each year. Not all the pregnancies enumerated in the Table occurred in unmarried students, but accumulating experience at Newcastle supports Finlay's observations.

There is no doubt that problems of personal relationships, marriage, and child-bearing are occurring with increasing frequency in university health practice. It is important to get them into perspective, however. Hitchens and James (1965), using data derived from the Registrar General for England and Wales relating to 1961, gives rates for extramaritally conceived maternities—that is, illegitimate maternities plus those occurring within nine months of marriage—per 1,000 unmarried women at risk. For the age groups 15–19 and 20–24 these were 27.3 and 63.3 per 1,000 respectively. Since an unknown proportion of pregnancies—variously estimated at between 12 and 20% (Macnaughton, 1966)—end in abortion, the rates for extramaritally conceived maternities must be a good deal lower than the pregnancy rates. Assuming an annual pregnancy rate among unmarried women students (age range, say, 18–25) to be currently of the order of 3%, there is little evidence to support the view that they suffer this particular consequence of sexual misbehaviour or misadventure disproportionately by comparison with other women of similar age.

Group XVII

Serious injury among students, often resulting in prolonged absence, and, especially in cases of head injury, sometimes presenting the most difficult problems of rehabilitation, was most commonly caused by road traffic accidents. Among less serious injuries (multiple lacerations, contusions, concussion, etc.) sometimes requiring only overnight admission, again the road traffic accident and—a sinister social commentary—the unprovoked assault figured more prominently than athletic injuries.

Deaths

Lastly, there is the "melancholy list of deaths" (Paget, 1869) given at the foot of the Table. This refers only to deaths occurring while *in statu pupillari,* and the contribution of trauma—that is, road traffic accidents—to mortality in this age group is underlined. In some instances the student was dead on arrival at hospital, and these ought strictly, perhaps, to have been excluded from the total of hospital admissions, but the picture would have been incomplete without them. Two students were "found dead" in circumstances which aroused suspicion of suicide—a surprisingly small number bearing in mind the size of the population at risk over a three-year period and experience at other universities (Rook, 1959).

Conclusion

The report of the W.H.O. Expert Committee and a report of the Royal College of Physicians (1966) both recommended that university health services should provide their own accommodation, preferably centralized, for the treatment of certain categories of sickness among students. This is not the place for a description of how such accommodation might best be organized or of the undoubted advantages it confers. It will suffice to say that in common with a number of universities this service is now being developed at Newcastle upon Tyne, and some cases which might formerly have been admitted to hospital will in future be admitted to it.

This note should not, of course, be thought to reflect the scope and volume of clinical and preventive work in a comprehensive university health department the facilities of which are extended, in one form or another, to all members of the university community. It is clearly incomplete even as a prevalence study of morbidity among students. But if it does nothing else, at least it should dispose of the notion, still evidently held in some quarters, that—psychological disorders apart—a description of illness among students is adequately covered by "influenza, the occasional inflamed appendix, and athletic injuries" and that students are seldom really ill at all.

This work, part of a larger study into the implications of morbidity among university students, was supported in part by a grant from the Nuffield Provincial Hospitals Trust.

References

Brit. Med. J., 1967, **2**, 457.
Finlay, S. E. (1965). Proceedings of the British Student Health Association. (Private circulation.)
—— (1966). *Abortion in Britain. F.P.A. Conference Proceedings*, p. 46. London.
Grant, G (1960). *Proc. roy. Soc. Med.*, **53**, 1054.
Hitchens, R. A. N., and James, E. B. (1965). *Pub. Hlth (Lond.)*, **79**, 258.
Kidd, C. B. (1965). *Brit. J. prev. soc. Med.*, **19**, 143.
Maclay, I. (1967). *Brit. J. Psychiat.*, **113**, 329.
Macnaughton, M. C. (1966) *Abortion in Britain. F.P.A. Conference Proceedings*, p. 7. London.
Paget, Sir James (1869). *St. Bart Hosp. Rep.*, **5**, 238.
Rook, Sir A. (1959). *Brit med. J.*, **1**, 599.
Royal College of Physicians (1966.) Report of subcommittee on the Student Health Service. Social and Preventive Medicine Committee. London.
World Health Organization, 1966, *Techn. Rep. Ser.*, No. 320.

NEW APPLIANCES

New Alarm for Treatment of Nocturnal Enuresis

Mr. H. J. TERRY, Department of Medical Electronics, St. Bartholomew's Hospital, London E.C.1, writes: Alarms for the treatment of nocturnal enuresis, as described by Gillison and Skinner (1958), are in widespread use. The first aim in designing a new one was to minimize the risk of "buzzer ulcers," which were investigated by Borrie and Fenton (1966). The opportunity was taken to make the unit not only safer but also more reliable and more easily used and maintained than types employing relays, bells, or buzzers. Since high-quality silicon transistors now cost only two or three shillings, the cost of construction is only slightly increased.

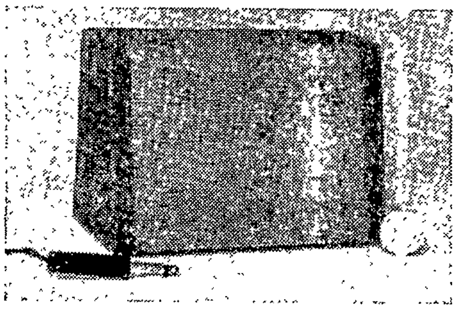


FIG. 1.—Enuresis alarm unit and a two-shilling piece.

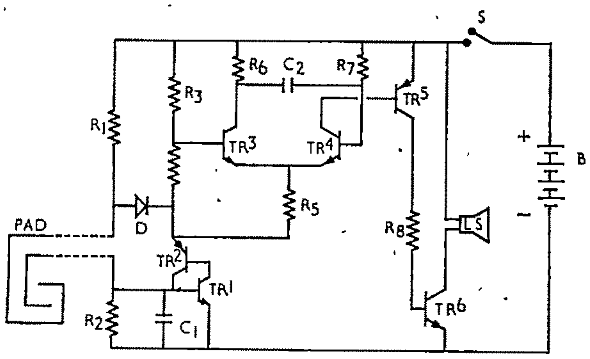


FIG. 2.—Enuresis alarm circuit. Components list: R 1, 5,600 ohms. R 2, 1,000 ohms. R 3 and 4, 4,700 ohms. R 5 and 6, 820 ohms. R 7, 470,000 ohms. R 8, 220 ohms. C 1 and 2, 0.01 microfarad. TR 1, 3, and 4, 2N 3710 (Texas Instruments). TR 2 and 5, 2N 3702 (Texas Instruments). TR 6, 2N 3706 (Texas Instruments). D, 1S940 (Texas Instruments). L S, loudspeaker 25–35 ohms. Battery, 4 cells, U 12/D 14.

Operation of the alarm has been made as simple as possible. As in earlier systems, a pad with two isolated electrodes is placed under the bottom sheet in the patient's bed and connected by a length of flex to a jack plug. Pushing the jack plug into its socket closes the switch, and the alarm is then ready for use. When the alarm is triggered by urine reaching the pad the loudspeaker wakes the patient with a steady note. This is switched off by simply unplugging the pad, and the alarm is again ready for use as soon as a dry pad is plugged in. The unit is powered by four pen-torch cells, which are sufficient for several months' use.

In answer to a letter in the *British Medical Journal* (Terry, 1966) 16 inquiries were received from doctors interested in trying out the new alarm. Nineteen alarms were built and sent out, with forms on which the user was asked to record each day whether the bed had been wet in the night and if the alarm had functioned correctly. Records of 40 months' use of alarms have so far been received, and as a result of the favourable reports by doctors and patients the alarm is being produced commercially.*

The unit is shown in Fig. 1 and the circuit diagram in Fig. 2. For those interested in electronics, TR 1 and TR 2 act as a switch, which responds to a current through the pad of about 400 microamps. With TR 1 and 2 conducting, TR 3 and 4 act as an emitter-coupled astable multivibrator. TR 5 and 6 merely amplify the square wave so produced, and drive the loudspeaker. Two safety features are included. R 1 ensures that, even if a fault occurs elsewhere in the circuit, the current through the pad cannot exceed 1 milliamp. The diode, D, provides the further safeguard that once the alarm has been triggered the potential across the pad cannot exceed 1 volt. To avoid false alarms when switching on it may be necessary to add a capacitor, similar to C 1 and C 2, between the base and emitter of TR 2.

I wish to acknowledge the help given by members of the Department of Medical Electronics in making the alarms, and by the medical officers, general practitioners, and patients in testing them. I am also grateful to the Endowment Fund of the hospital for financial support.

References

Borrie, P., and Fenton, J. C. B. (1966). *Brit. med. J.*, **2**, 151.
Gillison, T. H., and Skinner, J. L. (1958). Ibid., **2**, 1268.
Terry, H J. (1966). Ibid., **2**, 363.

---

* By Astric Products Limited, 261 Queen's Park Road, Brighton 7.

Correspondence

Letters to the Editor should not exceed 500 words.

Medicine in Burma

SIR,—Professor A. W. Woodruff's most informative article "Medicine in Burma Today" (26 August, p. 551) will interest many who feel profoundly towards that lovable land and people. May I, however, with the double interest of a founder professor of Rangoon University and of a former medical adviser to the British Government on Colombo Plan affairs, point out that by electing to leave the Commonwealth Burma did not deprive herself of British and Commonwealth aid. Both the Colombo Plan and the British Council gave generous help to Burma over the years and we still receive Burma nationals freely for specialist training and provide technological aid on the spot.

The London School of Hygiene and Tropical Medicine has played a most prominent part in shaping Burmese thought in medical administration, but tribute should be paid to the Edinburgh colleges—especially the Royal College of Physicians—for training the new generation of teachers. The outstanding claim for British influence rests on the Royal College of Obstetricians and Gynaecologists, whose members—male and female—are playing such an important part in modern Burma.

With the historical example of Judson, the pioneer American missionary who opened up Burma, and the great record of America in fostering education in Burma (we in British University College faced American Judson College on the university campus in the 'twenties) it is a matter for profound regret that the Burmese have felt it advisable to refuse further American aid, but with Thailand and Viet Nam round the corner their attitude is understandable. Professor Woodruff's own contribution to Burmo-Britannic concord is outstanding and his sympathetic study is therefore very welcome.—I am, etc.,

Ewell, Surrey. GEORGE R. MCROBERT.

SIR,—It was very heartening to read the paper by Professor A. W. Woodruff "Medicine in Burma Today" (26 August, p. 551). His paper gives an excellent survey of the medical services in that country. Naturally one would not expect from a professor of tropical medicine (any more than from a professor of radiology) an account that did not have an emphasis towards his main interests—in this case towards tropical medicine. This letter is written in no spirit of criticism, but merely to emphasize some of the aspects not fully covered in Professor Woodruff's paper.

The medical services in Burma have indeed undergone a revolution, and this has happened in particular since the present revolutionary council took over the government of the country. All medical practice is concentrated on hospitals and health centres. There is no longer general practice as we know it in Britain. In the larger towns, where under previous regimes there was general (and private) practice for the privileged few who could afford to pay for it, this has been discouraged or eliminated, and all medical practice is now concentrated within the Government medical service.

The medical school based on Rangoon General Hospital has always had a high reputation and produced doctors of high calibre. This now applies also to the new well-equipped medical schools at Mingaladon and Mandalay. However, as doctors trained in hospital where there are reasonable ancillary facilities were continuing to work subsequently in other hospitals, whether those hospitals were divisional or township hospitals, the demand for the continuance of ancillary facilities was considerable, though at the time the ability to satisfy these demands was minimal or non-existent. Thus an Institute of Paramedical Sciences was set up at Rangoon General Hospital to train laboratory technicians, radiographers, physiotherapists, and pharmacists. This Institute has been in action for nearly three years and is now producing a flow of trained technicians in these disciplines. I have been concerned with this concept since its beginning and visit it regularly year by year. In modern medical practice medicine cannot be practised satisfactorily without ancillary aids, and it is important in the context of Burma to realize that this essential "substructure" of medicine is now being established.

With the "substructure" of medicine established, and with the excellent medical schools, described by Professor Woodruff, already in existence, it only remained to plan the "superstructure" of the specialist fields. This has now started, and Professor Woodruff described one of these—that in tropical medicine. However, in addition, apart from the major fields of surgery, medicine, and obstetrics and gynaecology, the specialist fields of child health, pathology, anaesthetics, orthopaedic surgery, and radiology are now being developed. Already there are diploma courses for a Burmese diploma in anaesthetics and another in clinical pathology. These, together with the present course in tropical medicine, and the possibility of developing further postgraduate courses in other fields such as radiology, make it seem possible that Rangoon may well grow into a postgraduate centre of considerable significance in South-east Asia.

All these advances have taken place in Burma during the past five years, in a country which already had a first-class medical school whose medical degrees have recently been given full recognition by our own General Medical Council. The substructure and superstructure are now being built, just as they were in Britain many years after the undergraduate teaching hospitals were established. There is a considerable fund of good will in Burma towards Great Britain besides the traditional medical links that have existed for many years. It is to be hoped that the United Kingdom will continue to provide training facilities and hospitality for those Burmese doctors and medical technicians who come here for further experience, and in addition will continue to second medical and paramedical personnel at all levels to Burma to help them with the exciting developments that are now taking place.—I am, etc.,

J. H. MIDDLEMISS.

Department of Radiodiagnosis,
University of Bristol.

SIR,—Professor A. W. Woodruff's article "Medicine in Burma Today" (26 August, p. 551) refers to the recognition by the General Medical Council of Burmese medical degrees but does not tell the whole story.

It would seem that in 1964 the Burmese Government refused to permit foreign graduates of the Burmese School to practise in Burma unless they had 14 years' previous Government service. This has had the result that non-Burmese nationals qualifying in Rangoon are unable to obtain full registration in Britain because they are no longer permitted to practise in Burma. This political decision has meant that, while Burmese nationals qualifying in Rangoon may obtain full registration here, non-Burmese nationals who passed precisely the same examination are no longer so entitled.

Two points arise: firstly, should not the relevant section of the 1956 Medical Act 18(1)(c), which entitles persons holding certain foreign degrees to obtain full registration in Britain, be so amended as to avoid anomaly of a person's entitlement to registration here being dependent upon what appear to be purely political considerations? Secondly, should Burmese nationals be granted rights in Britain while their Government shows such discrimination?—I am, etc.,

HERBERT CONSTABLE,
Secretary,
Medical Protection Society.

London W.1.

Penicillin Encephalopathy

SIR,—Your leading article on penicillin encephalopathy (12 August, p. 384), while drawing attention to the hazards of intravenous penicillin therapy, makes little attempt to indicate how these hazards may be avoided or to define the indications for using penicillin G in this way.

In July my colleagues from Boston and I described eight patients treated with high doses of intravenous penicillin G in whom there was evidence of neurotoxicity.[1] These patients were compared with seven others treated similarly in whom toxicity was not observed. All patients were assessed as regards renal function, electrolyte imbalance, plasma, and cerebrospinal fluid penicillin levels. Major differences were noted between the two groups in respect of amount of penicillin administered and penicillin C.S.F. concentration; the group with fits tended to have lower serum sodium values than those without fits. No patient with a lumbar C.S.F. penicillin concentration less than 10 units/ml. had a fit; clearly, whatever the state of renal function or the blood/C.S.F. barrier it is unwise to exceed this concentration of penicillin in the C.S.F. The other complications of infusion of large doses of penicillin G are fluid and electrolyte imbalance, which can be avoided or corrected, and haemolytic anaemia, which is quite rare.

Intravenous penicillin G in doses of 20 to 100 million units per 24 hours is not only a useful form of therapy for septicaemia due to *Clostridium welchii* and selected Gram-negative species but may be the only effective therapy in certain patients with endocarditis. For those who may wish to administer these doses it is important that indiscriminate use is avoided and that the limitation of dosage based on C.S.F. penicillin levels be understood.—I am, etc.,

HILLAS SMITH.

Royal Free Hospital,
Infectious Diseases Department,
London N.10.

REFERENCE

[1] Smith, H. G., Lerner, P. I., and Weinstein, L., *Arch. Intern. Med.*, 1967, 102, 47.

Treatment of Staphylococcal Endocarditis

SIR,—Your leading article (4 March, p. 515) concluded that the best treatment for staphylococcal endocarditis is a combination of a penicillin or cephalosporin with an aminoglycoside (streptomycin or kanamycin). The patient with poor renal function presents a special problem in that the dosage of the aminoglycoside must be carefully monitored by assays of blood levels in order to avoid toxic side-effects.

A chance finding led to the realization that both cephaloridine and cloxacillin in serum can be neutralized by an excess of *Bacillus cereus* penicillinase. A patient with "sterile" endocarditis being treated with penicillin G and streptomycin was having serum streptomycin levels assayed daily. The penicillin was destroyed with commercial penicillinase (Neutrapen) and the streptomycin assayed by a microbial method. The levels remained surprisingly constant even after cephaloridine had been added to the regimen unbeknown to the laboratory.

As a result of this I set up a chessboard titration to compare the action of the penicillinase against varying concentrations of methicillin, cloxacillin, cephaloridine and penicillin G. The antibiotics were dissolved in phenol-red broth, and concentrations of penicillinase varying from 2 up to 400 units were added. Destruction of the antibiotic was indicated by the growth of a small inoculum of the Oxford staphylococcus after 18 hours' incubation. The results are shown in the Table.

Weight of Antibiotic	Penicillin G	Cephaloridine	Cloxacillin	Methicillin
500 μg.	16	160	>400	>400
50 „	16	80	400	>400
5 „	<2	16	80	400

Penicillinase units needed to neutralize the antibiotic.

An average blood level of antibiotic would be 5 μg./ml., and it can be seen that 400 units of penicillinase destroyed this amount of all four antibiotics. Similar results were obtained with a different make of penicillinase (Distillers), and also after the addition of 25% human serum to the medium.

These results agree with biochemical studies on penicillinases in general and bacterial work on the staphylococcal enzyme.[1 2] Whether there is a single beta-lactamase or separate penicillinase and cephalosporinase enzymes is still in doubt[3]; certainly the enzymes produced by different species of bacteria vary in their relative activities against penicillins and cephalosporins.

I conclude that the readily available *Bacillus cereus* penicillinase is a definite help to the medical microbiologists for the neutralization of cephaloridine, cloxacillin, and possibly methicillin in the blood of a patient when either blood levels of other antibiotics or blood cultures are required.—I am, etc.,

S. W. B. NEWSOM.

Papworth Hospital,
Papworth Everard,
Cambridge.

REFERENCES

[1] Ayliffe, G. A. J., and Barber, M., *Brit. med. J.*, 1963, 2, 202.
[2] Benner, E. J., Bennett, J. V., Brodie, J. L., and Kirby, W. M. M., *J. Bact.*, 1965, 90, 1599.
[3] Sabath, L. D., and Abraham, E. P., *Biochem. J.*, 1966, 98, 11C.

Mortality of the Ambulance Ride

SIR,—On Christmas Eve, 1966, my father, who was not a doctor, died of a coronary in the Postgraduate Hospital at Hammersmith. On the way to the hospital he asked me to try to alter the design of ambulances for cardiac cases, in as much that with the head-first position the abdominal contents rode up towards the chest every time the driver applied the brakes. This caused my father a considerable increase in his pain.

On reflection surely it would be better if all patients were carried in ambulances with their feet nearest to the driver, as even in the unconscious case the legs and body would protect the head from injury in an accident, whereas in the present system the head is smashed against the partition behind the driver. Facing the engine is often preferable in railway trains, and the only reason I can assume for our present policy of the patient lying facing the rear door of the ambulance is the reluctance of the authorities to agree to stretchers being carried feet first, possibly because the old expression "They carried him out feet first" has the connotation of dying or death.—I am, etc.,

JOHN R. GLOVER.

Department of Social and
Occupational Medicine,
Welsh National School
of Medicine,
Cardiff.

SIR,—I missed Dr. D. Lamont's letter (6 May, p. 374), but the letter of Dr. C. H. Cullen and colleagues (12 August, p. 438) deserves a comment from a totally different angle. In the first world war it was widely known and recognized that many cases of serious gunshot wounds often had better recovery prospects when they had been left for longish periods exactly where they were wounded.

I can speak from personal experience. I was crashed when flying in France as a passenger and became conscious before my squadron ambulance arrived. I was able to recognize that I was extensively paralysed. Being at that time aware of the benefit of no movement at all for a longish period, I forbade my anxious orderly to en-stretcher me, and made him cover me with rugs until an M.O. from the officers' hospital in St. Omer came and personally supervised my transport two hours after the crash.

The Army consultant, General Dawson (later Lord Dawson of Penn), attributed my ultimate recovery largely to this period of immobility.

All this is now 51 years ago. Years and years passed, and I had the misfortune to witness a motor-cyclist near Barnet involved in a bad accident. I remember vividly the difficulty I had in preventing him being immediately lifted on to one of those two-wheeled horrors, then in common use by the St. John Ambulance. He made a good recovery, thereby sparing the driver of the car involved in the accident standing a possible trial for manslaughter. The report of the casualty surgeon at the hospital to Lord Trenchard, then Commissioner of Police, produced a personal letter from Trenchard asserting the view that a longish period of immobilization had been of material help in this cyclist's recovery.

I wonder if the value of immobility at the site of injury with a resuscitation tent has ever been explored, before even a short motor journey, however good the springing.—I am, etc.,

C. B. HEALD.

Chipping Campden,
Glos.

SIR,—The plea of Mr. C. H. Cullen and his colleagues for improvements in ambulance suspension (12 August, p. 438) deserves strong support.

A few weeks ago I had occasion to accompany a patient who had suffered a subarachnoid haemorrhage a day or two previously to a neurosurgical centre. The journey covered 25 miles of good road which I know well, but I was appalled at the rough ride experienced, which was reminiscent of travel in a farm-cart.

I was greatly apprehensive that the shaking the patient received might restart the haemorrhage, and I felt the back of a saloon car would have been a far safer place in which to carry her.

New ambulances are, I understand, to have much better suspension of a pneumatic type, but could not something be done to improve the existing ambulances, which will be with us for many years to come?—I am, etc.,

J. HORTON.

St. Albans,
Herts.

Problems of Accident and Emergency Services

SIR,—It was refreshing to read Dr. K. C. Easton's comments on road accidents at the B.M.A. Bristol Meeting (22 July, p. 230). For some years a few general practitioners have been emphasizing the value of a doctor on the site of an incident, if this can be attained without delay.[1]

Unfortunately there has developed a widespread misunderstanding of what is possible in primary treatment by the general practitioner on the site, and how they can help to reduce the possible 20% preventable deaths in transit.

In my area the present policy of the accident service has produced a Gilbertian situation. The police, who are the organizers of the medical care at an incident, have been advised by the Medical Officer of Health that it is undesirable to inform a local general practitioner of an accident near him if the patient is alive, as this would cause delay in treatment by the accident hospital unit. However, the local doctor may well be informed if the patient is dead—to certify death.

Factual evidence of saving life, when a doctor has attended on site at an accident by chance, has made no impression on this policy. In this practice three, possibly four, lives have been saved during the past few years in the small percentage of accidents attended. Admittedly there are pros and cons on the subject. But any local accident medical organization that has as its policy "call the local doctor if the patient is dead, but don't call him if he's alive" must be suspect.

Some of us hope that a wind of change may start blowing through the opinions of the higher echelons of the accident service organizers as a result of Dr. Easton's talk.—I am, etc.,

ROBERT HOWARD.

Burley,
Ringwood, Hants.

REFERENCE

[1] Howard, R., *J. Coll. Gen. Practit.*, 1965, **9**, 48.

Mercury Perchloride in Surgery of Bowel Cancer

SIR,—Mayo Robson[1] drew attention to the problem of seedling implantation in radical cancer surgery. To avoid this implantation during mastectomy Sampson Handley[2] advised flushing the wound with 1:2000 perchloride of mercury solution. Miles[3] used a stronger 1:500 solution of perchloride of mercury after radical resection of the rectum, for its antiseptic rather than its anticancer action.

The use of the solution as an anticancer agent in colon and rectal surgery was popularized by several workers[4-6] and has been found efficacious. Keynes[6] stated that there was no evidence of mercury poisoning in any of the cases he had studied, but he gave no details of blood or urinary mercury levels. Royle[7] described a case of alleged mercury intoxication following the use of 200 ml. of 1:500 perchloride solution during the excision of a tumour of the renal pelvis, and this report prompted study of the question.

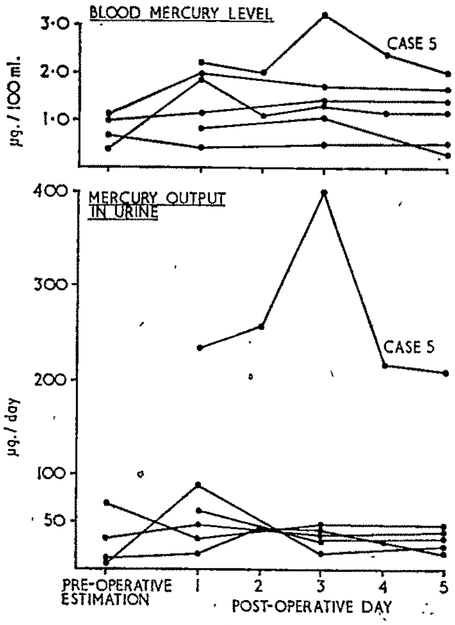
Six patients with rectal adenocarcinoma were studied (see Table). The urine output of mercury and the blood level of mercury were measured pre- and post-operatively. The technique of rectal restorative surgery employed was essentially that described by Goligher *et al.*[4] In this about 1 litre of 1:500 mercury perchloride solution is used to wash out the rectal stump, while a further 300 ml. is used to mop the lumen of the proximal colon when it is divided, and also to wash the edge of the mesentery and the exposed perirectal tissues in which malignant cells released by lymphatic division and direct tumour extension may lie.

When radical resection was performed the cut edge of the mesentery, the perirectal and perineal tissues, and the divided proximal end of the colon were mopped with the solution, which was dried up before the abdomen was closed. Again the surgeon was allowed only 300 ml. of 1:500 mercury perchloride for all these needs.

Details of Patients Studied

No.	Sex	Age	Clinical Details	Maximum Urinary Mercury Concentration (μg./litre)
1	F	54	Carcinoma rectosigmoid Restorative resection	58
2	M	74	Carcinoma rectal ampulla Abdominoperineal resection	26
3	M	50	Adenoma sigmoid colon Local resection	24
4	M	66	Carcinoma rectal ampulla Abdominoperineal resection	24
5	M	60	Carcinoma rectosigmoid Solitary metastases dome of bladder Restorative resection with partial cystectomy and wide pelvic fat clearance	232
6	F	66	Carcinoma rectal ampulla Abdominoperineal resection	38

Details of the six patients studied are shown in the Table, and the results are shown graphically (see Fig.). No patient showed clinical evidence of mercury intoxication, and six of the cases showed an inappreciable uptake of mercury into the blood. Case No. 5, however, showed higher urine values than the others, which were possibly due to the mercury put inside the bladder and "contaminating" the urine, to the more extensive pelvic dissection and the difficulty of drying the mercury out adequately, or to a selective uptake of mercury occurring in the bladder. Because the blood levels were only slightly raised we suspect that the first of these possibilities was responsible. Thus mercury fixes exposed cells such as those in the bladder, and these would be shed over the ensuing days, leading to the higher urine levels demonstrated in this case. Though the evidence for increased mercury uptake by bladder epithelium is slight, three previous cases of mercury intoxication involving bladder surgery are reported by Page and Wilson,[8] though they used mercury oxycyanide.



Lane[9] states that the normal urine mercury content is up to 80 μg./l., and that quantities in excess of 100 μg./l. are abnormal. Moreover, he further points out that symptoms of mercurialism develop when the level exceeds 300 μg./l. The highest level found in the series was 232 μg./l. in Case No. 5 within 24 hours of operation. No patient, however, showed any signs of mercurialism, and it is therefore concluded that mercuric perchloride is a safe anticancer agent when it used, as described above, in large bowel surgery.

I am grateful to Mr. R. W. Nevin and Mr. H. E. Lockhart Mummery for permission to study patients under their care and to Dr. R. B. McSwiney for biochemical facilities.

—I am, etc.,

H. BRENDAN DEVLIN.

Dept. of Surgery,
St. Thomas's Hospital,
London S.E.1.

REFERENCES

[1] Robson, Mayo, Bradshaw lecture Royal College of Surgeons, England, 1904.
[2] Handley, W. S., in *Modern Operative Surgery* ed. by H. W. Carson, **1**, p. 421, 1924, London.
[3] Miles, W. E., *Cancer of Rectum*, p. 61, 1926, London
[4] Goligher, J. C., Dukes, C. E., and Bussey, H. J. R., *Brit. J. Surg.*, 1951, **39**, 199.
[5] Morgan, C. N., *J. Roy. Coll. Surg. Edinb.*, 1955, **1**, 112.
[6] Keynes, W. M., *Ann. Surg.*, 1961, **153**, 357.
[7] Royle, J. P., *Aust. N Z. J Surg.*, 1964, **34**, 71.
[8] Page, B. H., and Wilson, C., *Lancet*, 1940, **1**, 640.
[9] Lane, R. E., *Brit. Med. J.*, 1954, **1**, 978.

Elusive Popliteal Pulse

SIR,—You have done an important service to your readers (5 August, p. 326) by raising a matter of such practical importance, and, while the consensus of opinion is that there are several best ways of palpating for the popliteal pulse (19 August, p. 495), no mention is made of a much more exact technique for obtaining the information which the popliteal pulse is meant to supply. I refer to oscillometry.

Like sphygmomanometry, oscillometry greatly enhances the accuracy of what at best can be regarded as only a subjective impression.—I am, etc.,

F. E. WEALE.

Surgical Professorial Unit,
St. Bartholomew's Hospital,
London E.C.1.

Nalidixic Acid and Intracranial Hypertension

SIR,—In a letter (5 August, p. 370) Dr. O. D. Fisher reports a case of raised intracranial pressure in a child during treatment with nalidixic acid. He states, "In the present case the dosage of nalidixic acid prescribed for the infant was twice the recommended one of 100 mg. per kg. body weight per day, and this was used in the second course to see if the condition could be reproduced."

The dose of 60 mg./kg. body weight is the one recommended by us and is the one which appears regularly in our literature. On this basis you will see that the doses used in the case reported by Dr. Fisher were in fact over three times the recommended dose of 60 mg./kg. body weight.

Nalidixic acid is widely used in hospital and general practice for the treatment of urinary tract infections, both in children and in adults, and it would indeed be unfortunate if doses other than those recommended by the manufacturers were quoted in medical journals and used unsuspectingly by doctors. —I am, etc.,

S. A. STEPHEN,
Medical Controller,
Bayer Products Company,
Surbiton, Surrey.

Achondroplasia and Leukaemia

SIR,—We were interested in the Clinicopathological Conference (3 December 1966, p. 1371) describing immunologic deficiency and aplastic anaemia in an infant with achondroplasia. Dr. V. A. Fulginiti and associates (22 April, p. 242) and Dr. J. A. Davis (8 July, p. 110) have written of similar cases, prompting us to report the case history of an achondroplastic child who developed leukaemia, and to speculate on a relation between this complication and the other disorders observed with achondroplasia.

On 3 January 1965 a boy aged 5 years was admitted to the Children's Cancer Research Foundation in Boston with the abrupt onset of a superior vena caval syndrome. A classical picture of achondroplasia had been evident since birth, in the absence of a family history of dwarfism or congenital defects, and during infancy the patient had respiratory difficulty, which was attributed to a deformed thoracic cage. In addition to achondroplastic dwarfism examination showed facial oedema, venous distension in the neck and chest wall, and hepatomegaly. The white-cell count was normal with 40% lymphocytes. *X*-rays revealed an anterior mediastinal mass and bony changes consistent with achondroplasia. A presumptive diagnosis was made of lymphosarcoma. Because of rapidly increasing dyspnoea, the patient was treated with *x*-ray therapy and adrenal steroids, followed by dramatic improvement. Intravenous vincristine, 0.6 mg. weekly, was given in an attempt to prevent conversion of lymphosarcoma to leukaemia.

On 4 April the patient complained of headache and vomiting. The white count was 13,000 with 4% blast cells, and bone-marrow aspiration showed acute lymphocytic leukaemia. Lumbar puncture revealed meningeal involvement with leukaemia, which was treated with intrathecal methotrexate. One month later the white count was 19,400 with 44% blast cells, and the platelet count was 7,000. Despite treatment with methotrexate, cytoxan, and adrenal steroids the subsequent course was progressively downhill, and the patient died on 12 September 1965. Necropsy revealed the osseous abnormalities of congenital achondroplasia, extensive leukaemic infiltration of organs, a haemorrhagic diathesis due to thrombocytopenia, and terminal bacteraemia.

To our knowledge there have been no previous reports of achondroplasia and leukaemia occurring in the same person, so that this case may represent a combination of chance events. Its signifiance is enhanced, however, by the concurrence of achondroplasia with immunologic deficiency and marrow aplasia, conditions which independently appear to carry an excess risk of leukaemia or lymphoma.[1] Thus leukaemia may be an added manifestation of an immuno-haematologic defect occurring in certain patients with achondroplasia.

If this association is not due to chance one may wonder about the role of chromosomal abnormalities which have been observed occasionally in achondroplasia.[2] It is of interest that the congenital disorders which are at high risk of leukaemia (Bloom's syndrome, Fanconi's syndrome, and mongolism) have chromosomal abnormalities in association with skeletal defects or dwarfism.[1] However, the recent description of osteogenesis imperfecta and childhood leukaemia in two siblings[3] suggests that the relation of leukaemia to heritable disorders of the skeletal system need not be mediated by cytogenetic defects. As noted by Dr. Davis, the disorders associated with achondroplasia seem to extend the list of syndromes which bring together genetically determined diseases of the bone and bone marrow.—We are, etc.,

JOSEPH F. FRAUMENI, JUN.,
Epidemiology Branch,
National Cancer Institute,
Bethesda, Maryland, U.S.A.

MIRIAM D. MANNING.
Children's Cancer Research
Foundation,
Boston, Massachuetts, U.S.A.

REFERENCES

[1] Fraumeni, J. F., jun., and Miller, R. W., *J, Nat. Cancer Inst.*, 1967, **38**, 593.
[2] Zellweger, H., and Taylor, B., *Lancet*, 1965, **85**, 8.
[3] Gilchrist, G. S., and Shore, N. A., *J. Paediatrics*, 1967, **71**, 115.

Smallpox Revaccination

SIR,—In our county the health authorities are advocating routine revaccination against smallpox of children between 8 and 9 years of age.

My partners and I think this is against modern teaching. Besides carrying a slight risk to the child, so many people require yet a further revaccination in their late teens owing to foreign travel. This appears to make procedure at 9 years superfluous.

We have written to our medical officer of health saying that we are advising parents against this routine procedure. He has replied suggesting that we alone are upsetting the records for the county. Are we really being "square" or are there other general-practitioner nonconformists ?—I am, etc.,

Horsham, Sussex. E. PERKINS.

Changed Character of Osteomyelitis

SIR,—I had not intended to enter into correspondence on your leading article (29 July, p. 255), as I have previously discussed most of the controversial points.[1-4] However, I have been unable to resist the temptation to make a few comments.

My own experience supports the opinion of Mr. J. H. Bulmer (19 August, p. 497) that cloxacillin is the antibiotic of choice before the sensitivity of the organism is known, and in this context Mr. J. H. Green's paper (13 May, p. 414) was a most helpful contribution. I am quite convinced that bacteriostatic antibiotics such as the tetracyclines have no part to play in the management of staphylococcal osteomyelitis, and there is no better one than cloxacillin for use against the penicillinase-producing staphylococcus. A further disadvantage of the tetracyclines is their relative inability to diffuse into dead bone.[5] I have shown quite conclusively that penicillin and methicillin diffuse readily through thick-walled abscesses and remain in the infected tissue long after the blood level has fallen to zero.

I regret that I cannot be equally enthusiastic in support of Mr. J. H. Bulmer's view that aspiration of subperiosteal pus is an efficient method of drainage. Aspiration can in fact be very difficult, because the pus may be deep-seated and impossible to localize; nor is it a complete decompression, which requires drilling of the bone, and in any case it may well have to be repeated—an important consideration, particularly in children. Surgical drainage, on the other hand, is simple and produces a complete decompression. The bone must be drilled because pus under considerable tension is often present before a subperiosteal abscess forms. Prompt relief of pain and prevention of bone death is the result of surgery at this early stage of the disease.

With regard to the development of secondary infection and sinus formation after surgery I can only repeat that it has not been my experience. It certainly occurs in some patients when surgery is performed late (after about the third or fourth day of the illness), by which time the story of the disease has been written. I think this is the reason for the difference of opinion on this aspect of the problem. It is important, therefore, when referring to surgery to indicate when it is performed and what we mean by early and late. My own series indicated that the blood culture is negative in at least 50% of patients with acute osteomyelitis. It is an unreliable method of obtaining the organism for culture and sensitivity tests, and most laboratories cannot give a report in less than 48 hours, which is far too long to wait. A report on pus can be given in less than 24 hours, and is therefore of some practical value.

Finally, Sir, it is encouraging to note that most of your correspondents think that surgical decompression has an important part to play in the management of acute osteomyelitis in its early stages, as Trueta advocated 13 years ago[6] and supported by my own studies five years ago. The best method of treatment, despite all that has been written in the past, is now a controversy not so much among surgeons but rather between physicians and surgeons. Acute osteomyelitis is only one of many examples of this phenomenon, which is both stimulating (though sometimes frustrating) and inevitable when two such disciplines are involved.—I am, etc.,

London W.1. NIGEL H. HARRIS.

REFERENCES

[1] Harris, N. H., *J. Bone Jt Surg.*, 1960, **42B**, 535.
[2] —— and Kirkaldy-Willis, W. H., ibid., 1965, **47B**, 526.
[3] —— *Brit. med. J.*, 1962, **1**, 1440.
[4] —— ibid., 1964, **1**, 237.
[5] Frost, H. M., Villanueva, A. R., and Roth, H., *Henry Ford Hosp. Bull.*, 1960, **8**, 255.
[6] Trueta, J., and Morgan, J. D., *Brit. J. Surg.*, 1954, **41**, 449.

National Kidney Centre

SIR,—As one of the founder trustees of the National Kidney Centre I would refer to the letter (22 July, p. 241) written by our medical director, Dr. S. Shaldon, and the news paragraph (p. 252) "Kidney Centre to Close." In this connexion I would draw your attention to a press denial by the trustees that the centre is to close. This is a decision which still has to be discussed by the trustees in the light of the resignation of Dr. Shaldon, which is to take effect from 1 July 1968. Obviously, if a suitable replacement for Dr. Shaldon could be found within a reasonable period of time the centre could continue to function, but if perchance this is not possible inevitably and regretfully it would have to close.

On 9 May last a meeting took place with representatives of the Minister of Health to discuss a Ministry of Health circular, No. H/A 190/14, where the Minister advised chairmen of medical committees of teaching hospitals and senior administrative officers that, while regional hospital boards have the power to refer patients to the National Kidney Centre and pay for treatment outside the N.H.S., it was the unanimous recommendation of the meeting that patients should not be referred, as this form of treatment should be based only on hospitals with full supporting facilities. At this meeting a plan to provide chronic dialysis in the United Kingdom based on the use of home haemodialysis, which would integrate the National Kidney Centre within the National Health Service, thereby making all the medical equipment and financial resources available to the National Health Service, was submitted for consideration, and to date no reply to this plan has been received.

The attitude of the trustees of the National Kidney Centre and its medical director has always been an unselfish one, and the result of Dr. Shaldon's research into home dialysis was quite staggering in its potential in the terms of numbers which could be treated. We therefore feel that by integration with the N.H.S. the maximum number of people suffering from this disease in the United Kingdom could receive benefit.

Regretfully, it is the complete lack of interest and approach to this matter which has developed cumulative frustration in our medical director which now results in his resignation. I would have thought that from a national point of view there must be a strong case for the retention of the National Kidney Centre until such time as a better form of development could be substituted in its place. Should the train of events now result in the eventual closure of the National Kidney Centre it would be a national tragedy.

The result during the last seven weeks has already proved disastrous, as the programme of the centre was to accept 60 patients by the end of the year. During the past three weeks any patients referred have not been accepted. By the end of the year, if the situation continues, some 30 prospective patients will die needlessly.

The National Kidney Centre has been established as a charitable, non-profit-making organization to provide artificial kidney treatment to as many patients as possible. The centre is concerned with providing treatment under ideal circumstances—one unit, one patient, at home and freed from the need for repeated hospital attendance, involving travel and pressure on bed space and nursing staff in the already overburdened Health Service hospitals. Though the effectiveness of artificial kidney treatment for those with incurably diseased or damaged kidneys is medically accepted beyond dispute, the National Health Service will be unable to provide this form of treatment for more than 5 to 10% of those who could benefit in the next few years. This means that 5,000 to 10,000 sufferers in this country will die unnecessarily in that time.

The National Kidney Centre was set up by a group of individuals who were dissatisfied with the Health Service plan and who wished to demonstrate an alternative approach —home dialysis—which would, through private funds, provide hope for the majority who are doomed to die and for whom no Government help is foreseeable.—I am, etc.,

MURRAY MEDWAY.

London N.3.

*** See leading article at p. 631.—ED., *B.M.J.*

Amphetamine

SIR,—I have been most pleased to see in "Today's Drugs" on the prevention of motion sickness (12 August, p. 422) that you and your expert contributors say that any drug combination containing amphetamine is of itself open to objection. On turning overleaf (p. xii) I was dismayed to see an advertisement for an anti-obesity drug containing just such a combination.—I am, etc.,

Harrogate. T. G. REAH.

The "Pill" and Deep-venous Thrombosis

SIR,—Mr. K. Hæger and colleagues (19 August, p. 493) query the reliability of diagnosis of venous thrombosis in the Royal College of General Practitioners series of non-fatal cases discussed in the Medical Research Council report (6 May, p. 355) and other reported non-fatal cases. Their remarks do not apply to any of the reported deaths, all of which have come to necropsy, as will have most of those studied by the Dunlop Committee. Even in the Royal College of General Practitioners cases, as the same practitioners were caring for both patients and controls, an increased incidence of *something* (pseudothrombosis ?) has been found. Conversely, about 66% of deep-venous thromboses are not diagnosed in life[1] (my own observations agree) and it is as likely that the incidence is understated as overstated.

Interpreting broadly the term "coagulation patterns" in their last sentence, many studies have revealed a variety of changes in oral contraceptive users. To take one line of thought, your leading article (19 August, p. 449) says: "Platelet adhesiveness . . . has been shown to be increased in . . . venous thromboembolism." Puerperal venous thromboses are commonest about the tenth day, when both platelet count and platelet adhesiveness are maximal.[2] Platelet adhesiveness in the presence of encephalitogenic factor is increased in users.[3]

The platelet count in users is not increased.[4 5] This was claimed as evidence against any thrombotic risk, but Dr. J. Ll. Burton (22 July, p. 214) suggests that agglomerins (notably fibrinogen) cause rouleaux formation and raised erythrocyte sedimentation rate in users. Very likely they play a part in thrombosis. If, as your leading article suggests, platelet adhesiveness is an index of other blood changes it may in users connote a liability to thrombosis.—I am, etc.,

ROBERT J. HETHERINGTON.

Summerfield Hospital,
Birmingham 18.

REFERENCES

[1] Richards, R. L., *Brit. med. J.*, 1966, 2, 217.
[2] Carroll, J. D., Leak, D., and Lee, H. A., *Quart. J. Med.*, 1966, 35, 347.
[3] Caspary, E. A., and Peberdy, M., *Lancet*, 1965, 1, 1142.
[4] Pepper, H., and Lindsay, S., *Amer. J. Obst. Gynec.*, 1963, 86, 737.
[5] Hetherington, R. J., *Lancet*, 1967, 1, 1385.

Surgery in Acquired Cardiac Disease

SIR,—Perhaps I may draw attention to an error in the report on my communication on the place of surgery in acquired cardiac disease at the Annual Meeting in Bristol in July (22 July, p. 233). I am reported as saying that: "Patients with mitral incompetence tended to run a more rapid downhill course after the *arrest* of symptoms . . . ." This should of course read "after the *onset* of symptoms . . . ." The change in the word of course completely alters the sense of the message.

I was anxious to point out that, since operations for mitral incompetence are more complex and hazardous than mitral valvotomy, patients should not be advised to have open operations unless the symptoms due to mitral incompetence were demanding. Thus I stated that many patients with mitral incompetence were capable of managing satisfactorily without surgery for a number of years and in them operation could often be postponed.—I am, etc.,

Royal Postgraduate
Medical School,
London W.12.

J. F. GOODWIN.

Protective Helmets and Traumatic Epilepsy

SIR,—I am very grateful for Mr. W. Bryan Jennett's helpful comments and information on traumatic epilepsy (29 July, p. 308). The following information may be of interest to him regarding his request for data on the incidence of head injuries in men wearing helmets.[1]

During a period of six months in a coal mining area where 16,732 were employed 324 men voluntarily reported to the colliery medical treatment centres injuries which had occurred to that area of the head normally covered by the helmet. Of these, 299 accidents occurred underground and 34 on the surface. The wearing of helmets was virtually 100% in underground workers; it was the exception rather than the rule for those working on the surface. The distribution of accidents which occurred at the underground working place, according to the site of the head injury, was 60% frontal, 17% side, 8% back, and 16% top of the head. Surface workers had a different distribution—namely, 24% frontal, 9% side, and 68% top.

These figures demonstrate the efficiency of the helmet in protecting the top of the head. Unfortunately, the design and wearing fashion of the helmet did not give the same degree of protection to the front of the head in underground workers. The helmet will only protect the head from injury if it is worn correctly and is designed to prevent those injuries which are foreseen. It must always be regarded as a second line of defence; accident prevention must be the primary aim.

Mr. Jennett is in error when he states that V. S. Caviness's conclusions[2] were based solely on a study of first world war gunshot wounds. In the statement I quoted from reference was made to the work of W. F. Caveness,[3] who investigated 356 young adult males who sustained head injuries in the Korean war campaign. Of these, 159 had non-missile head injuries. The report deals with the occurrence of epileptic attacks in the first 8 to 11 years following head injuries. W. F. Caveness stated, "While mode of injury is an important factor in the onset of fits, there is no significant difference between missile- and non-missile-injured men as regards the cessation of fits. A common clinical impression has been that the earlier the fits take place the less likely are they to persist. This has been held especially for those fits that occur within a few hours or days after injury. Conversely, it has been thought that those attacks that begin after one year seldom cease. In the current series neither is borne out."

Because Mr. Jennett's investigations[4] were of civilian head injury cases, his views are of great importance to those assessing prognosis, and especially his statement, "Early epilepsy (within a week of injury) has a 75% chance of permanent remission, but epilepsy developing later (whether or not there has been early epilepsy) persisted in more than 80% of 200 patients followed up for more than two years after their first fit."

Knowledge that seizures may cease can be an important factor when resettling patients. Unfortunately, to many managers the word "fit" is synonymous with unemployability. The possibility that seizures can cease may prevail on them to find suitable work, especially if the injury was the result of a works accident. Reduction of status and earnings are a deterrent to a proud craftsman from accepting the usual only available employment—for example, labouring. Acceptance of this work is made more likely when management undertake to upgrade a patient to his old skills if seizures cease permanently.—I am, etc.,

R. H. P. FERNANDEZ,
Regional Medical Officer,
Bristol. Central Electricity Generating Board.

REFERENCES

[1] Fernandez, R. H. P., *Brit. J. industr. Med.*, 1964, 21, 158.
[2] Caviness, V. S., in *Head Injury Conference Proceedings*. Ed. W. F. Caveness, and A. E. Walker, 1966, p. 220, Philadelphia.
[3] Caveness, W. F., *J. Neurosurg.*, 1963, 20, 570.
[4] Jennett, W. B., *Epilepsy after Blunt Head Injuries*, 1962, London.

Recognizing Early Myxoedema

SIR,—The facial appearances of patients with well-marked myxoedema have long been familiar to clinicians, but the earliest manifestations of this are not easy to recognize.

Considering this problem recently, I realized that a personal method of assessment that I have long used might be of value to young general practitioners. (It is of no value to those seeing such patients for the first time.) It is, quite simply, the fact that on seeing such a patient my first thought has been: "Mrs. So-and-so is losing her looks."

This is most obvious in the 45–55 age group.

The woman whose face is getting plumper does not provide this thought, nor do the tragic sufferers from depression.—I am, etc.,

Leeds. A. U. MACKINNON.

Investigating Hypertension

SIR,—My letter (29 July, p. 306) was intended primarily to offer critical comment on your leading article (1 July, p. 4) which I had found not particularly helpful or informative. In that article you chose to quote Chamberlain and Gleeson's paper,[1] and I offered certain criticisms of their paper to which they have now replied (19 August, p. 495). Although they state that they "would not wish to advocate diagnostic nihilism but merely recognition of the limitations and potential dangers of a particular diagnostic technique," their comments are apt to be taken up and used as evidence against the value of aortography—as in your leading article and in recent correspondence elsewhere.[2] In my view their paper had certain limitations which should be recognized.

I share their view that the outcome of surgical treatment of hypertension may be unpredictable or disappointing—but I repeat the comment that the value of aortography should not be judged on this alone. If the procedure adds to the diagnostic data and enables one to exclude certain disorders (for example, fibromuscular dysplasia) and assists in obtaining a likely explanation for the hypertension (for example, "essential hypertension" with renal arterial anomalies) then there has been a useful gain. Further, I believe that medical management may be influenced in a number of ways by the aortographic findings—if only in providing a once-in-a-lifetime survey of the renal and intra-abdominal vascular tree and relieving the physician of the misgiving that he may be overlooking some important disorder. I have seen the sad consequences of inadequate investigation too often to feel confident in advising my patients after incomplete assessment.

Drs. Chamberlain and Gleeson chose to quote only our first and smaller series[3] in an implication that our series was somewhat unrepresentative (with a 9-to-1 male to female ratio, and two-thirds of the patients being Service personnel). The second paper which they mentioned[4] but did not quote in this context studies almost three times as many patients (341 as against 121), and 1 in 4 of the patients was female. As a matter of fact over the eight years which our unit has been working the proportion of Service to civilian patients is almost exactly 50%.

Their own work presented an interesting analysis of a retrospective study on a relatively small number of aortograms. We were not told of the period of time from which these results were collected, nor from how many hypertensive patients their 107 cases were selected—nor indeed how they were selected. Presumably since their text states "records of all aortograms were available and through these a retrospective study . . . was possible," the figure of 107 represents all patients subjected to angiography for hypertension at the Westminster Hospital since angiography was first introduced. It would be unusual if there had not been many hundreds, if not thousands, of hypertensive patients attending for advice, investigation, and treatment over this period—so my comment that their series was highly selected must stand.

Whether our own papers described a selected series of patients is not relevant to the discussion on angiography, though it might be to any discussion on hypertension. Any series is in fact initially selected by geographical, environmental, and other features—but we did describe the findings from a large number of unselected angiograms (since all patients under investigation for hypertension were angiographed) in a prospective study. This seems to me a much more acceptable method of assessing the value of the procedure.

If Dr. Chamberlain and Dr. Gleeson would care to visit our unit at any time they will be most welcome, and we would hope to show them that our work is not founded on "uncritical . . . aortography in the hope that this will provide a diagnostic answer that it is incapable of doing." Further, they would see that a large amount of evidence has accumulated over the past seven or eight years in support of our contention that renal dysplasia, often familial, is associated with much clinical disorder, including hypertension. Papers on these and other aspects of the work are in an advanced state of preparation.—I am, etc.,

P. W. ROBERTSON.

Royal Air Force Hospital,
Wolverhampton, Staffs.

REFERENCES

[1] Chamberlain, M. J., and Gleeson, J. A., *Lancet*, 1965, 1, 619.
[2] Ledingham, J. G. G., *Hosp. Med.*, 1967, 1, 1076.
[3] Robertson, P. W., Klidjian, A., Hull, D. H., Hilton, D. D., and Dyson, M. L., *Lancet*, 1962, 2, 567.
[4] —— Hull, D. H., Klidjian, A., and Dyson, M. L., *Amer. Heart J.*, 1967, 73, 296.

Progestin Therapy of Breast Cancer

SIR,—Dr. B. A. Stoll (5 August, p. 338) has to be congratulated for his very worthwhile attempt at screening the efficacy of various progestational preparations in the treatment of advanced breast cancer. The paucity of satisfactory responses in his series of seven compounds tested should not discourage the search for more effective agents. The smallest change in the chemical structure of these steroids can markedly alter their clinical efficacy. For instance, the negative impression gained in the earliest trial in this country with norethisterone oenanthate was dispelled by a very similar compound having a shorter side chain and giving improved clinical results. Similarly the addition of 5 mg. oestradiol benzoate to progesterone 50 mg. by daily injection proved successful in 7 of the 15 cases with breast cancer treated by Landau *et al.*[1]

In this department further experience was gained from the combination of progesterone (19-nor-17α-hydroxyprogesterone caproate) 100 mg., with oestradiol valerate, 30 mg. Twenty-five patients (four premenopausal) with advanced cancer of the breast in whom previous surgery, radiotherapy, oestrogens, and androgens have either failed to arrest the progress of the disease or ceased to be effective were treated with this compound for periods of one to 14 months, receiving intramuscular injections weekly, later increased to twice weekly. In 8 cases (32%) a moderate to good response was noted with regression of visible skin and glandular neoplastic infiltration, disappearance of oedema, and amelioration of general conditions. In no case, however, did the arrest of the disease last for a period longer than ten months. No untoward side-effects were noted except in one patient who did not tolerate the agent on account of nausea. A detailed report on this trial will be published shortly.

Of the possible modes of action of progestins in breast cancer listed by Dr. Stoll probably the most important—that is, the action of progestational compounds on target organs via changes in mesenchymal structures so prominent among the known effects in endometrial carcinoma—has not been mentioned.

Theorizing in the context of the rationale of treatment is very important, as none of the synthetic progestational compounds possesses all of the known properties of natural progesterone, and, since the various properties are present in varying degrees in the compounds on trial, different criteria must be employed for testing their efficacy.

In this regard, according to Swyer *et al.*,[2] in premenopausal women only the cessation of menstruation is of value to give data for a probit analysis. Other tests such as vaginal smear changes, depression of karyopyknotic index, inhibition of ovulation, etc., do not help in establishing potency ratios with fiducial limits of error. Effects on vaginal smears are not likely to be more reliable in this regard in post-menopausal women, and caution should be exercised in drawing conclusions for the selection of patients suitable for this type of hormone therapy.

Department of Radiotherapy,
General Hospital,
Northampton.

B. JOLLÈS.

REFERENCES

[1] Landau, R. L., Ehrlich, E. N., and Huggins, C., *J. Amer. med. Ass.*, 1962, **182**, 632.

[2] Swyer, G. I. M., Sebok, L., and Barns, D. F., *Proceed. Roy. Soc. Med.*, 1960, **53**, 435.

G.P.s and Health Centres

SIR,—In view of the interest in health centres, we circularized all general medical practitioners in the London Borough of Redbridge (population 248,000), asking whether they would be prepared to consider transferring their practice premises to a health centre, assuming that the proposed site of the health centre was satisfactory.

Type of Practice	No. of Replies	No. of Practices	Practices Willing to Consider Transferring Sole Surgery Whole Time	Practices Willing to Consider Transferring Main Surgery Whole Time	Practices Willing to Consider Transferring Branch Surgery Whole Time	Practices Willing to Consider Transferring Branch Surgery Initially and Main Surgery Later	Practices Unwilling to Consider Transfer	Other
Single-handed, sole premises ..	28	28	15	—	—	—	10	3
Partnership, sole premises ..	22	12	6	—	—	—	5	2
Single-handed, more than one surgery ..	3	3	—	—	—	2	—	1
Partnership, more than one surgery	20	13	—	5	4	—	4	—
Totals ..	73	56	21	5	4	2	19	6

One hundred and forty-seven questionaries were despatched and 73 replies (50%) were received. The information received is shown in the Table.

We do not claim statistical validity for the information, because we do not know the views of the 50% who did not reply. It is interesting to note, however, that 32 out of the 56 practices which replied (57%) were willing to consider some form of health-centre practice. It is possible that many of those who did not reply were unwilling to commit themselves at an early stage, but, if experience in other areas is any guide, once a health centre is built there are often requests from general practitioners to be allowed to participate.—We are, etc.,

I. GORDON.
A. SHAW.

Health and Welfare Department,
London Borough of Redbridge,
Essex.

Importance of Medical Administrators

SIR,—It would be true to say that since 1948 medical administrators at hospital level have had a very thin time, in many cases being unwanted by management committees and their posts being dispensed with by hospital boards. Those who remained, and with more than a minimal number of sessions allocated to administration, found these sessions priced at an appreciably lower level than their clinical sessions.

It is therefore encouraging to note the increasing, if tardy, recognition of the importance of medical administration and the need for appropriate remuneration and training, as expressed in the Memorandum on the Current Problems of Hospital Medical Staff (*Supplement*, 13 May, p. 93, para. 32).

Likewise, it is welcome news that the Health Departments and the professions are agreed on the importance of this work, and are united in a desire to see an increase in the number of doctors qualified by training and experience to be medical administrators, as expressed in the Joint Second Report on the Negotiations with N.H.S. Hospital Doctors and Dentists (*Supplement*, 19 August, p. 119, para. 8).—I am, etc.,

NORMAN V. WILLIAMS.

Cefn Mably Hospital
St. Mellons, nr. Cardiff.

Opportunities in British Medicine

SIR,—I read in the Australian-printed edition of the *B.M.J.* that the Ministry are to woo doctors back from overseas (15 July, p. 128). The very fact that the Australian edition exists is a pitiful commentary on the Ministry's previous efforts related to practice in Britain. After considerable experience of English general practice and lately sufficient sight of Australian practice in a town of some 40,000 people, may I offer some advice to two sections of your readers. Firstly, to any young doctors who are contemplating English general practice: Don't! Give up the idea and leave as soon as possible.

Secondly, to the Ministry officials who are going overseas: You may possibly have some success with the older migrants who have deep roots in Britain, provided that you offer them access to hospital in some reasonable form. They will, however, look at you in amazement when you explain that the immense experience they have gained overseas will be rewarded by loss of seniority.

There are some quite good administrative posts overseas, so it is to be hoped a second Ministry team is not necessary to get the first one back.—I am, etc.,

Albury, N.S.W.,
Australia.

F. W. B. BREAKEY.

Points from Letters

Temporary Residents and the Casualty Department

Dr. G. W. GRIFFITHS (Bangor, N. Wales) writes: Often in areas whose temporary population is increased owing to its popular holiday appeal patients (young and old) use the overburdened casualty/accident units as "casual surgeries." By this I mean patients (and I refer particularly to children) who are brought in with non-urgent, non-traumatic illnesses.

For this service the general practitioner claims a fee—quite rightly and properly. The poor casualty officer, however, cannot claim even a shilling—and has a further burden of responsibility to carry on his often relatively inexperienced shoulders.

Infectivity of Scabies

Dr. J. O'D. ALEXANDER (Glasgow) writes: I observe with regret that my colleague Dr. R. W. Carslaw (12 August, p. 437) has misinterpreted my remarks on the diagnosis of scabies (17 June, p. 766). I said, "Above all it depends on the constant suspicion that an itchy patient may have scabies, even though the evidence is scanty." This is not advocating the *treatment* of a case of itching as scabies without confirmation. Suspicion will make the physician even more careful in his examination. It will prompt him to look for further evidence and critically to assess what evidence he has. The risk of not diagnosing a case of scabies will be reduced. I am in entire agreement that treating all cases of itching as scabies as a blanket cover for possible errors is unwise. I would go further and say it is foolish, because it creates far more difficulties than it solves.

On the other hand, Dr. Carslaw's remarks about the infectivity of scabies should not pass without comment. I think he is perhaps stretching a point when he says that infectivity from clothing and bedclothes is a myth. Mellanby[1] showed quite clearly that there was a risk if volunteers slept in the beds previously occupied by scabetics. The risk was small (he put it at 1 in 200) but nevertheless could occur. It should not therefore be stated to be a myth.

REFERENCE

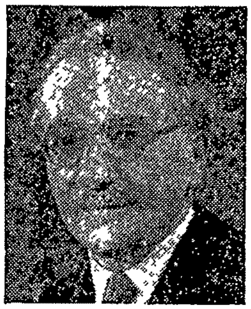
[1] Mellanby, K., *Scabies*, 1943, London.

Obituary Notices

TERENCE EAST, M.A., D.M., F.R.C.P.

Dr. C. F. T. East, formerly consultant physician and physician-in-charge of the cardiological department at King's College Hospital, and consultant physician to the Woolwich War Memorial Hospital, London, died very suddenly at his home in North Cornwall on 27 August. He was 73.

Charles Frederick Terence East, son of Dr. C. H. East, of Malvern, was born in Malvern on 20 June 1894, and was educated at Winchester and New College, Oxford. His studies were interrupted by the first world war, during which he served as lieutenant in the Northamptonshire Regiment and was twice severely wounded. After demobilization in 1918 he returned to Oxford, and graduated B.A. in 1919, winning the Welch prize, and proceeded M.A. two years later. For his clinical studies he entered King's College Hospital Medical School in 1919, having been awarded the Burney Yeo scholarship. He graduated B.M., B.Ch. in 1921, and took the Conjoint diploma the same year. He also studied at the Universities of Freiburg and Lausanne. He took the M.R.C.P. in 1922, and was awarded the Murchison scholarship by the Royal College of Physicians. After serving early house appointments at King's College Hospital, he was appointed medical registrar in 1923, and the following year was Radcliffe Travelling Fellow, University College, Oxford. In 1924 he was appointed concurrently junior physician, senior medical tutor, lecturer in morbid anatomy, and curator of the museum at King's College Hospital.


[King's College Hospital Gazette

Terence East had early developed a special interest in cardiology, and on the retirement of Dr. Harold Wiltshire in 1924 East took over the work of the department, becoming physician-in-charge. In 1931 he was appointed full physician, and in 1945 he became senior physician and director of medical studies in the medical school. He proceeded D.M. in 1927, and was elected F.R.C.P. in the same year. He also held additional appointments of consulting physician to the London County Council, the Woolwich War Memorial Hospital, and the Bute Hospital, Luton.

He was an examiner in the final B.M., for Oxford University, was a councillor of the Royal College of Physicians in 1949–50, elected censor in 1951, and senior censor in 1954. He gave the FitzPatrick lecture in 1956 and 1957, quoting freely from early authors whose works on congenital heart disease he had read in the original Latin. He gave the first Wiltshire lecture at King's College Hospital in 1960, a year after he retired, taking as his title "Forty Years of Cardiology."

Terence East was generally regarded as a somewhat lonely man, but he had a number of close friends from his student days at Oxford and King's. A physician of the old school, he paid great attention to accurately described physical signs, which enabled him to build up a diagnosis in a logical manner. He was keenly interested in teaching, and it was unfortunate that his habit of speaking in a low voice, almost as if talking to himself, enabled only those immediately around the bedside to hear what he said. There was always great competition to be his house physician, and a number of modern cardiologists owe their early interest in heart disease to him.

Sensitive and kindly, Terence was a countryman at heart. For many years he lived near Wimbledon Common, and it was his habit to walk there before breakfast to study plant and bird life. He was a keen botanist, and many King's men will remember with pleasure visits to the Chelsea Physic Garden, where he would hold forth on the properties of the "excellent herbs" grown there, with stories of those whose names were associated with them.

He retired to St. Merryn, where he could pursue his enjoyment of the pleasures of the country and watch birds, sail, read, and paint. He is survived by his wife, his daughter, and two sons.—R. S. B. P.

H. O. BLAUVELT, M.D., C.M., F.R.C.S.

Mr. H. O. Blauvelt, formerly senior surgeon to Chase Farm Hospital, Enfield, and surgeon to the North Middlesex Hospital, Edmonton, died on 7 August. He was 70.

Hugh Osmond Blauvelt was born on 18 August 1896 at Windsor, Nova Scotia, and spent his early years in Canada. He graduated M.D., C.M. from Dalhousie in 1918 and became a lieutenant in the Canadian Army. After demobilization he practised at Lockeport, Nova Scotia, for a few years and then came to England. He took the Conjoint diploma in 1927 and the F.R.C.S. in 1930.

He was appointed to a surgical post at the North Middlesex Hospital, and flourished in the progressive atmosphere where hard work was rewarded with plenty more work to do. His ascent of the professional ladder was not by any academic steps but by learning the art of surgery from leading exponents on the staff of the hospital such as Ivor Lewis, R. L. Galloway, and K. A. K. Hudson. At this time he wrote several good papers, and one of them is commemorated in Blauvelt's sign (subcutaneous fat necrosis in acute pancreatitis).

For a brief period he went to Middlesbrough as honorary assistant surgeon to the North Ormesby Hospital, but he soon returned to London to rejoin the staff at the North Middlesex Hospital as a senior member. He later moved to Chase Farm Hospital, Enfield, where he built up his surgical reputation. From his surgical colleagues in the municipal hospital service he learned his art, and he was a safe surgeon for whom mere feasibility alone was never the indication to operate. He outshone his colleagues in his ability to teach, and for years his fellowship classes were a Mecca for surgical postgraduates.

After retirement he continued to do some surgical work in the Highlands and Islands service. He enjoyed country life and fishing at Drumnadrochit, and was able to devote time to the hobby in which he excelled—wood-carving and the restoration of old furniture.

Hugh Blauvelt was a man of high principles who would take a firm stand when he thought fit. He had no enemies and was widely respected by colleagues and patients. By his death British surgery has lost a fine exponent and numerous folk in Enfield and Edmonton a trusted friend. His last short illness was clouded by the sudden loss of his wife. To his son and daughter we extend our sincere sympathy in the loss of their parents.—C. A. B.

W. K. HAMILTON, M.B., CH.B., F.R.C.S.ED.

Mr. W. K. Hamilton, former consultant ear, nose, and throat surgeon at Walsall General Hospital, and consultant ear, nose, and throat surgeon to the Guest Hospital, Dudley, and to other hospitals in the Dudley and Stourbridge group, died suddenly on 11 August, aged 67 years.

William Keith Hamilton was born in Timaru, New Zealand, on 23 December 1899. His education was interrupted by the first world war; he joined the Army at the age of 16 years, and had risen to the rank of captain when he was demobilized. He returned to New Zealand, and entered Otago University Medical School, graduating M.B., Ch.B. in 1924. Shortly afterwards he came to Edinburgh, and became a Fellow of the Royal College of Surgeons of Edinburgh in 1927. After a period in general and urological work in London he went to Oswestry, and for three years was assistant to Sir Robert Jones at the Robert Jones and Agnes Hunt Orthopaedic Hospital. He returned to New Zealand on the death of his mother, but after three years went to America for further postgraduate study, working in Chicago and at the Mayo Clinic at Rochester, New York. He then returned to England and took up the specialty of otolaryngology, studying at Golden Square Hospital, Bradford Eye and Ear Hospital, and the Royal Hospital, Wolverhampton. In February 1937 he became consultant ear, nose, and throat surgeon to the Guest Hospital, Dudley, and the Walsall General Hospital. He was a member of the British Association of Otolarygnologists and a member of the Midland Institute of Otology.

To Bill Hamilton the two things in life that mattered most were his work and his family—he was devoted to both. He was a quiet man endowed with great charm. He died suddenly while on his way to the coast of North Wales, on holiday with his family.

He leaves his widow and three children, the eldest of whom, Philip, has recently qualified as a doctor. We extend to them our deepest sympathy.—R. G. H.

L. MORRIS, M.D., F.R.C.S.

Mr. L. Morris, formerly senior orthopaedic surgeon to the Leicester group of hospitals, died at his home on 19 August. He was 67.

Leslie Morris was born on 23 June 1900, and was educated at the school in Ashton-under-Lyne where his father was headmaster. Entering Manchester University, he graduated M.B., Ch.B. in 1923, and took the Conjoint diploma the following year. In 1925 he took the F.R.C.S. The M.D., with commendation, was conferred upon him by his university in 1928 for a masterly thesis on the anatomy of the Gasserian ganglion and the treatment of fifth-nerve neuralgia by alcohol injection using the anterior approach to the ganglion. This was at the time when recognized neurologists were still employing the somewhat ineffectual lateral approach to the nerve divisions. His interest in the subject was maintained for many years, and his success with his own technique was such that patients were referred to him for treatment long after he had become established as an orthopaedic surgeon.

His Leicester appointment came after periods as assistant resident surgical officer in Manchester Royal Infirmary, and as registrar at the Royal National Orthopaedic Hospital, London. At this time he developed a lifelong admiration for Sir Robert Jones, and throughout the years Sir Robert's profile in plaster occupied a prominent place in his private consulting-room. Morris was responsible for the initiation of the orthopaedic section of the Leicester school clinic in 1930, and for its future development. In addition to his main appointments at the Royal Infirmary and the General Hospital at Leicester he was senior orthopaedic surgeon to the Kettering General Hospital, had a close association with Melton Mowbray and the Miners' Rehabilitation Centre at Higham Grange, and was an associate surgeon at Harlow Wood Orthopaedic Hospital. For many years he was the consultant surgeon to Leicester City Football Club, rarely missing a home match. He retired just over two years ago.

A conscientious surgeon whose name became a household word, Leslie was rarely late for any appointment. He was loyal and true to his friends, and a friendship once made was lasting, but to those holding a different viewpoint he could be firm and expressive without being impolite. Outside his professional work his great interests were in music, and as a collector of antiques and pottery. He played no instrument himself, but as a regular visitor to the Royal Opera House in Covent Garden with his wife, who shared his enjoyment, he had an outstanding interest in opera and the ballet. In all that he did he was sincere, and he was devoted to his family of four married daughters, his home, his garden, and to the countryside of England, especially to his beloved Cornwall. —E. R. F.

S. G. CORNER, M.A., M.D., D.O.M.S.

Dr. S. G. Corner, a former Essex ophthalmic surgeon, who had been living in Umtali, Rhodesia, since 1948, died on 27 July, aged 87.

Samuel Gordon Corner was born in Inverness of Highland parentage on 12 January 1880, and was educated at the Inverness Royal Academy. He entered Edinburgh University, and in 1902 took the M.A., his studies having been interrupted by service with the University contingent of the Imperial Yeomanry in the South African war, an episode in his life which was to leave a lasting liking for that country. In 1906 he graduated M.B., Ch.B., and after serving as house-surgeon at the Essex County Hospital, Colchester, he worked for a time in Coggeshall before moving to Chelmsford, where he settled down in general practice. He proceeded M.D. in 1910. The first world war saw him again in South Africa, this time as a captain in the R.A.M.C. After demobilization he returned to his practice in Chelmsford. Between the wars he began to specialize in ophthalmology, after which he gave up general practice. He took the D.O.M.S. in 1940, and held an honorary appointment at Moorfields Eye Hospital, London. From 1937 to 1946 he was chairman of the Mid-Essex Division of the British Medical Association. His connexion with Essex and Chelmsford lasted for over forty years.

During the second world war he volunteered for active service, but was turned down on account of age. However, he was appointed lieutenant-colonel in the medical section of the Home Guard.

About 1948 Corner moved to Umtali, in Southern Rhodesia, where he continued to do ophthalmic work, and he lived there until his death. He had been a keen shot in his early days (he even carried his shotgun to the South African war), and was a good golfer. All his life he had a love for natural history and botany, the basis of which was laid in open-air studies in Inverness and the Highlands. On his last visit home he was very pleased when the director of the Edinburgh Botanic Gardens accepted a collection of plants made on his tours of Rhodesia. His house was full of memories of Essex and Scotland, and was frequently visited by Essex people who had settled in Rhodesia. He married Miss Gladys Benham, of Colchester, who died in 1928. He is survived by his daughter and by his son.—Wm. C.

J. T. W. writes: Sam Corner came to Chelmsford about 1912, and established himself successfully as a general practitioner. He was exceedingly generous to the younger men, and purposely cultivated a delightful habit of calculated forgetfulness. His patients all adored him, and he was always at their beck and call. His hobbies were books and golf, and, on his holidays in his native Scotland, fishing. A man much loved and admired by us all in Chelmsford, he retired from his work in Essex after the inception of the National Health Service and went to live with his daughter in Rhodesia, where he continued to work as an ophthalmologist.

W. J. ADAM, M.B., CH.B.

Dr. W. J. Adam, for many years in general practice in Marden, Kent, died in Eastbourne on 24 July. He was 71.

William James Adam was born in Aberdeen, the third son of Dr. Wilson Adam, who practised in Crown Street, Aberdeen. He was educated at Robert Gordon's College and at Aberdeen University. His medical studies were interrupted by the first world war and he saw service as an ambulance driver in Mesopotamia. After the armistice he returned to Aberdeen and graduated M.B., Ch.B. in 1922. For six years he acted as assistant to Dr. Oliphant in Bucksburn, Aberdeen, then obtained his own practice in Marden in 1928, where he remained until his retirement in 1958.

Dr. Adam had many of the attributes that make for success in family practice—a deep understanding of people and of the effects that illness could have upon them and their families, an unerring ability to tell when patients—especially children—were really ill and required assistance beyond what he could give, an easy manner and capacity to deal happily with patients from all social classes, and a deep knowledge of the community in which he worked. During the last war he held the rank of captain in the R.A.M.C. and was responsible for the medical training of Home Guards and Red Cross personnel in the Marden area. In his retirement he turned to gardening and philately, building up a large and carefully selected collection of stamps. Dr. Adam is survived by his wife.—J. K. R.

D. M. FORSTER, M.B., CH.B.

Dr. D. M. Forster, formerly in general practice in Brownhills, Staffordshire, died at his home on 21 June. He was 54.

Donald Makepeace Forster was born in Exeter on 9 April 1913, and was educated at Dudley Grammar School and at Birmingham University Medical School, graduating M.B., Ch.B. in 1940 and qualifying with the Conjoint diploma in the same year. After holding house appointments at the Queen's Hospital, Birmingham, he entered the Indian Medical Service with the rank of captain. In 1942 he married Miss E. M. Murdoch, and four years later joined Drs. Bradford and Patterson in practice at Brownhills. In addition to his duties as a general practitioner he became honorary divisional surgeon to the St. John Ambulance Brigade and police surgeon to the Brownhills subdivision of the Staffordshire County Constabulary. He was a founder member of the Brownhills Rotary Club and later its president in 1961–2. He was elected chairman of the Walsall Division of the British Medical Association in 1966.

Dr. Forster was a friendly and instantly likable man, whose qualities of kindness and good humour became even more evident on closer acquaintance. He had an active and inquiring mind, which he applied not only to his daily work but to all medical affairs and to his varied hobbies. In addition to being a keen fisherman he also interested himself in photography, music, and electronics, and in 1958 won first prize in the electrical section of the doctors' hobbies exhibition by building an electronic organ. He will be greatly missed by his patients, of whom he took such thoughtful care, never sparing his own health in order to look after theirs. His colleagues all regarded him with affection, and admired in him the rare qualities which made him a family doctor of such high calibre.

He is survived by his widow, a son recently qualified in medicine, and a daughter, to whom we extend our sympathy.—J. P. L.

J. C. WILLIAMS, L.M.S.S.A.

Dr. J. C. Williams, a former medical officer to the British Shipping Federation, died in London on 13 July. He was 62.

John Claude Williams was born in Cape Town on 12 August 1904, and was educated at Malvern College and Worcester College, Oxford. He became a licentiate in medicine and surgery of the Society of Apothecaries of London in 1933, and was elected to the Livery of the Society of Apothecaries in 1935. He set up in private practice in Devonshire Street, London, where many eminent personalities became his patients. The outbreak of the second world war found him in the U.S.A. He returned immediately, booking the first available passage home to join the Emergency River Service. For the last two or three years of the war he was medical officer in one of H.M. cable-laying ships, and although he was never forthcoming about his exploits either to members of his family or to his friends, he took part in at least one memorable attempt to sail a disabled tanker back to the United Kingdom. After the war he joined the Prison Service as a medical officer, and was concerned with the Heath, Haigh, and Christie trials. He found the strain of this work, and attendances at executions, too much for him, and after resigning from the service he joined the British Shipping Federation as a medical officer, where he remained until his health failed, and he was able only to manage an occasional locum.

He had a wide circle of friends who enjoyed his unfailing sense of humour. He will be sadly missed by all those who knew him. He died a bachelor.—P. A. W.

G. J. MURRAY, M.D., M.R.C.P. D.T.M.&H.

Dr. G. J. Murray, senior physician at Hexham General Hospital, died on 10 August, at the age of 57.

Gerard John Murray was born on 9 December 1909, at Blackhill, Co. Durham, and was the elder son of Dr. John Murray, a well-known general practitioner. He received his education at St. Joseph's College, Dumfries, and later at the medical school of Durham University at Newcastle upon Tyne, graduating in 1932 with second-class honours, and proceeding M.D. two years later. He spent the next five years in various hospital appointments, and in 1937 he joined the Colonial Medical Service and spent two years in Uganda. During his student days he had, like several of his friends, joined the R.N.V.R., and at the outbreak of the second world war he was mobilized, and spent the next six years with the Royal Navy, serving in the hospital ship *Oxfordshire* as pathologist, with the rank of surgeon lieutenant-commander. Later he was attached to the Wentworth Hospital in Durban, and finally to the Royal Naval Hospital at Newton Abbot, Devon, and while there was admitted M.R.C.P. in 1943. On demobilization he came to Newcastle, and became a medical registrar at the Royal Victoria Infirmary, but his previous experience abroad seemed to develop a restlessness in his nature and he joined the Esso Oil Company as chief medical officer, and travelled extensively. He took the D.T.M.&H. in 1946. With the inception of the National Health Service in 1948 he was appointed physician-in-charge to the Hexham group of hospitals in Northumberland.

I was privileged to know Gerry Murray very well. Our friendship began in the early days of our undergraduate training, and continued throughout the years. As visiting paediatrician to his hospital I saw him regularly, and we discussed paediatric and other problems with mutual interest and enjoyment. He was a very capable and kind doctor; his manner was always serene and calm, and he never appeared to be ruffled, even in the most urgent situations. He was always accessible to his medical and nursing staff alike. In his student days he was a very good all-round sportsman, but the demands of his work restricted these pursuits, although he did find time occasionally to continue with his latter sport of yachting, especially at Bassenthwaite.

In the past few years he was dogged persistently by ill-health, which he bore with great patience and fortitude. A man of strong religious convictions, his faith was a source of great comfort and strength to him. Towards the end of his life he was almost completely disabled, and yet there appeared to be no rancour, but the calm acceptance of fate. He was indeed a gentle man. To his wife and family, who formed such a happy unit, we extend our deepest sympathy.—E. G. B.

M. L. KAIN, M.D.

Dr. M. L. Kain, an American anaesthetist engaged on research training at the University of Leeds, his wife and son, together with his wife's parents, were killed instantly in a motor accident in Holland on 9 August. He was 27.

Martin Lee Kain was born in 1940, and graduated M.D. in 1963 from the University of Chicago. He was an intern at the Mary Hitchcock Memorial Hospital in Hanover, New Hampshire, after which he proceeded to a two-year residency in anaesthesiology at the Presbyterian Hospital, New York, under Dr. E. M. Papper. He then sought a formal training in research, and was perhaps the first American anaesthetist to do so in England. In June 1966, he came to the department of anaesthesia of the University of Leeds, and registered as a Ph.D. student. His wife had her Master's degree in history, and she also registered as a Ph.D. student in the department of modern history of the same university.

At an early stage of his career it was apparent that Martin Kain was a man of exceptional ability. He had set his sights on a career in academic anaesthesia, and his talents were well suited to this. He was highly intelligent, had a quick mind, and an immense capacity for sustained hard work. He soon grasped the fundamentals of experimental design, and at an early stage was initiating his own studies. He was a competent linguist, fluent in German, and well versed in Russian, Spanish, French, and Italian. He will be well known to many for his published translation of one of the classical papers of von Neergaard and Wirz. He was also an amateur musician, and played regularly in a string quartet. Dr. Kain combined his exceptional talents with a delightful personality. His courtesy never left him, and his ability was unusually concealed beneath an exterior of genuine modesty, with his cheerful and easy manner giving little hint of his acute perception.

Those who knew Martin Kain in this country have experienced a tremendous personal loss. However, their loss is no greater than that of anaesthesia as a whole. The specialty has lost a man who was surely destined to be an international leader in the years to come. His many friends in this country extend their deepest sympathy to his parents, and to the relatives of all those concerned in this tragic accident.—J. F. N.

E. B. VERNEY, M.A., M.D., F.R.C.P. F.R.S.

G. B. writes: When Basil Verney (obituary, 2 September, p. 621) came to St. Bartholomew's from Cambridge for his clinical work he soon came under the influence of that remarkable teacher Dr. J. H. Drysdale, and this influence was apparent throughout his professional and personal career. The brilliance of his laboratory work, both in conception and in technique, is a matter for others to assess. Sufficient it is to mention that he made a unique contribution to the understanding of the mechanisms controlling the secretion of pituitary hormones concerned in urinary excretion.

He was a firm opponent of intellectual compromise and a champion of scientific truth, for which he would have fought to the death. He was once sued by the antivivisectionists for cruelty, but was entirely vindicated. There hung in his laboratory for years a framed and faded poster from the *Star*: "Professor *v.* Dog Result," a cherished souvenir.

As an examiner in pharmacology for the third M.B. he gained a reputation for strictness. He was strict, but only to the point of affirming that a candidate must know the dangers to his patients of drugs and measures, and never to the extent of insisting upon a knowledge of irrelevant minutiae.

When Verney became house-physician at Shadwell I was physician there, and Ruth Conway was resident medical officer and Basil's senior. This collaboration had a happy outcome, for they later became engaged, and I had the pleasure of being best man at their wedding, the first milestone in a long and valuable friendship. Through all the years since, a scintillating characteristic of Basil's companionship has been a keen sense of humour, never far from the surface.

A modest man, retiring by disposition, he never hungered after money or worldly status. He bore through life the shining grace of a personality true to the uttermost depth, and to have known him was a privilege and a joy.

News and Notes

EPIDEMIOLOGY

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **19 August** (No. 33) and corresponding week 1966.

Figures of *cases* are for the countries shown and for Greater London. Figures of *deaths* and *births* are for the whole of England and Wales (London included). Greater London, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0		0	0	0	0	
Dysentery ..	253	35	42	2	3	278	71	70	4	5
Encephalitis, acute ..	0	0		0		1	0		0	
Enteric fever: Typhoid ..	4	1	1	0		3	0	3	0	
Paratyphoid	7	0	0	0		4	0	0	0	
Food-poisoning	191	41	41	4		133	31	6	11	
Infective enteritis or diarrhoea under 2 years				13	44				12	52
Measles* ..	2,643	185	6	32	67	6,930	828	55	50	81
Meningococcal infection ..	4	0	1	1		8	1	3	1	
Ophthalmia neonatorum	3	0	1	0		14	3	0	0	
Pneumonia† ..	80	6	46	0	1	67	8	59	2	
Poliomyelitis, acute: Paralytic ..	1	0	0	0		1	1	0	0	
Non-paralytic	0	0	0			0	0	0		
Puerperal fever§	70	24	1	0		108	51	9	0	
Scarlet fever ..	132	21	5	8	7	194	23	8	0	5
Tuberculosis: Respiratory ..	208	43	26	2		219	45	42	5	
Non-respiratory ..	55	10	11	2		48	12	10	6	
Whooping-cough	840	125	61	6	72	446	57	39	12	14

DEATHS	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0		0	0	0	0		0		0
Dysentery ..	0	0		0		0	0			
Encephalitis, acute ..					0					0
Enteric fever ..	0	0	0	0		0	0	0		
Infective enteritis or diarrhoea under 2 years	3	0	0	0	1	4	0	0		0
Influenza ..	4	2	0	0	0	2	0	0		0
Measles ..	0		0	0	0	0		0		0
Meningococcal infection ..			0					0		
Pneumonia ..	497	92	17	13	4	527	92	16		10
Poliomyelitis, acute ..	0	0		0	0	0	0			0
Scarlet fever ..	0		0	0	0	0		0		0
Tuberculosis: Respiratory ..	39	8	3	0	2	40	4	1		0
Non-respiratory ..				0	1					0
Whooping-cough	2	0	0	0	0	3	0	0		0
Deaths 0–1 year	250	51	16	8	7	250	43	22		6
Deaths (excluding stillbirths)	8,670	1354	494	104	187	9,048	1430	559		117
LIVE BIRTHS	15,364	2566	883	261	385	16,135	2755	892		401
STILLBIRTHS	207	26	11			240	49	19		

* Measles not notifiable in Scotland, whence returns are approximate. † Includes primary and influenzal pneumonia. § Includes puerperal pyrexia.

MEDICAL NEWS

First Woman President

Dame KATHLEEN LONSDALE, F.R.S., has been elected president of the British Association for the Advancement of Science. She will preside at next year's annual meeting. Dame Kathleen is professor of chemistry and head of the department of crystallography at University College, London.

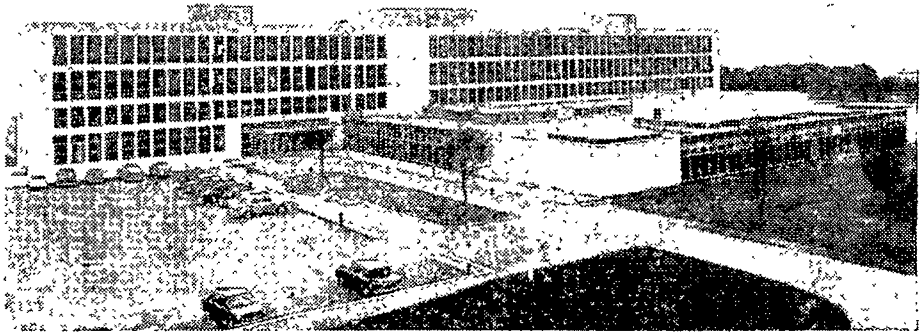
Sir PETER MEDAWAR, F.R.S., director of the National Institute for Medical Research, has been nominated president-elect of the association for 1968–9.

Postgraduate Medical Education

At a meeting on 21 July the Central Committee on Postgraduate Medical Education (see *B.M.J.*, 24 June, p. 833) incorporated "(Great Britain)" in its title, in recognition of its concern with Scotland as well as England and Wales. It decided to invite a representative of the Royal Medico-Psychological Association to attend its meetings. A preliminary paper bringing together members' views on the organization of post-registration training (the first three years) was discussed. The Committee agreed to invite the Ministry of Health to send representatives to the next meeting to consider the relation of postgraduate training to the career structure of the hospital service.

New Plastic Surgery Unit

A plastic and reconstructive surgery unit, which has cost about £1m. to build and equip, was opened last week at Canniesburn, Glasgow. It consists of a main block containing wards, outpatient department, staff and lecture rooms, and an adjoining single-storey area with operating-theatres and dental, *x*-ray, and other special departments. There are 138 beds. Facilities include four in-patient theatres with intensive care unit, an outpatient theatre and day-stay ward, maxillofacial department, and suite of consulting-rooms. Provision is made for research. The unit is designed to ensure privacy. For



patients arriving by ambulance a special reception department with direct access to the wards has been provided at the rear of the building. The completion of the project brings together facilities hitherto spread throughout the region.

Psychotropic Drugs

The Committee on Safety of Drugs published its sixth note in the adverse reaction series on 8 September. It draws attention to the large number of prescriptions for psychotropic drugs—43 million were issued by general practitioners in the N.H.S. during the three years ending June 1967—and states that 1,200 reports of suspected adverse reactions to these drugs, with 91 deaths, were received in the three-year period.

History of Medicine

The sixth British congress on the history of medicine was held from 6 to 9 September at the University of Sussex, Brighton. The theme was "Medicine and Science in the 1860s." At the inaugural session an address was given by Dr. DOUGLAS GUTHRIE, president of the British Society for the History of Medicine. An exhibition of illustrations, arranged by the Wellcome Historical Medical Museum and Library, was on view throughout the congress.

Health Services in Scotland

Expenditure on the National Health Service in Scotland has risen about 52% in the last 10 years according to the 1966 report of the Health and Welfare Services (H.M.S.O., Cmnd. 3337, 9s.) In 1965–6 the gross cost of the Service was about £145m., compared with £130m. in the previous year. Excluding capital expenditure, the cost of the hospital and specialist services was £78m., an increase of £7m. The hospital building programme "maintained its impetus," the total capital investment in hospitals being nearly £10m.

In 1966 the birth rate (18.6 per 1,000 population) was the lowest since 1956. The illegitimate live birth rate rose to 6.4% (provisional), the highest recorded since 1946. Stillbirths fell by 246, giving the lowest stillbirth rate so far recorded (16.2 per 1,000 total births). The infant mortality rate (23.2 per 1,000 live births) was slightly higher than the record low rate in 1965 (23.1). In 25 local authority areas fewer than 10% of births took place at home, and in 21 other areas fewer than 20% of births were home confinements. The total number of births in these 46 areas accounted for 90% of the total births in the country.

Deaths from lung cancer rose from 3,009 in 1964 to 3,120 in 1965, the increase among women being proportionately greater. Bronchitis accounted for 2,066 male deaths (83 per 100,000) and 788 female deaths (29 per 100,000). The figures were little better than the all-time high of 2,171 and 881 respectively recorded in 1963. The report notes "disquieting trends" in the admission of people suffering from the effects of poisons, usually self-administered. By far the largest increase occurred among young women. A tendency towards an increase in cases of otitis media and mastoiditis is noted.

Expenditure on mental health continued to rise more rapidly than in any other field of local authority health and welfare work during 1965–6, with an increase of 28% over the preceding year. The number of patients admitted to mental hospitals with a diagnosis of alcoholism was the highest recorded (2,755). According to the report more than a quarter of all male admissions to mental hospitals are for alcoholism.

Hospital geriatric services are stated to have been increased, with special emphasis on rehabilitation and return to life in the community. Residential accommodation in local authority welfare homes rose from 7,428 places at the beginning of 1966 to 7,639 places at the end of the year.

Between October 1965 and September 1966 640,950 patients were discharged from N.H.S. hospitals. This was 10.9% more than in 1960–1. The average weekly cost per inpatient was £23 5s. 5d., compared with £21 4s. 1d. in the previous year, and the average length of stay for each period of treatment was 31 days.

The number of principals providing general medical services was 2,594, compared with 2,618 at the end of 1965. As a result, the average number of patients in each doctor's list rose from 2,066 to 2,089. At September 1966 3,478 doctors were employed in hospitals, compared with 3,118 in 1961, an increase of 11.6% in five years. There were 1,335 consultants, an increase of 32.5% in the same five-year period. The number of nurses and midwives was higher than ever before.

In 1966 27.53m. prescriptions were dispensed, an increase of 7.5% over the figure for the previous year.

Appendices to the report give details of research programmes supported by Exchequer funds, of hospital building schemes completed and in progress, and statistical tables.

News in Brief

The provisions of the Road Safety Act referring to drink and driving will come into force on 9 October.

Grants and Awards

Grants for research projects at Glasgow University include £9,000 from the British Empire Cancer Campaign for Research for work in the biochemistry department and £7,500 from the Tobacco Research Council for research in the department of medical cardiology, Royal Infirmary, into smoking and lipid metabolism.

Coming Events

Davos Medical Association.—International symposium on tuberculosis, climate, asthma, and chronic bronchitis, 8–10 October, Davos. Conference fee about £3. Applications by 15 September.

Systematic Course in Psychological Medicine and Related Basic Sciences 1967–8.—Designed to provide instruction for Parts 1 and 2 of the D.P.M., starts 21 September. Details from Physician Superintendent, Runwell Hospital, Wickford, Essex.

Norfolk and Norwich Institute for Medical Education.—Symposium on pitfalls in rheumatic disease, 23 September, St. Michael's Hospital, Aylsham. Course recognized by Cambridge University Postgraduate Medical School for purposes of allowances to general practitioners.

Chemotherapy of Tuberculosis in Developing Countries.—Symposium sponsored by Smith and Nephew Associated Companies Ltd., 25–27 September, Royal College of Surgeons of England, Lincoln's Inn Fields, London W.C.2. Attendance is primarily limited to those with special knowledge of treatment of tuberculosis overseas, but further information can be obtained from Mr. E. M. BAVIN, Smith and Nephew Research Ltd., Gilston Park, Harlow, Essex.

King's College Hospital Medical School.—Inaugural address by Sir BASIL SPENCE, O.M., 29 September, 2.30 for 3 p.m., Medical School, Denmark Hill, London S.E.5.

King Edward's Hospital Fund for London.—Conference, "Estimating the Needs for Hospital Beds," 18 October, Hospital Centre, 24 Nutford Place, London W.1. Fee £1. Completed application forms by 6 October. This conference is the first of a series of three on making better use of hospital resources.

Societies and Lectures

For attending lectures marked ● a fee is charged or a ticket is required. Applications should be made first to the institution concerned.

Monday, 11 September

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 5.30 p.m., clinical meeting.

KINGSTON-UPON-THAMES MEDICAL CENTRE.—5.15 p.m., Dr. M. E. A. Powell: Slide Seminar—Breast.●

Tuesday, 12 September

B.B.C. 2 TELEVISION.—1.15 p.m., medicine today: Fits (sponsored by A.S.M.E.).

KINGSTON-UPON-THAMES MEDICAL CENTRE.—1 p.m., Dr. W. E. Medd: "Sandwich" Seminar—Pulmonary Infarction (a tape recording).

ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Mr. L. C. Oliver: Head Injuries.

WEXHAM PARK HOSPITAL, SLOUGH.—At Lecture Room, School of Nursing, 8.45 p.m., Mr. A. H. C. Ratcliff: Fractures of the Femoral Neck in Children.

Wednesday, 13 September

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 12 noon, surgical meeting (buffet lunch).

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Queen Charlotte's Hospital, 2 p.m., Mr. S. Davidson: Diabetes in Pregnancy.●

ROYAL FREE HOSPITAL.—5.15 p.m., Dr. C. Merskey (New York): Thrombosis, Defibrination and Fibrinolysis.

Friday, 15 September

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. J. R. Bignall: clinical demonstration.

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Chelsea Hospital for Women, 3 p.m., Mr. D. M. Wallace: Cystoscopy and the Gynaecologist.●

Deaths

Laing.—On 27 August 1967, John Kidd Collier Laing, M.B., B.S., D.P.M., of 37 Heathclose Road, Dartford, Kent, aged 76.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON W.C.1. TELEPHONE: 01-387 4499. TELEGRAMS: *Aitiology, London W.C.1.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs.

ADVERTISEMENT AND SUBSCRIPTION ORDERS should be addressed to The Manager at B.M.A. House, London, or at 415 Bourke Street, Melbourne, Victoria, Australia.

MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the British Medical Association, B.M.A. House, London, or to the Scottish Secretary, B.M.A. Scottish Office, Drumsheugh Gardens, Edinburgh.

BRITISH MEDICAL JOURNAL

LONDON SATURDAY 16 SEPTEMBER 1967

Pointers

School Record Collated with Obstetrical History: Only five of the obstetrical complications considered by Drs. D. J. P. Barker and J. H. Edwards appeared to affect intellectual performance in 50,000 children studied in Birmingham, and impairment was slight. Multiple births were excluded (p. 695).

Importance of the Paraproteins: Dr. J. R. Hobbs finds that observing the level over years can aid in diagnosis of malignancy in doubtful cases (p. 699).

Lymphocytes in Hodgkin's Disease: Transformation response found to be low irrespective of therapy, but cells with anomalous chromosomes were attributable to radiation, and changes were not specific to Hodgkin's disease, according to Dr. Sylvia D. Lawler and colleagues (p. 704).

Hazard of Mushroom Cultivation: Dr. A. Sakula describes four patients with respiratory symptoms and miliary mottling on chest *x*-ray which cleared on removal from the environment (p. 708). Leader at p. 691.

Iron and Anaemia: Dr. R. H. Davis and colleagues found no relation between iron intake and haematological status in normal subjects, and concluded that iron loss is the determinant factor in haemoglobin levels (p. 711).

Acro-osteolysis: Raynaud's phenomenon and osteolysis of terminal phalanges reported in two workers dealing with polyvinyl chloride by Drs. D. K. Harris and W. G. F. Adams (p. 712).

Sickling and HbO: Two siblings showing both traits reported from the Sudan by Drs. S. A. Ibrahim and D. Mustafa (p. 715).

New Spirochaetosis: Drs. W. A. Harland and F. D. Lee describe 10 cases of spirochaetal infection of intestine (p. 718).

Weed-killer Death: Fatal poisoning from paraquat reported by Drs. Ch. Almog and E. Tal (p. 721). Leader, p. 690.

Further Case Reports: Volvulus of small intestine (p. 719). Trophoblastic activity as precipitating cause of pre-eclampsia (p. 720). Treatment of allergy to insulin (p. 722). Fragmentation of blood column in retinal vessels (p. 722). Avulsion of uterine fibroid (p. 723).

The Occasional Fit: Article supplementing television programme seen on 12 September and to be repeated on 19 September on B.B.C. 1. (p. 725).

Left-over Drugs: Dr. W. A. Nicholson reports on some 43,000 tablets collected from private houses (p. 730).

Legislation on Drugs: Summary of Government's White Paper (p. 734). Leader this page.

Vocational Training for General Practice: Summary of Advisory Committee's conclusions (*Supplement*, p. 129).

Control of Drugs

The great potency of many drugs now in common use has meant that against the benefit they offer must continually be weighed the risk they bear. Only last week the Dunlop Committee on Safety of Drugs drew attention to adverse reactions to psychotropic drugs (tranquillizers and antidepressants).[1] In the three years to June 1967, during which general practitioners had written 43,000,000 prescriptions for drugs in this group, the Committee had received over 1,200 reports of suspected adverse reactions to them, including 91 that were fatal. The Dunlop Committee itself came into existence on the recommendation of a joint subcommittee of the English and Scottish Standing Medical Advisory Committees set up after the thalidomide tragedy. And it has been the unanimous view of both the medical and pharmaceutical professions that it has carried out its task in exemplary fashion.

Now the Government's White Paper discussing forthcoming legislation on drugs and medicines[2] foreshadows substantial extensions of statutory measures to control their manufacture, import, quality, testing, and marketing. A brief summary of it is given at page 734. The Government proposes to set up a Medicines Commission. This body would advise the Ministers of Health and Agriculture on matters of policy, on the " pattern of expert committees " and their terms of reference, and on important technical points of principle in connexion with licensing, and it would be responsible for the preparation of the *British Pharmacopoeia* (instead of the General Medical Council). The Commission is to be " kept to a reasonable size," and its members will be appointed by the Minister after consultation with appropriate organizations. These would include the Royal Colleges, the G.M.C., the Medical Research Council, and the B.M.A., as well as bodies representing the veterinary surgeons and the pharmaceutical industry. A licence will be required for the marketing, importation, or manufacture of drugs, and for wholesale dealing in them, and the authority for licensing will rest with the Ministers of Health and Agriculture.

Nor does the Government intend to stop at controlling the manufacture and distribution of drugs, for the Ministers will also be empowered to make regulations controlling the advertising of them—to the general public, as at present, but in addition to professional audiences. " The content, format, and manner of presentation of advertisements for drugs " is to be within the scope of the proposed legislation, so that " those to whom the advertisement is directed are given adequate information about the drug."

In saying that the voluntary system, which is in operation at present, " has had the full support of the pharmaceutical industry and the medical and pharmaceutical professions " the White Paper is doing no more than endorse the annual reports issued by the Dunlop Committee and express the views of medical men and drug manufacturers. In fact the system has functioned exceedingly well, partly because the Committee, in addition to working with commendable efficiency, is an independent body that all

© *British Medical Journal*, 1967. All reproduction rights reserved.

concerned are confident to trust, partly because the absence of bureaucratic control has enabled advice and decisions to be given quickly, and, if necessary, informally. Why then does the Government now consider that statutory backing " would give greater reassurance and should not be further delayed " ? One reason advanced is that the Dunlop Committee itself has said it believed " the arrangements ought to be given permanence within the framework of legislation."[3] But it seems very questionable whether the Committee, in suggesting further statutory backing, had in mind anything like the all-pervasive Governmental control now proposed. A second reason for introducing the new legislation is that it is " believed to be broadly compatible with the arrangements " that will be laid down for the European Economic Community under the Treaty of Rome—that is, the Common Market. But, since other arrangements might be equally compatible, the ones set out in the White Paper should not be regarded as the last word in that respect.

That thorough checks on the manufacture and marketing of drugs are needed must be beyond dispute. At present they are satisfactorily exercised by the pharmaceutical industry in the course of research and manufacture, by the Dunlop Committee, and by the doctors who test and prescribe drugs. Despite the White Paper's expressed intention " to retain the flexible administration that has been so effective under the voluntary scheme," the ability of this or any Government to carry it out must arouse misgivings. Bureaucratic control rarely allows flexible administration. Nor is it clear how a system that vests in a Minister, a member of a political party, such complete control over the development and supply of drugs can command the confidence that the Dunlop Committee enjoys.

Some indication, perhaps no more, of the way the wind is blowing may be noted in the White Paper's remarks on the *British Pharmacopoeia*—to be taken over from the G.M.C. by the proposed Medicines Commission. " It is not intended," says the White Paper, " to prohibit the publication by other bodies of similar compendia . . . but as the scope of the compendia prepared under the aegis of the Commission widens, the scope of other compendia might diminish." The difficulty is to prevent much more than the scope of " compendia " from diminishing when control becomes centralized in Whitehall. The great danger is a deadening of the impulse to research that has revolutionized therapeutics in the last 30 years.

---

[1] *Brit. med. J.*, 1967, **3**, 688.

[2] *Forthcoming Legislation on the Safety, Quality and Description of Drugs and Medicines.* Cmnd. 3395. 1967. H.M.S.O.

[3] Committee on Safety of Drugs, *Report for the Year Ended 31 December 1965.* 1966. H.M.S.O.

Poisoning from Paraquat

The question of differentiating " toxicity " from " hazard " is no more clearly illustrated than in the case of the herbicide paraquat (1,1′ dimethyl-4,4′-dipyridilium). In Great Britain there has been no death among people occupationally exposed to pesticides since 1953, and in each year fewer than 20 cases of poisoning are reported to the Ministry of Agriculture by their vigilant inspectors. These reported cases are mostly trivial—rashes or the effects of splashes in the eye—with one or two cases of systemic poisoning.[1]

The dipyridilium herbicides are a British invention, which could in some circumstances revolutionize agriculture by removing the need for the plough. The herbicides of this group act immediately on plants and are inactivated on coming into contact with soil. They are widely used for general control of weeds among plantation crops in Britain and overseas, and also for defoliation to facilitate harvesting of crops like cotton and potatoes. Workers applying these substances have sometimes suffered some nose bleeding owing to inhalation of spray droplets, but nothing more serious. The extraordinary activity of these compounds as weedkillers has led on several occasions to the illicit removal of concentrates from bulk and their diversion to private hands in small containers. When the container was a beer bottle two casualties resulted,[2] and other similar cases have been reported to the manufacturer.

At page 721 of the *B.M.J.* this week Drs. Ch. Almog and E. Tal record an unusual case of suicide by the subcutaneous injection of a 20% solution of paraquat. Animal experiments indicate that once absorbed into the body above a certain dose paraquat induces an irreversible disease process[3] despite the fact that over 90% is excreted within 24 hours.[4] The disease process—a cellular proliferation of the lungs—develops remorselessly and seems to represent a progressive chronic inflammation. Only paraquat does this. The pathogenesis of this lesion requires further study, and from work already published it is clear that the manufacturers of the herbicide are devoting considerable efforts to discovering more about its mode of action on the mammalian cell.

Meanwhile what sort of hazard does such a compound present ? Repeated small doses have no effect on laboratory animals, and repeated exposure seems to have no effect on agricultural workers, except that local irritation may occur after prolonged contamination of the skin. Yet the accidental ingestion of a single small quantity can provoke a fatal disease within two to three weeks. The only case known so far in which ingestion did not result in death is one in which a man swallowed the contents of the home garden pack of Weedol, containing 2.8 g. of paraquat formulated as granules.[5] Clearly a few drops from a watering-can containing this weedkiller are not likely to be dangerous to the suburban gardener. Nevertheless, the concentrate as issued to farmers and market gardeners can be very dangerous in a way that may mislead doctors owing to the delay in the onset of its effects. In a recent case (unreported) a child drank from a Coca Cola bottle in which its parent had put some paraquat illicitly obtained from a market garden. The child appeared to recover from the acute effects, was sent home, but died two weeks later.

Many modern herbicides have a very low acute toxicity to man. The immediate effects of paraquat are mild, but fatal poisoning may be delayed in onset. In any case of suspected suicide or accidental poisoning from swallowing of a weed-killer the doctor would be well advised to make certain that the preparation was not a dipyridyl type of herbicide before assuming that an early recovery from poisoning will be permanent. A sample of urine should be analysed as soon as possible, and if this shows that the patient has absorbed any significant amount of paraquat he should be treated, in the absence of any known specific measures, on general principles. These would include stomach wash-out and the promotion of diuresis by mannitol. If there are signs of renal failure, dialysis should be considered. Unfortunately no treatment has yet been found effective once the lung lesions develop.

---

[1] Ministry of Agriculture, Fisheries, and Food. *Reports on Safety, Health, Welfare and Wages in Agriculture,* 1961–1965. H.M.S.O.

[2] Bullivant, C. M., *Brit. med. J.*, 1966, **1**, 1272.

[3] Clark, D. G., McElligott, T. F., and Hurst, E. W., *Brit. J. industr. Med.*, 1966, **23**, 126.

[4] Daniel, J. M., and Gage, J. C., ibid., 1966, **23**, 133.

[5] Unpublished information.

Allergic Alveolitis

Mushroom-worker's lung, like bird-fancier's lung,[1] is one of a group of pulmonary allergic diseases due to inhaled organic dusts, for which the term "extrinsic allergic alveolitis" has been suggested. Farmer's lung is the classical example.

The inhalation of organic dusts may cause two main forms of allergic disease, affecting either the bronchi, with the production of asthma, or the peripheral lung tissues, with the production of a mainly alveolar reaction. An analysis[2] of the factors which determine these important differences shows that atopic persons give bronchial asthmatic reactions which are mediated by non-precipitating, reaginic antibody (type I allergy[3]), whereas non-atopic persons give predominantly alveolar reactions, provided the dust particles are small enough to penetrate to the alveoli. These reactions are mediated by precipitating antibody (type III allergy[3]).

Many organic dusts cause allergic alveolitis. The diseases include farmer's lung,[4] bagassosis,[5] maple-bark disease due to the fungus *Cryptostroma corticale*,[6] lung disease due to the grain weevil *Sitophilus granarius*,[7] bird-fancier's lung due to avian antigens,[8] and pituitary snuff-taker's lung due to porcine and bovine posterior pituitary powder.[9] In the *B.M.J.* this week (page 708) Dr. Alex Sakula adds another—namely, mushroom-worker's lung, due to actinomycetes that flourish in hot, damp vegetable matter. In all of these diseases precipitins have been found in the serum against the relevant antigens. Other similar diseases in which precipitins have either not yet been found or not certainly identified include suberosis due to cork dust, paprika-splitter's lung, smallpox-handler's lung,[10] and the chronic lung disease of New Guinea natives attributed to dust from thatched roofs.[11]

Extrinsic allergic alveolitis, whatever its cause, has a common pattern of clinical symptoms, all of them present in the patients suffering from mushroom-worker's lung. They are entirely different from the wheezing of the asthmatic patient, in whom pulmonary function tests show airways obstruction. Systemic reactions are an important feature of allergic alveolitis, and may consist of fever, chills, and malaise, with aches and pains, followed by a marked loss of weight. The pulmonary symptoms and signs are those of a chiefly alveolar reaction. They consist of cough, and of dyspnoea, which is often severe and out of proportion to the paucity of the crepitant rales which may be heard. Tests of pulmonary function show a restrictive defect, with impairment of gas transfer and decrease in lung compliance, with little, if any, evidence of airways obstruction.[4, 12, 13] Such tests are now becoming an essential part of the investigation of patients with lung disease.

Radiographic examination in the early stages usually shows nodular shadows, frequently micronodular, and of a wide distribution, as might be expected from the inhalation of large amounts of finely particulate dust capable of reaching the alveoli. In the late stages there is radiographic evidence suggestive of fibrosis, with diffuse honeycomb changes, affecting particularly the upper lobes.

Histological examination of the lungs shows, in the early stages, infiltration of the alveolar walls with polymorphonuclear, lymphoid, and plasma cells, and in the later stages epithelioid-cell granulomata and fibrosis are present. In about one-quarter of patients with farmer's lung bronchiolitis obliterans was also found.[14]

The disease may present in two ways.[4, 8] The classical form consists of systemic and pulmonary symptoms appearing five to six hours or more after exposure to the dust. Such attacks may subside rapidly, only to recur on re-exposure. The disease may also have an insidious onset and is then, if anything, the more dangerous, because the relationship of the symptoms to the causal exposure is far less likely to be suspected. The gradual development of the disease results in the patient's seeking medical attention when fibrosis is far advanced and irreversible. The differences in the mode of onset appear to be related to the frequency and intensity of exposure to the dust. Inhalation tests in both groups of patients provoke the same classical attacks of the disease, coming on after five to six hours or so.[8]

Management of the disease must be based on avoidance of the antigens. This makes it imperative that inhaled dusts should be considered as possible causes in patients with disease affecting the alveoli or with pulmonary fibrosis. Fortunately, the precipitin test offers a means of identifying the antigen, though the presence of precipitins can be taken in the first place only as evidence of exposure to the antigens. Inhalation tests help to confirm the cause by reproducing the disease, and when a new dust is recognized such tests are needed to establish the clinical relevance of the immunological findings. Once the significance of the serological tests has been established, inhalation tests may reasonably be omitted. Farmers can avoid exposure to thermophilic actinomycetes by keeping down the moisture content of the hay.[15] Mushroom workers face greater difficulties, because in the making of their compost many actinomycete spores are inevitably produced.[16] Masks are of limited value, because of the very small size of the spores of the thermophilic actinomycetes—only about 1 μ in diameter.[17]

[1] *Brit. med. J.*, 1967, **2**, 713.

[2] *Medical Research Council Annual Report, 1966–67*, 1967, p. 74. H.M.S.O.

[3] Gell, P. G. H., and Coombs, R. R. A., *Clinical Aspects of Immunology*, 1963. Oxford.

[4] Pepys, J., and Jenkins, P. A., *Thorax*, 1965, **20**, 21.

[5] Salvaggio, J. E., Seabury, J. H., Buechner, H. A., and Kundur, V. G., *J. Allergy*, 1967, **39**, 106.

[6] Emanuel, D. A., Wenzel, F. J., and Lawton, B. R., *New Engl. J. Med.*, 1966, **274**, 1413.

[7] Lunn, J. A., and Hughes, D. T. D., *Brit. J. industr. Med.*, 1967, **24**, 158.

[8] Hargreave, F. E., Pepys, J., Longbottom, J. L., and Wraith, D. G., *Lancet*, 1966, **1**, 445.

[9] Pepys, J., Jenkins, P. A., Lachmann, P. J., and Mahon, W. E., *Clin. exp. Immunol.*, 1966, **1**, 377.

[10] Morris Evans, W. H., and Foreman, H. M., *Proc. roy. Soc. Med.*, 1963, **56**, 274.

[11] Blackburn, C. R. B., *Lancet*, 1966, **2**, 1396.

[12] Rankin, J., Jaeschke, W. H., Callies, Q. C., and Dickie, H. A., *Ann. intern. Med.*, 1962, **57**, 606.

[13] Williams, J. V., *Thorax*, 1963, **18**, 255.

[14] Emanuel, D. A., Wenzel, F. J., Bowerman, C. I., and Lawton, B. R., *Amer. J. Med.*, 1964, **37**, 392.

[15] Gregory, P. H., Festenstein, G. N., Lacey, M. E., Skinner, F. A., Pepys, J., and Jenkins, P. A., *J. gen. Microbiol.*, 1964, **36**, 429.

[16] Fergus, C. L., *Mycologia*, 1964, **56**, 267.

[17] Corbaz, R., Gregory, P. H., and Lacey, M. E., *J. gen. Microbiol.*, 1963, **32**, 449.

[18] Pepys, J., Longbottom, J L., and Jenkins, P. A., *Amer. Rev. resp. Dis.*, 1964, **89**, 842.

While in farmers and mushroom workers antigens from micro-organisms are the cause of the allergic alveolitis, it is worth noting that organic dusts from any source are possible causes of similar serious disease. There is evidence that precipitins are commonly present in persons exposed to a wide range of vegetable dusts.[18]

Doctors for Industry

There are about 2,000 appointed factory doctors in Britain, most of whom are general practitioners. They examine young persons entering industry, advise both the employer and the employee in cases where a disease or disability is likely to be affected by working conditions, and have various other statutory duties. Last year a Ministry of Labour report[1, 2] recommended that these part-time factory doctors should be replaced by a much smaller group of 100 " A doctors," still responsible to the Ministry of Labour.

The report has been the subject of much controversy, both among doctors in industry[3, 4] and elsewhere, and the Industrial Health Committee of the Royal College of Physicians[5] has now commented on it. The Royal College report agrees " that the present Appointed Factory Doctor Service does not meet the needs of the working population," but goes on to point out that the envisaged 100 A doctors will serve only that part of the working population covered by the Factories Acts, whereas those covered by the Shops, Offices and Railway Premises Act will be left out, as will many other groups of workers, such as fishermen.

The Royal College report suggests that as the A doctors' role would be mainly to give advice they should answer to the Ministry of Health and not the Ministry of Labour. As well as emphasizing the advisory function of A doctors this would improve their career structure and facilitate their recruitment from the National Health Service, especially as they might be part-time in the first instance. A doctor could have secretarial assistance and trained ancillary services provided by the N.H.S. for carrying out radiological, physiological, and haematological investigations. The Royal College report suggests that an industrial hygiene service could be organized by regions, preferably based on the universities.

The most contentious proposal in the original report from the Ministry of Labour was that school doctors should issue all school-leavers with a standard certificate, which would make the examination at entry to industry unnecessary. The Royal College Committee agreed that the numerous young persons' statutory annual examinations at present carried out by the appointed factory doctors are largely a waste of time and took the view that the pre-employment medical certificate was a satisfactory substitute.

However, the B.M.A. Occupational Health Committee is far less happy with the idea of the certificate and has made its views known to the Minister of Labour. At any pre-employment examination of a young person by an industrial medical officer or an appointed factory doctor, not only is the employer already chosen but the actual job that the school-leaver is going to do is known to the examiner. If the School Medical Service issues a certificate of fitness for most leavers and a small group receives a " disabled " certificate it may lead to the employer deciding which jobs are " heavy " or have a " high dermatitis hazard," and may also make it easy for an unscrupulous employer to refuse all but the healthy school-leavers. This is an interference with the individual's freedom to apply for any sort of occupation which he himself chooses, and another step in the creation of a State dossier on each citizen. This restriction is to be foisted on school-leavers as part of an inescapable administrative scheme, and is based only on the evidence of a school doctor at the beginning of this person's working career. The doctor may err, or the patient's condition may improve.

The solution put forward by the B.M.A. is that a handbook should be issued for the guidance of school medical officers, listing the medical handicaps which might be hazardous for school-leavers in open industry. Young persons with these disabilities could be referred to the A doctor for his advice. He could then take the matter up with the general practitioner and the youth employment officer and eventually with the proposed employer.

The Association of Certifying Factory Surgeons, which is the recognized body of the appointed factory doctors, has not yet committed itself to print but seems to be viewing its members' demise with equanimity, while at the same time regretting that all the emphasis has been placed on the time-wasting statutory examinations of young persons and that no mention has been made of the valuable service that appointed factory doctors have already carried out in the field of occupational health.

However, the climate of expert opinion appears to favour the appointment of A doctors, if they will become occupational health advisers under the Ministry of Health serving on area health boards as envisaged by the Porritt Committee.[6] These men could then become the basis of a national occupational health service, a service which the Treaty of Rome demands in a field where Britain lags behind most other civilized countries.

---

[1] *The Appointed Factory Doctor Service.* Report by a Subcommittee of the Industrial Health Advisory Committee. H.M.S.O. 1966.

[2] *Brit. med. J.*, 1966, **2**, 539.

[3] *Trans. Soc. occup. Med.*, 1966, **16**, 37.

[4] Ibid., 1967, **17**, 81.

[5] *The Appointed Factory Doctor Service,* Report of the Royal College of Physicians, 1967.

[6] *A Review of the Medical Services in Great Britain,* Social Assay, London, 1962.

Treatment of Addicts

The Dangerous Drugs Bill was introduced to " provide for the control of drug addiction." Moving the second reading in April, Miss Alice Bacon[1] claimed that the Bill paved the way for a major change in the organization of treatment for addicts. Fundamental to that change was the establishment of treatment centres in hospitals. However, until there are enough of these centres to cope with the number of cases there is no possibility of getting away from the existing practice of individual doctors prescribing heroin and other drugs as they see fit.

Government spokesmen have repeatedly stated that plans for the provision of these centres are proceeding smoothly, and that they hoped that the regulations limiting prescription of drugs to addicts would be introduced in 1968. But the Ministry of Health has refused[2] to provide hospital boards with the money for treatment centres, and there is little evidence that they are being established. The Ministry refuses to name the hospitals where the centres are to be or to give any details of their progress. The existing outpatient facilities for addicts in the London area are certainly inadequate to meet the demand that will be created when the regulations forbidding private prescribing come into operation.

---

[1] *Brit. med. J.*, 1967, **2**, 187.

[2] Ibid., 1967, **3**, 58.

[3] Edwards, G., ibid., 1967, **3**, 425.

[4] Ibid., 1967, **2**, 498

Recent discussion[3] [4] in the *B.M.J.* of British and American experience has made it clear that the best treatment for addicts is not yet agreed. If the Government really means to tackle the growing problem of drug addiction it must make money available to equip and staff treatment centres, which could then be used to assess the merits of different ways of treatment—the use of differing degrees of compulsion, the value of drugs such as methadone and cyclazocine, and the use of community-centred programmes. The profession has been assured[2] that the new regulations will not be brought into operation until there are adequate centres. It is equally important for the Government to show some practical evidence of its professed sense of the urgency of the problem by providing the money needed to cope with it.

Australian Doctors in Vietnam

The pressing needs of the civilian population in Vietnam for the benefits of modern medicine are apparent from a recent Australian study. A symposium on the work of Australian surgical teams there, reported in full in the *Medical Journal of Australia*,[1] provides a story which is both tragic and inspiring. It is tragic because of the amount of human suffering concentrated in Vietnam ; inspiring because of the help which these teams are bringing to that country.

Two problems in particular stand out: a primitive existing medical service which can provide only the most sketchy facilities—so that the disease picture is nineteenth-century or earlier—coupled with a large number of civilian casualties produced by all the refinements of modern warfare from napalm-charring to the multiple wounds of Claymore mines.

The bare outlines of the medical situation in South Vietnam are as follows. There is a population of about 15 million people, of which about 10% are refugees. The average life-expectancy is 38 years, and about one-quarter of infants born alive are dead before the age of 5. Causes of death include tuberculosis, pneumonia, malaria, typhoid fever, and the dysenteries. Other major diseases include cholera, plague, leprosy, and worm infestations. In December 1965 there were only 244 doctors available for the civilian population (180 of these were Vietnamese and 64 from other countries). The present proportion of doctors to population is 1 to 61,000.

Australia's assistance with financial non-military medical aid is second only to that of the U.S.A., and in addition since 1964 she has sent from Melbourne surgical and medical teams totalling 75 doctors together with nurses and technicians who work a three- to six-month tour of duty. At present there are 28 teams in South Vietnam from 13 countries, of which Australia provides three. Only three other countries provide more than one team, and these are Korea (7), the Philippines (5), and the U.S.A. (4). The United Kingdom has one paediatric unit at present serving in Vietnam.

The bare statistics provided by P. G. Large in this symposium give some idea of the amount of work to be done. In 15 months the Australian teams carried out over 4,000 operations, a total of 270 cases per month, of which three-quarters were major. About half the cases were emergencies, of which two-thirds were traumatic in origin. Individual case histories help fill in the background to these figures—children injured playing with a grenade, an amputation case arriving two days later with artery forceps still attached to the stump of the leg, a woman with a bullet wound involving the common carotid artery who travelled 36 hours and 100 miles (160 km.) to reach the hospital, and patients arriving with their wounds stuffed with tobacco.

The report from the plastic surgeon, John Snell, shows that there are only two civilian plastic surgeons in the whole of Vietnam, neither specially trained. Three Australian plastic surgeons have battled with the vast array of advanced deformity. The tasks of the nurses are also immense, as reported by Miss Susan Terry ; in provincial hospitals there may be three nurses to tend 500 patients.

Summing up the symposium, J. D. Villiers gives the three aims of these Australian teams: firstly, humanitarian, the care of civilian sick and wounded ; secondly, diplomatic, in that the teams are tangible evidence of Australia's concern for her less fortunate neighbours in South-east Asia ; and, thirdly, the training of Vietnamese personnel. A primary function of the team is to leave behind it a structure capable of continuing its work.

---

[1] *Med. J. Aust.*, 1967, 2, 331.

Disc Protrusion and the Bladder

It is well known that lesions of the lower spinal cord and the cauda equina may interfere with neurological control of the bladder. Congenital defects, trauma, pressure from neoplasms, and inflammatory conditions are responsible for most of the cases. The role of lumbar disc protrusions is less clearly defined, and a diagnosis of bladder dysfunction from this cause when the characteristic features of local muscular spasm and referred pain are absent might at first sight appear questionable.

In a recent report from the Mayo Clinic J. G. Love and J. L. Emmett[1] described three cases in which urinary retention was attributed to asymptomatic lumbar disc protrusions and in which normal function was restored by appropriate surgery. All the patients were women and somewhat fat. All had suffered from enuresis in childhood, but no other neurological factor had been suspected and neither physical examination nor myelography had shown any abnormality. At cystoscopy there was a large vesical residue, but suspicion was aroused by the absence of sensation on instrumentation and the lack of discomfort on further distension of the bladder. In each case the bladder was smooth and could expel urine normally through the cystoscope. Laminectomy was done to explore the filum terminale and in each case it revealed a protruded lumbar disc which proved to be the cause of the symptoms.

It is worth noting that all the patients were women. Urinary retention is relatively uncommon in women, except when due to gynaecological causes or cystitis, and it is prone to be ascribed to "hysteria." Clinical experience indeed suggests that in many instances the condition is transient and is permanently relieved by simple catheterization. But there are none the less some patients in whom dysfunction persists despite elimination of any urinary infection and treatment with cholinergic drugs. The usual management of these cases has been to carry out a limited perurethral resection of the bladder neck to relieve a hypothetical obstruction. It seems surgeons should now first investigate the termination of the spinal cord in more detail in such resistant cases.

---

[1] Love, J. G., and Emmett, J. L., *Mayo Clin. Proc.*, 1967, 42, 249.

Hypotonia and Obesity Syndrome

Lack of muscle tone in the newborn infant is a common problem. Usually there is a history of foetal distress, followed by the delivery of an apnoeic hypotonic infant requiring resuscitation. During the ensuing weeks or months it becomes clear whether any permanent cerebral damage has occurred.

A difficult delivery, not necessarily a breech, with excessive traction on the neck may damage the spinal cord, usually in the lower cervical region, causing initially a flaccid paralysis of trunk and legs. Occasionally a widespread poliomyelitis may develop in utero as a result of a maternal infection during pregnancy; or there may be a transient myasthenic phase in an infant whose mother has myasthenia gravis. If a previous child was severely hypotonic at birth and died at an early age the possibility of the infantile form of degeneration of the anterior horn cells of the spinal cord (Werdnig–Hoffmann disease) should be considered. Less commonly the picture may merely mimic disease of the anterior horn cells, but there is a gradual improvement, though this is not always complete. This is the condition or group of conditions known as "benign infantile hypotonia"; a familial incidence is uncommon. Marked weakness of sucking, with a bilateral convergent squint, usually indicates a form of Möbius's syndrome, with agenesis of the motor nuclei of the sixth and seventh (and occasionally other) cranial nerves.

There remains a small group of infants with extreme hypotonia from birth, an almost complete lack of spontaneous movement, and an inability to suck. B. M. Laurance[1] has recently surveyed the literature, and has reported nine cases of his own, describing a condition which begins in this way but evolves in a curious manner. In the males the external genitalia are very small and the testes are small or impalpable. As these infants get older muscle power improves, but they remain hypotonic, and it soon becomes apparent that their delayed motor development is due partly to muscle weakness and partly to mental retardation. By the age of 4 to 5 years they are usually dwarfed and extremely fat, and from the age of 12 years onwards they tend to develop diabetes. This syndrome was first described from Zürich by A. Prader, A. Labhart, and H. Willi[2] in 1956. Other reports from Sweden,[3] England,[4] and Belgium[5] suggest that it is not uncommon.

In most of the families studied so far there has been no indication of a genetic basis, though J. C. Gabilan[6] found two affected children in one family. Nor has any significant environmental factor been discovered. Systematic investigation has not been of much help. It has been observed that the majority of the affected children have a similar facial appearance, with "almond-shaped eye sockets with slightly overhanging lids, a high cranial vault above the ears when seen in profile, prominent foreheads, retroussé noses, and slightly open fish-like mouths"[1]; the hands and feet are small and narrow. The possibility of a chromosomal abnormality has been considered, particularly as the angle between the palmar triradii is the same in some cases as that found in Down's syndrome (mongolism). H. G. Dunn and his colleagues[7] reported a minor chromosomal abnormality in one case, but the significance of this finding is uncertain, as neither Laurance[1] nor H. Forssman and B. Hagberg[3] found any such abnormalities in their cases. Electroencephalography has shown no constant abnormality, nor has electromyography. Muscle biopsies were done in two of Laurance's cases: in one the appearance was normal and in the other Dr. A. L. Woolf suggested there was a "dysplasia of the lower motor neurones" or an "actively progressive degeneration." Glycogen content and muscle enzymes have been shown to be normal in another case. In one patient a biopsy of the testis showed an appearance consistent with the age of the child, who was prepubertal.

Investigations of the function of the pituitary and adrenal cortex have given normal results in most cases, but in Forssman and Hagberg's case there was a reduced response to A.C.T.H. The diabetes which develops in these children appears to be less acute than is usually seen in children, and ketosis is often absent. These observations led P. R. Evans[4] to suggest that an insulin antagonist[8] might be present, interfering with the uptake of glucose by skeletal muscle but enhancing its uptake by adipose tissue.

It is not clear whether the small external genitalia and testes (and presumably ovaries) are an expression of primary or secondary hypogonadism. Puberty is delayed and incomplete, and in one of the Swiss cases[2] the excretion of gonadotrophin was abnormally high, suggesting a primary gonadal deficiency. If there is a persisting hypogonadal state, either primary or secondary, production of growth hormone may also be deficient, as a eunuchoid state does not develop. There is still much that is obscure in this interesting syndrome, and it remains to be seen whether there is a single basic abnormality or whether the syndrome comprises several different but similar conditions.

---

[1] Laurance, B. M., *Arch. Dis. Childh.*, 1967, **42**, 126.
[2] Prader, A., Labhart, A., and Willi, H., *Schweiz. med. Wschr.*, 1956, **86**, 1260.
[3] Forssman, H., and Hagberg, B., *Acta paediat. (Uppsala)*, 1964, **53**, 70.
[4] Evans, P. R., *Guy's Hosp. Rep.*, 1964, **113**, 207.
[5] Hooft, C., Delire, C., and Casneuf, J., *Acta paediat. belg.*, 1966, **20**, 27.
[6] Gabilan, J. C., *Journées pediat.*, 1962, **1**, 179.
[7] Dunn, H. G., Ford, D. K., Auersperg, H., and Miller, J. R., *Pediatrics*, 1961, **28**, 578.
[8] Vallance-Owen, J., and Lilley, M. D., *Lancet*, 1961, **1**, 804.

Guide to Hospitals

Following the example of Baedeker, many diligent guides have set out to help the newcomer find his way round with pleasure and enlightenment. Culture and sport, eating and sleeping—these and other human aspirations and frailties are the subject of many an instructive handbook. One of special interest to doctors seeking hospital junior appointments is *The Hospital Gazetteer*, published by the British Medical Association.[1] It contains a mass of information about the hospitals of Great Britain, Northern Ireland, and the Isle of Man. The traveller in this bewildering world is given pithy guidance on the sort of reception and accommodation he may expect. For example, one hospital has "Catering very high standard; good facilities for meals at night." Another offers accommodation "above the minimum laid down" but "off-duty time inadequate." Some further samples are: "28 rooms too small, 24 have no wash-basins." "Social club with old-time and modern dancing, drama section, archery, photography." "H.P.s' sitting-room is used as dining-room by resident medical staff and visiting consultants." "Rooms have no desks, easy chairs, nor running water." Thus with the help of this book the young doctor seeking decent accommodation in which to live, work, and study should be able to pick out a congenial billet and keep clear of "accommodation inadequate."

---

[1] *The Hospital Gazetteer*, 3rd ed., 1967. British Medical Association, London. 25s. net (by post 26s. 6d.).

Papers and Originals

Obstetric Complications and School Performance

D. J. P. BARKER,*† M.B., B.SC., PH.D.; J. H. EDWARDS,* M.R.C.P.

Brit. med. J., 1967, **3**, 695–699

Little is known about the mental development of children who are exposed to obstetric complications and escape the immediate hazards of perinatal death or severe brain injury. This lack of knowledge results from the practical difficulties involved in collecting the obstetric histories of a large number of infants and relating them to school performance, or to some other index of intellectual development, several years later. During the past 16 years obstetric records have been compiled for all births within the City of Birmingham, and these now permit an analysis of the relation between obstetric history and performance in the verbal reasoning tests which form part of the selective examination for 11-year-old schoolchildren.

Since performance in verbal reasoning tests is determined by genetic endowment, prenatal environment, and the physical and social environment after birth, data relating small differences in performance to obstetric events can be interpreted only against a control population matched for similar hereditary, prenatal, and postnatal determinants. Therefore unless the differences are large sibs provide the only possible controls.

In this paper the verbal reasoning scores of children exposed to obstetric complications are compared with those of their sibs and of the population of 50,000 children to which they belong.

Method

The population comprised all children who were born in Birmingham during 1950–4 and subsequently took the "eleven-plus" examination there. It did not include children who left the city or died before the age of 11 years, or who did not take the examination because they were in private schools, special schools for the handicapped, or, though in ordinary schools, had been assessed as "borderline subnormal."

Eleven-plus candidates have to take two verbal reasoning tests. These are a form of group intelligence test, and the means of the two scores obtained are transformed and adjusted so that the scores of candidates born in different months have a mean of 100 and a standard deviation of 15. The present investigation is based on analysis of these age-adjusted verbal reasoning (V.R.) scores.

Obstetric data which have been recorded on punch cards for all births in Birmingham since 1950 (Charles, 1951) were converted into a constant format and transferred to magnetic tape. The eleven-plus results of all children who took the examination in Birmingham during 1961–5 were made available, and these also were transferred to magnetic tape. The records on the two data tapes were sorted into sequence depending on names and dates of birth, and the data were merged to form a third tape. An eleven-plus record was linked with a birth record if the first name, surname, and date of birth were identical when expressed in the Hogben numeric code (Hogben, Johnstone, and Cross, 1948). As a result of this procedure birth and examination records of 50,046 children were linked.

Children born during the last quarter of 1954 were too young to have taken the eleven-plus during 1965, and the population of 50,046 children was therefore restricted to those born from 1 January 1950 to 1 September 1954. Subsequent comparison of surnames and addresses on the combined birth and eleven-plus records led to identification of 12,959 sibs from 6,129 fraternities within the population.

Results

Plurality

Table I shows that the mean V.R. scores of twins and triplets are 4.8 and 13.3 units below the mean score of single-born children. This confirms the observations of Mehrotra and Maxwell (1949) and of Sandon (1957). As multiple pregnancies impose a peculiar prenatal environment, and the survivors have an unusual upbringing, further analysis in this paper is restricted to the 48,795 single-born children.

TABLE I.—*Mean V.R. Scores According to Plurality*

Single-born	Twins	Triplets
100·2 (48,795)	95·4 (1,233)	86·9 (18)

Numbers of children are given in parentheses.

Birth Rank

The number of previous livebirths and stillbirths was recorded for all except 50 of the children. Within the population the mean V.R. score falls with increasing birth rank, from 102.8 in birth rank 1 to 89.3 in birth ranks 10 or more (Table II). Comparison of mean scores of sibs in each birth rank with those of sibs in the preceding rank (Table III) shows that within fraternities the V.R. score falls with increasing birth order, with an average fall of 1.0 for each unit increase in birth order.

Duration of Gestation

The gestation period, calculated to the nearest week from the first day of the last menstrual period, was recorded for

TABLE II.—*Mean V.R. Scores According to Birth Rank*

Birth Rank									
1	2	3	4	5	6	7	8	9	10+
102·8 (17,065)	101·6 (13,803)	98·8 (8,122)	96·6 (4,378)	93·8 (2,296)	93·1 (1,303)	92·4 (748)	90·4 (439)	89·8 (270)	89·3 (321)

---

* Department of Social Medicine, Medical School, The University, Birmingham 15.

† Present address: Department of Medicine, Medical School, The University, Birmingham 15.

Table III.—*Mean V.R. Scores in Sib Pairs According to Birth Rank*

	Birth Rank									Total
	1	2	3	4	5	6	7	8	9	
Children in each birth rank (a)	—	100·2	98·1	95·7	93·2	91·5	93·1	91·0	90·3	97·7
Children in preceding birth rank (b)	—	101·7	99·1	96·0	94·1	92·4	92·0	91·4	88·8	98·7
Difference (a)–(b)	—	−1·5 (2,208)	−1·0 (1,293)	−0·3 (711)	−0·9 (413)	−0·9 (211)	+1·1 (126)	−0·4 (74)	+1·5 (49)	−1·0 (5,085)

41,452 children (85%). The mean V.R. scores of children born at term (38 to 41 weeks) are above average; but the children born after either longer or shorter gestations have mean scores below the average (Table IV). Table V shows the mean scores among pairs of sibs in consecutive birth ranks, of whom one member was born at term (term sib) and the other was born either before term (28 to 37 weeks) or after term (more than 41 weeks). Because of the relation between V.R. score and birth order within fraternities (Table III) the results are subdivided according to whether the term sib is the earlier- or later-born member of the pair. In the sib pairs which include one child born before term both sibs were born after pregnancies uncomplicated by antenatal disease and after labours of spontaneous onset. In the pairs in which one child was born after term both sibs were likewise born after uncomplicated pregnancies but sibs born after induced labours were not excluded.

Table IV.—*Mean V.R. Scores According to Duration of Gestation in Fortnights*

28–	30–	32–	34–	36–	38–	40–	42–	44+
80·1 (15)	95·8 (89)	93·5 (186)	96·3 (635)	97·4 (2,170)	100·3 (10,169)	100·7 (22,410)	99·4 (5,119)	97·1 (659)

In Table V the mean scores of affected children—that is, of sibs born before and after term—exceed those of their term sibs in the subsequent birth rank by 1.2 and 0.7 respectively. This may be attributed to the higher birth order of the term sibs. But when affected children are compared with term sibs in the preceding birth rank their mean scores are 2.5 and 1.8 lower. These differences exceed the average fall of 1.0 for each unit increase in birth order and, together with the lower mean scores in the population (Table IV), they suggest that shortened and prolonged gestation periods are associated with impaired performance on V.R. tests. There is, however, no marked difference in the percentage distribution of scores of children born before, at, or after term (Table VI).

Table V.—*Mean V.R. Scores in Sib Pairs of Whom One Member Was Born at Term (38 to 41 Weeks of Gestation) and the Other Either Before Term (28 to 37 Weeks) or After Term (More Than 41 Weeks)*

	Born Before Term	Born After Term
Affected children (a)	97·6	96·7
Sibs in subsequent birth rank born at term (b)	96·4	96·0
Difference (a)–(b)	+1·2 (120)	+0·7 (229)
Affected children (c)	95·0	96·9
Sibs in preceding birth rank born at term (d)	97·5	98·7
Difference (c)–(d)	−2·5 (163)	−1·8 (312)

Numbers of sib pairs are given in parentheses.

Antenatal Diseases

The presence or absence of antenatal disease was recorded for 45,650 children (94%), and Table VII shows the mean V.R. scores of children born after pregnancies complicated by toxaemia, non-toxic antepartum haemorrhage, or anaemia.

Table VII.—*Mean V.R. Scores According to Antenatal Disease*

Toxaemia	Non-toxic A.P.H.	Anaemia
101·9 (3,321)	97·9 (641)	97·4 (1,338)

In the compilation of the birth records the coding "toxaemia" was applied to all cases of hypertension or albuminuria during pregnancy. The mean V.R. score of children born after toxaemic pregnancies is above the population mean. But the incidence of toxaemia in birth rank 1 is twice that in the other ranks; and children in birth rank 1 have the highest mean V.R. scores (Table II). When children from toxaemic pregnancies are distributed according to birth rank, their mean V.R. score is consistently greater than the mean for all children in the same birth rank (Table VIII). Since, however, less intelligent mothers tend to neglect regular antenatal examination, there is probably a correlation between maternal intelligence and the diagnosis of toxaemia; and the intellectual performance of mothers and their children is known to be correlated.

Table VIII.—*Mean V.R. Scores of Children Affected by Toxaemia, According to Birth Rank*

	1	2	3	4	5	6+
Children affected by toxaemia	103·7 (1,855)	101·9 (725)	100·1 (325)	96·7 (186)	94·7 (93)	92·2 (136)
Whole population of children	102·8	101·6	98·8	96·6	93·8	91·9

Table IX, constructed in the same way as Table V, shows that the mean V.R. score of children from toxaemic pregnancies is only 0.5 above that of their sibs in the subsequent birth rank and is 2.0 below that of sibs in the preceding rank. This suggests that toxaemia is associated with an impaired V.R. test performance. Table X shows that in sib pairs, of which both members were born at term (38 to 41 weeks of gestation), children from toxaemic pregnancies were at a great disadvantage compared with their normal sibs. The association between toxaemia and impaired V.R. performance does not therefore seem to be secondary to the known association between toxaemia and a shortened period of gestation. In accord with their higher mean score the distribution of scores of children from toxaemic pregnancies differs slightly from that of the whole population of children (Table XI).

The mean V.R. score of children affected by non-toxic antepartum haemorrhage is 97.9 (Table VII). This may be compared with a mean score of 99.5 for children with the same

Table VI.—*Percentage Distribution of V.R. Scores According to Duration of Gestation*

Duration of Gestation	V.R. Score								No. of Children	Mean Score
	Below 70	70–	80–	90–	100–	110–	120–	130+		
28–37 weeks	3·5	8·4	18·4	26·4	25·1	13·0	4·5	0·9	3,095	96·8
38–41 "	1·6	5·8	14·7	25·1	25·7	17·6	7·5	2·0	32,579	100·6
42+ "	2·1	6·8	16·2	26·2	24·7	16·5	6·1	1·4	5,778	99·1

birth-rank distribution. However, the scores of affected children are not lower than those of their unaffected sibs (Table IX). "Non-toxic antepartum haemorrhage" is a description that was applied to antepartum bleeding which resulted from many causes but was not associated with toxaemia; and even some cases of threatened abortion were classified in this way. From the results in Tables VII and IX one can draw only the general conclusion that disturbances of the placenta which result in bleeding during pregnancy, in the absence of toxaemia, do not usually influence subsequent V.R. performance.

TABLE IX.—*Mean V.R. Scores in Sib Pairs According to Antenatal Disease*

	Toxaemia	Non-toxic A.P.H.	Anaemia
Affected children (a)	100·3	99·8	97·7
Unaffected sibs in subsequent birth rank (b)..	99·8	98·1	95·3
Difference (a)–(b)	+0·5 (180)	+1·7 (44)	+2·4 (92)
Affected children (c)	100·8	95·1	97·9
Unaffected sibs in preceding birth rank (d)..	102·8	94·5	98·7
Difference (c)–(d)	−2·0 (162)	+0·6 (66)	−0·8 (191)

TABLE X.—*Mean V.R. Scores in Sib Pairs Both of Whom Were Born at 38–41 Weeks of Gestation and One of Whom Was Affected by Toxaemia or by Non-haemolytic Jaundice*

	Toxaemia	Non-haemolytic Jaundice
Affected children (a)	100·8	102·0
Unaffected sibs in subsequent birth rank (b)	101·5	101·6
Difference (a)–(b)	−0·7 (87)	+0·4 (36)
Affected children (c)	101·0	104·7
Unaffected sibs in preceding birth rank (d)	103·2	105·0
Difference (c)–(d)	−2·2 (100)	−0·3 (42)

All types of anaemia were grouped together as "anaemia." The lowered mean V.R. score of children affected by anaemia (Table VII) may be partly or wholly the result of the known association between anaemia of pregnancy and poor social circumstances. There is no evidence that the V.R. performance of affected children differs from that of their unaffected sibs (Table IX).

Presentation at Onset of Labour

Table XII shows the mean V.R. scores of the 45,291 children (93%) whose type of presentation was recorded. Although the mean score of all children whose presentation was occipito-posterior is 100.4, the mean score of affected sibs is only 0.1 above that of unaffected sibs in the subsequent birth rank and is 2.5 below that of unaffected sibs in the preceding rank (Table XIII). This is evidence of an association between occipito-posterior presentation and an impaired V.R. performance. The percentage distribution of the affected children is similar to that of the whole population of children (Table XI).

In Tables XII and XIII there is no evidence of any marked association between other forms of presentation and V.R. performance, though the numbers of brow presentations and presentations caused by a transverse lie were too small to permit comparisons within sib pairs.

TABLE XII.—*Mean V.R. Scores According to Type of Presentation at Onset of Labour*

Normal Vertex	Occipito-posterior	Brow	Face	Breech	Caused by Transverse Lie
99·8 (41,929)	100·4 (2,232)	106·9 (35)	98·5 (116)	99·2 (913)	99·5 (66)

TABLE XIII.—*Mean V.R. Scores in Sib Pairs According to Type of Presentation at Onset of Labour*

	Occipito-posterior	Face	Breech
Affected children (a)	97·8	100·2	102·3
Unaffected sibs in subsequent birth rank (b)..	97·7	89·4	99·1
Difference (a)–(b)	+0·1 (188)	+10·8 (9)	+3·2 (56)
Affected children (c)	96·9	92·1	95·1
Unaffected sibs in preceding birth rank (d)..	99·4	93·2	97·6
Difference (c)–(d)	−2·5 (229)	−1·1 (12)	−2·5 (96)

Type of Labour

In the records of 46,236 (95%) of the children the type of labour was classified to show whether the onset was spontaneous or induced, and whether delivery was natural, instrumental, or by caesarean section.

The mean V.R. score of children born by instrumental delivery is 103.5 (±0.4) (Table XIV). This may be compared with a mean score of 102.0 for children with the same birth-rank distribution. The mean score of 103.0 (±0.5) for children born by caesarean section may be similarly compared with a mean score of 101.2. Within fraternities the mean score of children born by instrumental delivery is higher than that of sibs in both the subsequent and preceding birth ranks (Table XV). Though small numbers make interpretation difficult, Table XV also suggests that the V.R. performance of children born by caesarean section is better than that of their sibs.

TABLE XIV.—*Mean V.R. Scores According to Method of Delivery*

Natural	Instrumental	Caesarean Section	"Other"
99·6 (43,452)	103·5 (1,661)	103·0 (1,016)	101·7 (107)

TABLE XV.—*Mean V.R. Scores in Sib Pairs According to Method of Delivery*

	Instrumental	Caesarean Section
Affected children (a)	102·3	106·6
Unaffected sibs in subsequent birth rank (b)	100·0	96·5
Difference (a)–(b)	+2·3 (145)	+10·1 (9)
Affected children (c)	97·1	95·9
Unaffected sibs in preceding birth rank (d)	95·5	93·2
Difference (c)–(d)	+1·6 (34)	+2·7 (13)

TABLE XI.—*Percentage Distribution of V.R. Scores of Children Affected by Toxaemia, Occipito-posterior Presentation, or Delivery in an Ambulance*

	V.R. Score								No. of Children	Mean Score
	Below 70	70–	80–	90–	100–	110–	120–	130+		
Toxaemia	1·6	4·7	12·7	24·7	26·5	18·8	8·3	2·6	3,321	101·9
Occipito-posterior presentation	1·6	5·5	14·9	25·6	25·7	18·3	6·6	1·8	2,232	100·4
Delivery in an ambulance	5·2	9·2	20·4	31·2	18·8	10·0	4·8	0·4	250	94·3
Whole population of children	1·8	6·3	15·3	25·0	25·3	17·2	7·3	2·0	48,795	100·2

In the classification of type of labour the category "other" denoted labours and deliveries which were regarded as unusual. This category was not strictly defined, but its most frequent use was for labours which ended in breech extractions. The mean V.R. score of children born after "other" types of labour is 101.7 (Table XIV) and therefore exceeds that of the whole population. Numbers were too small to permit comparisons within sib pairs.

Precipitate Labour

In the compilation of the birth data a simple classification was used to denote the duration of labour. The time recorded was that from the beginning of the first stage until the completion of the second. For children born after labours completed in two hours or less (a precipitate labour) the mean V.R. score is 97.7 (Table XVI). This may be compared with a mean of 99.0 for children with the same birth-rank distribution. Although the mean score of affected children is 2.5 above that of sibs in the subsequent birth rank and only 0.5 below that in the preceding rank (Table XVII), these differences seem too small to justify the conclusion that precipitate labour and V.R. performance are associated.

TABLE XVI.—*Mean V.R. Scores of Children Born After Precipitate Labour, or Delivered in Ambulances or in the Absence of a Qualified Attendant*

Born After Precipitate Labour	Delivered in Ambulance	Delivered in Absence of Qualified Attendant
97·7 (2,985)	94·3 (250)	95·3 (981)

TABLE XVII.—*Mean V.R. Scores in Sib Pairs One of Whom Was Born After a Precipitate Labour, or Delivered in an Ambulance or in the Absence of a Qualified Attendant*

	Born After Precipitate Labour	Delivered in Ambulance	Delivered in Absence of Qualified Attendant
Affected children (a)	96·9	94·8	93·1
Unaffected sibs in subsequent birth rank (b)..	94·4	93·2	91·8
Difference (a)–(b)	+2·5 (200)	+1·6 (29)	+1·3 (107)
Affected children (c)	98·4	93·7	97·3
Unaffected sibs in preceding birth rank (d)..	98·9	96·9	97·4
Difference (c)–(d)	−0·5 (589)	−3·2 (90)	−0·1 (200)

Birth Attendant

Observations of the type of attendant present at birth—for example, hospital midwife or general practitioner—included cases where birth had occurred in an ambulance or before the arrival of a qualified attendant. The mean V.R. scores of the affected children are low (Table XVI). This may be partly or wholly the result of the known associations of inadequately supervised delivery with both precipitate labour and with poor social circumstances. The mean score of children born in ambulances is 1.6 above that of unaffected sibs in the subsequent birth rank, and 3.2 below that of sibs in the preceding birth rank (Table XVII). This is evidence of some direct association between impaired V.R. performance and birth in an ambulance. There is no evidence of a similar association with birth in the absence of a qualified attendant (Table XVII). The percentage distribution of children born in ambulances (Table XI) shows that a considerable excess of affected children (66%) have scores below the population mean (100.2).

Condition after Birth

This was recorded for 46,439 (95%) of the children. The mean V.R. score of children who had non-haemolytic jaundice is 100.2 (Table XVIII). Levels of serum bilirubin were not recorded. Table XIX shows that the mean scores of affected children are below those of sibs in the subsequent as well as the preceding birth rank; and this suggests that neonatal non-haemolytic jaundice is associated with an impaired V.R. performance. However, when comparison is restricted to sibs born at term (Table X) the association is no longer present, which suggests that it is secondary to the increased incidence of non-haemolytic jaundice among children born before term.

TABLE XVIII.—*Mean V.R. Scores According to Condition After Birth*

Non-haemolytic Jaundice	Birth Injury and/or Asphyxia
100·2 (903)	100·8 (909)

TABLE XIX.—*Mean V.R. Scores in Sib Pairs According to Condition After Birth*

	Non-haemolytic Jaundice	Birth Injury and/or Asphyxia
Affected children (a)	99·6	99·8
Unaffected sibs in subsequent birth rank (b)	100·0	95·1
Difference (a)–(b)	−0·4 (68)	+4·7 (56)
Affected children (c)	99·9	99·1
Unaffected sibs in preceding birth rank (d)	100·7	101·9
Difference (c)–(d)	−0·8 (117)	−2·8 (74)

A single coding was used to denote children who showed signs of trauma or asphyxia at birth. Therefore children who, for example, had cephalhaematomata, or were unusually cyanosed after birth, were coded in the same way. Such data permit only general conclusions. Nevertheless Tables XVIII and XIX provide no evidence that "birth injury and/or asphyxia" is related to academic performance in children within the normal range of intelligence.

Discussion

The results of this inquiry are based on an analysis of eleven-plus performance in a population of Birmingham-born children. This population did not include children who were of very low intelligence, who were in special schools for the physically handicapped, or who died before the age of 11 years. Children who had moved out of the city were also excluded, and the population was therefore unrepresentative of all eleven-plus candidates. However, it is difficult to see how this can affect the conclusions, which are mainly dependent on comparisons within fraternities.

Only five of the obstetric complications studied seemed to be associated with impaired V.R. performance: a short gestation period, a prolonged gestation period, toxaemia, occipito-posterior presentation, and delivery in an ambulance. Children born at term (38 to 41 weeks of gestation) had a higher mean V.R. score than children born after shorter or more prolonged gestation periods (Table IV); and comparison between sibs (Table V) suggested that in some cases impaired performance might be a direct consequence of birth before or after term. The results did not confirm those of Dale (1966), who, from a study of 179 children, concluded that "it is possible that a higher intelligence could be obtained by delivery before 40 weeks of gestation, provided the mother is obstetrically normal."

Children from toxaemic pregnancies were found to be at a great disadvantage compared with their unaffected sibs when they were born at term. The data did not permit further elucidation of this, but one interpretation of the finding is that induction of labour in cases of toxaemia may curtail a period during which the foetus sustains cerebral damage.

It it is accepted that the five obstetric complications—birth before and after term, toxaemia, occipito-posterior presentation, and delivery in an ambulance—do result in impaired academic performance among children at ordinary schools, it seems unlikely that they exert more than a small influence on the intellectual development of children exposed to them. The distributions of scores of affected children were unimodal (Tables VI and XI) and therefore provided no evidence of a substantial group of children whose development was greatly impaired; and there were only small differences in the mean scores of affected and unaffected sibs.

A previous analysis of the relation between obstetric complications and subnormal intelligence (an I.Q. below 75), based on the same obstetric data as the present analysis, revealed an association between educational subnormality and both precipitate labour and delivery in the absence of a qualified attendant (Barker, 1966). But neither of these complications seems to be associated with impaired performance within the normal range of intelligence.

The mean V.R. scores of children delivered instrumentally or by caesarean section were higher than those of the population and of their unaffected sibs. It seems reasonable to suppose that a child born by caesarean section may avoid cerebral damage sustained in a normal delivery; but it is difficult to explain the association between instrumental delivery and raised V.R. scores. The data are, however, too complex to justify the conclusion that instrumental delivery will improve school performance.

The finding that the mean V.R. score in the population declines with increasing birth rank (Table II) confirms numerous previous observations of the negative correlation between fraternity size and measured intelligence. But this inquiry has also shown that within fraternities there is an average fall of 1.0 in V.R. score with each unit increase in birth order.

Summary

Birth records of 50,000 children were linked with records of school performance at the age of 11. Twins and triplets showed marked impairment, and were excluded from this study. The verbal reasoning (V.R.) scores of single-born children exposed to obstetric complications were compared with those of the population and of their sibs. The results suggested that impaired performance was associated with only five of the obstetric complications studied: a short gestation period, a prolonged gestation period, toxaemia, occipito-posterior presentation, and delivery in an ambulance. In no case was the impairment very marked. Within fraternities there was a fall in average V.R. score with increasing birth rank.

It is a pleasure to thank Dr. E. L. M. Millar, Medical Officer of Health for Birmingham, and Sir Lionel Russell, Chief Education Officer for Birmingham, for permission to transfer records in their departments on to magnetic tape, and Dr. E. D. Acheson for lending a programme for converting names into the Hogben number. Computer Services, Birmingham, made their Univac 1107 available on generous terms; and we are particularly grateful to Mr. R. J. Milne for advice and for creating the tape files.

REFERENCES

Barker, D. J. P. (1966). *Brit. J. prev. soc. Med.*, **20**, 58.
Charles, E. (1951). *Brit. J. soc. Med.*, **5**, 41.
Dale, M. H. (1966). *Practitioner*, **196**, 430.
Hogben, L., Johnstone, M. M., and Cross, K. W. (1948). *Brit. med. J.*, **1**, 632.
Mehrotra, S. N., and Maxwell, J. (1949). *Popul. Stud.*, **3**, 295.
Sandon, F. (1957). *J. roy. Statist. Soc., Series A*, **120**, 440.

Paraproteins, Benign or Malignant?

J. R. HOBBS,[*] M.D., M.R.C.P., M.C.PATH.

Brit. med. J., 1967, **3**, 699–704

Paraproteins are those serum proteins which on electrophoresis are found to run as an abnormal narrow band between the positions occupied by the inter-α and post-γ protein fractions. Once it is confirmed that the paraprotein contains a heavy chain or a light chain, or both, of one class only—that is, a monoclonal immunoglobulin or fragment thereof—it may be assumed that it has come from a single clone of cells within the reticuloendothelial system. The question then remains, will this "monoclone" behave in a malignant fashion—invading bone (myelomatosis), lymphoid tissue (lymphomata), or the blood stream (leukaemia)—or will it, like a benign tumour, strike a balance with its neighbouring tissues and cause no harm to the patient?

Though much work (well reviewed by Hällén, 1966) has dealt with both malignant and benign conditions, less is known about the intermediate diseases owing to inadequate investigation during life or at necropsy. The present study includes 304 patients followed up to the time when a diagnosis of malignant disease was established or for at least three years. Prospective examination of fresh serum and urine from every patient has shown findings of prognostic value.

Investigation of Paraproteins

Serum

Serum was separated at 37° C. to avoid missing cryoproteins and then electrophoresed on cellulose acetate. False M bands due to fibrinogen or old or uraemic serum were excluded (Hobbs, 1966a).

The level of M protein was estimated as a percentage of the total uptake of amidoschwarz 10 *B* under standard conditions (Hobbs, 1965), great care being taken always to load the strip within a linear range, often set by the narrow bands of paraprotein. Strips were often run with decreasing applications until the percentage became constant. Usually no attempt was made to simulate peaks or subtract any underlying proteins—vertical cuts were made down the peaks. In this way reproducibility of ±2% was achieved. From the total protein by a biuret method (suitably diluted for high values) using Armour bovine albumin standard the percentage of paraprotein was converted to g./100 ml. in the case of γG, γA, and γD (where the dye-binding and biuret colour compared to albumin is reliable to within 5% overall). As the biuret method underestimates γM-paraproteins by 12%, the specific gravity gradient tube of Lowry and Hunter (1945) was used for determining the total protein in such cases. By the above technique pure isolated paraproteins calibrated by ultraviolet absorption could be added to normal serum and recovered with an absolute accuracy of ±0.2 g./100 ml.

By using our own monospecific rabbit antisera the presence of the paraprotein was confirmed by immunoelectrophoresis as an M bow of only one type of heavy or light chain, or both.

---

[*] Lecturer in Chemical Pathology, Postgraduate Medical School, London W.12.

After personally examining over 800 positive and very many negative samples, I have yet to see an M bow on immunoelectrophoresis that was not already apparent on cellulose acetate electrophoresis. Hence the latter method is a satisfactory screening test for paraproteins, though with paper electrophoresis small M bands can readily be missed.

In every case serum immunoglobulin levels of classes other than the paraprotein were measured by a modified Mancini method (Hobbs and Maatela, 1967), as a percentage of the mean level for that class determined in 107 normal adults. In Fig. 2 the average is plotted—for example, a patient with myelomatosis producing only Bence Jones protein had γG 44%, γA 50%, and γM 50% of mean adult normal; these results are plotted as "other immunoglobulins 48% mean normal."

γA-paraproteins have a shorter half-life (mean 6.4 days) than γG-paraproteins (mean 11.6 days) (Drivsholm, 1964); and for the same serum level have a faster turnover (10.8% of the total pool) than γG-paraproteins (6% of the total pool). Thus simple serum levels do not allow a true comparison between γA and γG classes. In order better to compare such patients, all of the latter have arbitrarily been assumed to weigh 70 kg., and to have a plasma volume of 50.7 ml./kg., and the plasma has been assumed to contain 71% of the total paraprotein pool —averages of available data in patients with myelomatosis (Gabuzda, 1962). Thus for a given serum level, M g./100 ml. the total pool would be $M/100 \times 70 \times 50.7 \times 100/71 = 50 \times M$ g.; and for patients in equilibrium the average daily productions of γA would be 10.8% of $50\ M = 5.4 \times M$ g. and of γG 6% of $50\ M = 3.0 \times M$ g. In γM-paraproteinaemia an average daily turnover is 13.3% of the intravascular pool of γM-globulin (Barth *et al.*, 1964), though these authors estimated the average plasma volume at only 45 ml./kg. Most of our patients were severely anaemic, so that an arbitrary plasma volume of 60 ml./kg. has been used, closer to that found in one patient of Gabuzda (1962) and in two patients of Olesen (1963). Thus, in equilibrium the daily production rate would be $M/100 \times 60 \times 70 \times 13.3/100 = 5.6 \times M$ g.

Any loss of Bence Jones protein was measured in a 24-hour specimen of urine; it was corrected for the patient's body weight and added to the above productions (or used by itself for patients producing only Bence Jones protein) to obtain the *approximate production of paraprotein* in g./70 kg. body weight/day. It is recognized that this value can be only approximate, since plasma and total body pools and the half-lives of paraproteins all show individual variation (mostly less than ±25% of the taken means) but this calculation is necessary to allow comparison of the different paraprotein classes in Fig. 2. Moreover, the large numbers of patients studied should help to overrule individual errors.

In Fig. 1 a value below the 2 S.D. lower limit of normal (for γG 54%, γA 52%, γM 50% of mean adult levels) has been recorded as "other immunoglobulins subnormal." This is particularly relevant for γM-globulin—which was the only protein having subnormal levels in 21 patients who were later found to develop a malignant process. This would not be detected simply by assessing the electrophoretic γ-globulin other than the paraprotein, as Hällén (1966) did.

Where desired the molecular sizes of the paraproteins were confirmed by using thin-layer Sephadex G200 (Hobbs, 1966a) or the ultracentrifuge.

Urine

Fresh urine (or preserved with toluene or azide) was examined in every case as follows. It was first cleared of bacteria by passage through a membrane filter with maximum pore size of 0.2 μ. Total protein was then measured by a biuret method on the redissolved precipitate from 10% trichloroacetic acid. Where significant, a 24-hour output was measured and the paraprotein content added into the total daily paraprotein production in Fig. 2.

The urine was suitably concentrated (up to ×500 within two hours by using Sartorius collodion shells attached to a vacuum pump) and electrophoresed alongside the patient's serum. Any M bands were measured as a percentage of the total protein and confirmed and typed by immunoelectrophoresis. When desired, the size of the M proteins was determined by using thin-layer Sephadex G75.

The interpretation of some of these methods has been described (Hobbs, 1966b) and, using them, it is easily possible to distinguish Bence Jones protein in the urine at concentrations of only 1 mg./100 ml. from normal light chains in the urine at concentrations of 0.25 mg./100 ml.

Biopsy Material

In some cases where serum and urine results were initially negative, bone marrow or other biopsy fragments (after thrice washing with 4% human albumin) were inserted into agar and then subjected directly to immunoelectrophoresis. In three patients with undoubted myelomatosis this investigation was negative. In two other patients positive results were obtained, and later confirmed by positive findings in subsequent sera and urine specimens. Hence this method is apparently the most sensitive test available.

Cold Agglutinins

All patients in whom γM-paraproteins were found were carefully investigated for cold agglutinins. Three patients proved to be suffering from primary cold-agglutinin syndromes and were not included in this study. The remainder did not have appreciable cold agglutinins present in their sera.

Material

All 146 patients whose initial specimens of sera and urine containing paraproteins were examined between October 1959 and June 1964 are included, together with a further 158 patients studied between June 1964 and March 1965 in whom a diagnosis was possible. The final classification of the patients' conditions was as follows:

I. Malignant	Myelomatosis	196
	Waldenström's macroglobulinaemia	19
	Lymphoma	6
	Chronic lymphatic leukaemia	2
II. Benign	Mainly static for at least three years ...	68
	Transient	2
III. Uncertain	... ...	11

I. Criteria of Malignancy

The assumed monoclone was thought to be malignant in 223 patients in whom the following diagnoses were established:

Myelomatosis (196 patients).—(1) Radiological evidence (87%)—discrete osteolytic lesions (61%), diffuse halisteresis with vertebral collapse or pathological fractures in the absence of other known causes (26%) (95% of these patients had a normal serum level of alkaline phosphatase). (2) Biopsy evidence—bone marrow or bone biopsy at operation or necropsy containing an excess of atypical plasma cells which in the opinion of the examining pathologist was characteristic of myelomatosis (92%). (3) Paraprotein detected in serum and/or urine and/or biopsy (γG 99, γA 50, γμ 41, γD 3) (98.5%). The diagnosis was never made on a single criterion only: in 78% all three were present, in the remainder at least two.

Waldenström's Macroglobulinaemia (19 patients).—(1) Severe lassitude with anaemia and neutropenia. (2) Bleeding unaccounted for by thrombocytopenia or a defect of clotting factors. (3) Mild to moderate splenomegaly, slight generalized lymphadenopathy. (4) Biopsy evidence—lymph nodes (architecture well preserved) and/or bone marrow infiltrated with atypical lymphoid cells consistent with the diagnosis in the view of the examining pathologist. (5) Monoclonal γM-globulin eventually greater than 2 g./100 ml.

Features 4 and 5 were found in every case, as were some or all of features 1–3. In eight patients atypical lymphoid cells were also found in the peripheral blood.

Lymphosarcoma (five patients: four γM, one γμ); *reticulosarcoma* (one patient, γA).—(1) Massive regional involvement of lymph nodes and/or spleen and/or liver. (2) Biopsy evidence—gross destruction of normal architecture by neoplastic lymphoid or reticulum cells. (3) In four patients unfixed material was studied with fluorescein-conjugated rabbit antisera specific to the heavy chain and light chain of the paraprotein class, which was thereby identified within the cytoplasm of scanty nests of cells within the tumour tissue. In all four cases only 5–15% of the tumour cell[illegible]e stained.

Chronic Lymphatic Leukaemia (two patients: one γG, one γμ).—(1) Peripheral blood lymphocyte counts above 40,000/cu. mm for over two years. (2) No evidence of bone lesions or involvement of lymph nodes, spleen, or liver. (3) Only the cytoplasm of a few of the circulating lymphocytes could be stained with fluorescent antibody specific to the paraprotein class.

II. Criteria of Benignity (68 patients)

(1) No symptoms related to the presence of paraproteins. (2) No palpable enlargement of lymph nodes, liver, or spleen. (3) Negative radiological survey, including at least the skull and axial skeleton. (4) Bone marrow—apparently normal or with an excess of plasma cells which, however, showed few, if any, atypical features. (5) Followed for at least three years, with no detectable change in the overall picture.

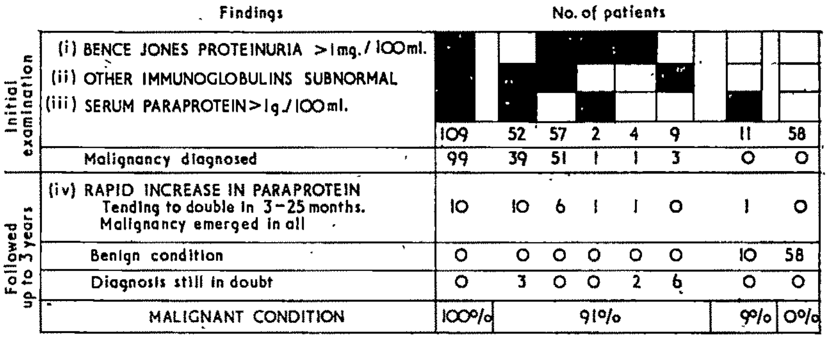
Transient (two patients).—The presence of a γG-paraprotein band was confirmed in the serum of each of these patients on at least three occasions. Nevertheless, the band disappeared within three and six months, and has not reappeared over two and eight years respectively. The first case has been reported in detail (Hobbs, 1966a) and neither is included in Fig. 1.

III. Uncertain (11 patients)

These patients had some of the features of malignancy—namely, clinical features (5) suggestive radiology (3), suspicious biopsies (7), recurrent infections owing to reduction of other immunoglobulins (4). Nevertheless, in no single patient could all the specialists concerned (physician, haematologist, radiologist, and biochemist) agree about the diagnosis, even by the end of the three-year period of observation—though it was agreed the condition could not be regarded as wholly benign.

Results

From Fig. 1 it can be seen that if at the initial examination findings (i), (ii), and (iii) were all present a diagnosis of malignancy was reached in all 109 patients. From the outset the diagnosis was in doubt in only 10 patients, and in them more definite evidence emerged within eight months. If findings (i), (ii), and (iii) were all absent the outlook appeared benign in all 58 patients three years later. Nevertheless, since this group of patients was selected for follow-up, one exceptional patient has been seen. He was first seen with a pain in the back due to collapse of a single vertebra; on investigation a γGK-paraprotein (0.2 g./100 ml.) was detected in the serum, but findings (i) and (ii) were absent. Skeletal survey and bone marrow were negative, but the vertebral biopsy revealed myeloma cells, and two years later there was evidence of recurrence; the serum paraprotein concentration had risen to 1.2 g./100 ml., while that of γM had fallen below normal.



	Findings	No. of patients							
Initial examination	(i) BENCE JONES PROTEINURIA >1mg./100ml.	■	□	■	■	■	□	□	□
	(ii) OTHER IMMUNOGLOBULINS SUBNORMAL	■	■	■	□	□	■	□	□
	(iii) SERUM PARAPROTEIN>1g./100ml.	■	■	□	■	□	□	■	□
		109	52	57	2	4	9	11	58
	Malignancy diagnosed	99	39	51	1	1	3	0	0
Followed up to 3 years	(iv) RAPID INCREASE IN PARAPROTEIN Tending to double in 3–25 months. Malignancy emerged in all	10	10	6	1	1	0	1	0
	Benign condition	0	0	0	0	0	0	10	58
	Diagnosis still in doubt	0	3	0	0	2	6	0	0
	MALIGNANT CONDITION	100%	91%					9%	0%

FIG. 1.—Outcome in 302 patients with paraproteins. Positive findings are shown in black. If (i), (ii), and (iii) were all positive the outcome was malignant in every patient, whereas if they were all negative the patients appeared to have benign conditions three years later. Between these black and white extremes, positive findings (i) and (ii) had a poor prognosis because 91% of patients showing these have had malignant conditions. In cases where the initial diagnosis is in doubt, follow-up observation for finding (iv) is of great value.

Bence Jones Proteinuria

This was detected initially in 172 patients (Fig. 1). Of these, 170 have already developed malignant conditions, and this group represents 73% of the total of 223 malignant cases studied. It must be emphasized that if urine had not been concentrated and thoroughly examined Bence Jones protein would not have been found in 90 patients. Albustix cannot be used for this, while sulphosalicylic acid gave a negative result in 65. Careful layering of cleared urine over concentrated hydrochloric acid (Bradshaw, 1906) has been found to be unsurpassed as a screening test (Hobbs, 1966b), and the presence of a white ring at the junction of the urine and the acid indicated that 162 urines required electrophoresis.

Nevertheless, in the case of six specimens of urine Bence Jones protein was present at concentrations of between 120 and 1,200 mg./100 ml. (estimated only after precipitation with ammonium sulphate) but gave negative results with all the screening tests, was not precipitated by 10% trichloroacetic acid, and was found only by electrophoresis.

The most striking results have been found with the γM paraproteins. Bence Jones proteinuria was associated with 32 of the 34 malignant cases, though it was present at concentrations of only 1 to 20 mg./100 ml. in 26 patients; in the eight benign cases none was detected.

Other Immunoglobulins

Subnormal serum levels of one or more of the immunoglobulins of classes other than that of the paraprotein were found initially in 227 patients, and of these 218 proved to have malignant disease. Only five of 223 patients with malignant conditions had normal levels.

In γG-myelomatosis subnormal levels of γM- and γA-protein were found to be the rule (86 out of 99 patients); seven patients had a concentration of γM within normal limits, seven had a normal γA level, but only one patient had both normal γM and γA. Among 53 patients with γA or γD-myelomatosis, the level of γM was subnormal in 44 and of γG in 42, and only one patient had normal levels of both γM and γG. In myeloma producing Bence Jones protein only, the γM level was subnormal in 40 out of 41 patients: normal levels of γG and γA were found initially in 10 and 9 patients, respectively, but only one patient had concentrations of all three within normal limits. All three patients with undoubted myelomatosis, in whom no paraprotein could be detected, showed subnormal levels of immunoglobulins. Thus among 196 patients who developed myelomatosis only three had normal levels of the other immunoglobulins when first seen. For each immunoglobulin taken separately these results are very similar to those reported by Bachmann (1966), who, however, does not state whether the few patients with normal γA also had normal levels of γM and other proteins.

Of the first 19 patients seen with Waldenström's macroglobulinaemia, two had normal levels of the other immunoglobulins. Among the total of 34 malignant γM-paraproteinaemia (Fig. 2) the levels of γG and γA were within normal limits in 16 and 10, respectively, though only six patients had normal levels of both γG and γA.

In Fig. 2 it can be seen that, though the concentration of the other immunoglobulins tends to decrease as the daily production of paraprotein increases, the presence of γG-paraproteins is associated with the most severe reduction (even less than 10% with daily paraprotein productions below 10 g.). The reduction is not so severe with higher daily productions of γA, γM, and Bence Jones paraproteins. This reduction was especially associated with the malignant group, for the concentrations of the other immunoglobulins, though sometimes at the lower limits, have remained within normal limits in 68 patients in the benign group.

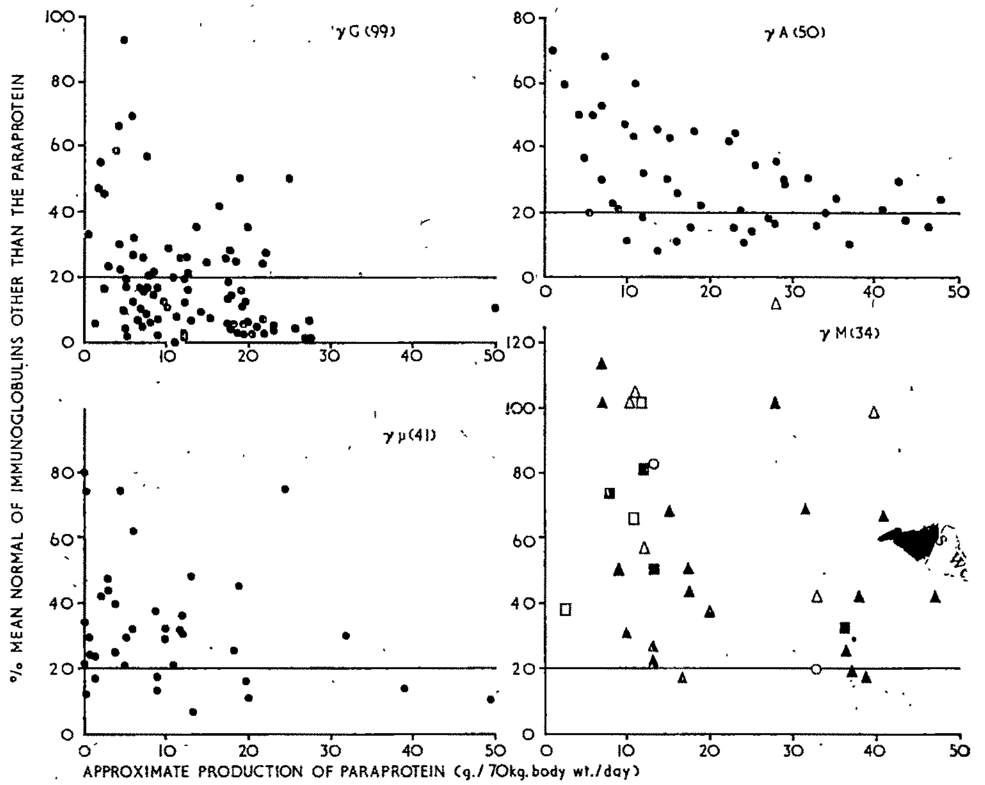


Fig. 2.—Reduction of normal serum immunoglobulins in relation to paraprotein production in patients with malignant conditions. Though there is some trend to lower values with increasing production, γG paraproteins are associated with the most severe reduction at lower production rates than γA and γM classes. The frequencies of patients under 20% agree with an increased incidence of infection presumably due to antibody deficiency (Hobbs *et al.*, 1966). Patients producing Bence Jones protein only (γμ, mostly without renal failure when first seen) present with lower production rates than the others, suggesting differentiation of their tumours. ●, Myelomatosis. ▲, Waldenström's. ■, Lymphosarcoma. (Open symbols indicate 11 additional patients (γM) not in the consecutive series.)

Levels of Serum Paraproteins

Apart from the 45 patients who produced only Bence Jones proteins, 175 patients with serum paraproteins were diagnosed as having malignant conditions, 161 (92%) of whom had levels greater than 1 g./100 ml. when first seen. This contrasts with the 68 patients whose conditions were regarded as benign, 58 (85%) of whom had levels of less than 1 g./100 ml.

Progress in Doubtful Cases

Of the 304 patients there were 110 in whom a firm diagnosis could not be reached initially. In these the paraprotein estimations were repeated at 3- to 12-monthly intervals. Within three years malignant conditions had developed in 29 patients, all of whom showed a significant (>0.2 g./100 ml.) and rapid increase in paraprotein level. In most cases only a second or third measurement was obtained before treatment was begun. Results in the patients who were followed the longest—and who clearly developed the bone lesions of myelomatosis—are shown in Fig. 3. By plotting the paraprotein level on a logarithmic scale against time on a linear scale, it can be seen that the rate of increase is exponential or only slightly curved: the doubling-time ranges from 4 to 25 months. This closely agrees with the data of Hällén (1966), many of whose 23 patients have had a longer follow-up: most of these showed exponential increases, and in 17 it was possible to estimate the doubling-time. Combining his results with the above nine, one obtains a median doubling-time of 12 months. The limit of likely detection of a serum paraprotein on cellulose acetate is about 0.2 g./100 ml. Average serum levels of paraprotein at the time of clinical presentation and diagnosis are γG 4.3 g./100 ml. and γA

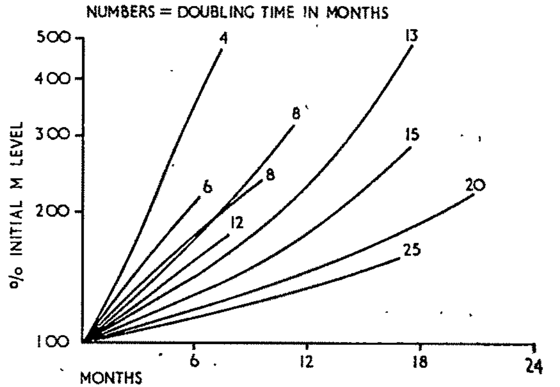


Fig. 3.—Progress in nine untreated patients in whom a diagnosis of myelomatosis was later established. The increasing serum paraprotein (M) level is shown on a logarithmic scale; there were at least four points on each line. The increase is exponential (straight line) or nearly so, enabling estimation of the doubling times in months as indicated above.

2.8 g./100 ml. (Hobbs *et al.*, 1966). Thus an exponential increase from the earliest serum level of chance detection to the average level when clinical diagnosis is certain could take between 18 months and nine years for γG and between 15 months and eight years for γA myelomatosis. Nevertheless, most patients will show significant increases (>0.2 g./100 ml.) in these levels within two years.

In contrast, 66 of the 68 patients classified as having benign conditions have not shown any persistent significant increase over three years. Two have shown increases (1.3 to 2.0 and 1.4 to 1.8 over three years). This finding again agrees well with that of Hällén.

Discussion

The natural frequency of the occurrence of serum paraproteins has been reported by Axelsson *et al.* (1966). Out of a population of 6,995, 64 subjects showed M proteins, and a malignant condition was at that time suspected in only four. Routine electrophoresis of serum obtained from 7,200 new patients at Hammersmith Hospital between December 1963 and June 1964 revealed the existence of 55 paraproteins. After three years' follow-up only 40% of these patients can be considered to have benign conditions, a malignant condition having been diagnosed in 53% and the diagnosis being uncertain in 7%.

From the results it can be seen that Bence Jones proteinuria in excess of 1 mg./100 ml. is of sinister significance. Of the normal daily production of 5 g. of immunoglobulin (Fahey, 1965) only 3.5 mg. (0.07%) appears as normal light chains in the urine, in a concentration of about 0.25 mg./100 ml. (Berggard and Edelman, 1963). Thus an increase in light-chain excretion reflects an inefficient process and probably implies that the synthesizing cells have lost their differentiation. The production of Bence Jones protein indicates further dedifferentiation and the prognosis is worse. These patients present with lower daily paraprotein production rates than those for the other classes (see Fig. 2), and most are dead within six months of diagnosis, though one exceptional patient who survived 15 years has been seen.

The other feature signifying an adverse prognosis is the loss of normal immunoglobulins, originally emphasized by Grabar *et al.* (1956). In four patients a severe reduction in immunoglobulin levels was detected one to three years before the malignant clone was large enough to produce detectable lesions or paraproteins (premyelomatosis).

The mechanism of the suppression of immunoglobulin production remains unknown. Displacement of normal antibody-producing cells seems unlikely; indeed, the production of γA-globulin—which is derived largely from the gut—may be severely reduced with no regional involvement of the gut. The presence of an excess of γG-paraprotein resulted in an increased turnover and a reduced level of normal γG-globulins in six out of the 11 patients studied by Solomon *et al.* (1963). Nevertheless, turnover of γM-globulin has not been shown to be affected (Barth *et al.*, 1964), so that increased catabolism cannot account for the usual severe reduction of γM-globulin levels. It seems probable that the synthesis of γM-globulin is impaired, as is that of γA-globulin. In two patients removal of an apparently solitary myeloma was found to restore the levels to normal (Hobbs, 1966a), and this suggests that the tumours release some humoral substance which inhibits the synthesis of normal immunoglobulins but not that of paraproteins.

Nathans *et al.* (1958)—confirmed by Osserman *et al.* (1964)—found that in mice there was a linear relation between the amount of plasmacytoma and the serum level of γ-paraprotein—which was produced at a daily rate of about 14 mg./g. well-differentiated tumour. This roughly agrees with the estimated rate of production of antibody by single cells (Nossal and Mäkelä, 1962). On average, patients with γG-myeloma have a serum level of this paraprotein of 4.3 g./100 ml. when first seen, and produce some 13 g. of paraprotein daily. This total production could require 930 g. of tumour to be present. Harrison (1962) estimated that for a 70-kg. man the total bone-marrow cellularity was 7.5×10^{11} cells. If the haemopoietic tissue is assumed to weigh a total of 1,625 g., each 1 g. would contain 4.6×10^8 cells, and 930 g. of γG-myeloma tissue could contain 4.3×10^{11} cells. The average 60-kg. man would have a bone marrow of 3,250 g. (Mechanik, 1926). Normally about half is haemopoietic. Patients with γG myeloma have on average 42% myeloma cells in bone marrow biopsies—that is, 685 g. if half the marrow is haemopoietic or 1,370 g. if the marrow is fully occupied. The independent estimate is similar to that based on paraprotein production. If the myeloma tissue is a clone derived from a single cell then it would take almost 39 doubling divisions to reach this number of surviving cells. If we now accept, in man as in the mouse, that the doubling-times of paraprotein levels (4–25 months, Fig. 3) reflect the doubling-times of the cells producing them, it could take 13 to 80 years before the amount of γG-myeloma was sufficient to produce symptoms.

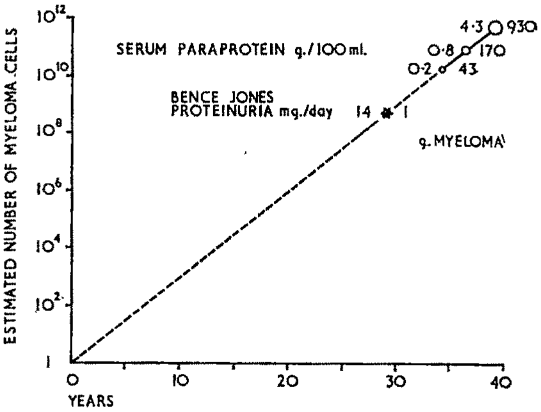


FIG. 4.—Schematic development of myelomatosis. The solid part of the line shows the observed exponential increase of serum paraprotein level from the lowest detectable level of 0.2 to the average level of 4.3 g./100 ml. found in patients presenting with γG-myelomatosis. At the median doubling-time of 12 months this would take about five years. The star indicates the earliest possible detection of myeloma 10.7 years before the usual time at this doubling rate. If it is assumed that the serum level reflects the myeloma mass and its contained cells, the extrapolated broken line shows that if it arose from a single cell and grew at the same exponential rate throughout it began some 39 years previously.

Hence chance detection of a serum paraprotein might not occur for 11 to 70 years (see Results)—though an isolated lesion, such as the collapse of one vertebra or the finding of Bence Jones proteinuria, could reveal the presence of an early myeloma, which might then take up to 20 years to declare itself clinically. These conclusions are summarized in Fig. 4 for a median doubling-time of 12 months: the dotted portion of the line is speculation based on results in the mouse. Similar extrapolations have offered accurate explanations for the latent periods observed between irradiation of humans and the subsequent clinical emergence of acute leukaemia and thyroid cancer (reviewed by Hobbs, 1963).

Such estimates assume that the growth of the cells is exponential throughout, and this is not always the case. Some tumours outgrow their blood supply and undergo necrosis, but myeloma is well placed to avoid this, though a change in growth rate has been seen in two patients. Furthermore, these estimates apply only to well-differentiated tumours, in which virtually all the neoplastic cells eventually produce paraprotein. Our own experience with fluorescent antisera suggests this is so in most cases of myelomatosis, though in the mouse Osserman *et al.* (1964) found that after multiple passages the cells comprising the plasmacytoma could become considerably less differentiated, producing less paraprotein and growing faster. A few patients with obviously extensive rapidly growing myeloma similarly produce little or even no paraprotein, especially those who produce only Bence Jones protein.

In lymphosarcomata and in chronic lymphatic leukaemia, on the other hand, it seems to be the rule that when paraprotein production occurs it involves only a small percentage of the tumour cells. MacKay *et al.* (1957) thought that the presence of macroglobulinaemia in such cases was a secondary phenomenon, and arose from a side-line of mutated cells. The presence of more than one paraprotein has been demonstrated in three of our six patients with lymphomata—an incidence that is in marked contrast to our findings in myelomatosis, five out of a total of 320 patients showing more than one paraprotein. These findings also agree with those of Imhof *et al.* (1966), and support the hypothesis that paraprotein production in the lymphomata reflects unstable, mutating cell populations.

Paraproteins are also found in association with other malignant diseases, but their frequency is no greater than would be expected (Hällén, 1966). Moreover, their levels rarely correlate with the removal or progress of the cancer, and our own experience suggests that this largely occurs by chance.

Summary

Examination of blood and concentrated specimens of urine for paraproteins, together with the measurement of the other immunoglobulins, can have prognostic value in some groups of patients. In doubtful cases, following the paraprotein level can indicate within one to three years which cases are likely to show malignancy, though up to 10 years may be required before the diagnosis is certain, and up to 20 years where solitary lesions or only a trace of Bence Jones proteinuria are the presenting features.

This article would have been impossible without the participation and encouragement of the Medical Research Council and its Myeloma Trial Working-party. Many other patients have been referred from other physicians, particularly my colleagues at Hammersmith, who have kindly provided full details and follow-up data. I am indebted to the staff of the haematology and radiological departments. I would also like to thank Professor I. D. P. Wootton, Professor J. V. Dacie, and Dr. D. A. G. Galton for their guidance ; Miss Hazel Gardner, Miss Susan Burtenshaw, and Mrs. Ann Kasler for their assistance ; and Mr. K. B. Cooke for early guidance in immunoelectrophoresis.

References

Axelsson, U., Bachmann, R., and Hällén, J. (1966). *Acta med. scand.*, **179**, 235.
Bachmann, R. (1966). *Scand. J. clin. Lab. Invest.*, **18**, 273 and 280.
Barth, W. F., Wochner, R. D., Waldmann, T. A., and Fahey, J. L. (1964). *J. clin. Invest.*, **43**, 1036.
Berggard, I., and Edelman, G. M. (1963). *Proc. nat. Acad. Sci. (Wash.)*, **49**, 330.
Bradshaw, T. R. (1906). *Brit. med. J.*, **2**, 1442.
Drivsholm, A. (1964). *Acta med. scand.*, **176**, 257.
Fahey, J. L. (1965). *J. Amer. med. Ass.*, **194**, 255.
Gabuzda, T. G. (1962). *J. Lab. clin. Med.*, **59**, 65.
Grabar, P., Fauvert, R., Burtin, P., and Hartmann, L. (1956). *Rev. franç. Étud. clin. biol.*, **1**, 175.
Hällén, J. (1966). *Acta med. scand.*, Suppl. No. 462.
Harrison, W. J. (1962). *J. clin. Path.*, **15**, 254.
Hobbs, J. R. (1963). M.D. Thesis, London, p. 15.
—— (1965). *Nature (Lond.)*, **207**, 292.
—— (1966a). *Sci. Basis Med. Ann. Rev.*, p. 106.
—— (1966b). *Biochem. J.*, **99**, 15P.
—— and Maatela, J. (1967). To be published.
—— *et al.* (1966). *Lancet*, **2**, 614.
Imhof, J. W., Ballieux, R. E., Mul, N. A. J., and Poen, H. (1966). *Acta med. scand.*, Suppl. No. 445, p. 102.
Lowry, O. H., and Hunter, T. H. (1945). *J. biol. Chem.*, **15[illegible]** 465.
MacKay, I. R., Taft, L. I., and Woods, E. F. (1957). *Brit[illegible]d. J.*, **1**, 561.
Mechanik, N. (1926). *Z. ges. Anat.*, **79**, 58.
Nathans, D., Fahey, J. L., and Potter, M. (1958). *J. exp. Med.*, **108**, 121.
Nossal, G. J. V., and Mäkelä, O. (1962). *Ann. Rev. Microbiol.*, **16**, 53.
Olesen, H. (1963). *Scand. J. clin. Lab. Invest.*, **15**, 497.
Osserman, E. F., Rifkind, R. A., Takatsuki, K., and Lawlor, D. P. (1964). *Ann. N.Y. Acad. Sci.*, **113**, 627.
Solomon, A., Waldmann, T. A., and Fahey, J. L. (1963). *J. Lab. clin. Med.*, **62**, 1.

Lymphocyte Transformation and Chromosome Studies in Hodgkin's Disease

SYLVIA D. LAWLER,* M.D., M.C.PATH. ; C. R. PENTYCROSS,† M.B., B.CH. ; B. R. REEVES,‡ B.SC.

Brit. med. J., 1967, 3, 704–708

The circulating lymphocytes in Hodgkin's disease are assumed to be immunologically deficient because of the poor response shown by the patients in delayed hypersensitivity tests. There is some evidence that this anergy is present even in the earliest stages of the disease (Aisenberg, 1965). The question therefore arises whether the lymphocytes are also abnormal in any other respect.

One way of testing a population of lymphocytes is to study the responses to stimulation in vitro by phytohaemagglutinin. When normal lymphocytes are cultured with phytohaemagglutinin a high proportion are stimulated to divide, and a cell showing the associated morphological changes is said to have "transformed." Recent studies (Hersh and Oppenheim, 1965) have shown that the response of the lymphocytes in Hodgkin's disease is sometimes depressed. At least three factors may influence the response: the lymphocyte count, which is often very low ; the stage of the disease at the time of investigation ; and the effects attributable to radiation or chemotherapy. We have attempted to assess the relative importance of these factors.

Another way of characterizing a cell population is to determine the chromosome complement. Apart from a single case of Spiers and Baikie (1966), in which the peripheral blood lymphocytes were found to be normal, no information about the chromosomes of the circulating lymphocyte in Hodgkin's disease is available. There is no doubt that chromosomal abnormalities are detectable in lymph node material (Ricci *et al.*, 1962 ; Spriggs and Boddington, 1962 ; Galan *et al.*, 1963 ; Baker and Atkin, 1965 ; Miles *et al.*, 1966 ; Spiers and Baikie, 1966). Various abnormalities have been described, including polyploid cells, presumed to represent Sternberg-Reed cells, and anomalous chromosomes, particularly of the E group, in diploid cells.

Materials and Methods

Twenty cases have been studied. Some of the patients are the same as those investigated by Goldman and Hobbs (1967). The method used in the lymphocyte transformation tests is that

---

* Senior Lecturer.
† Leukaemia Research Fellow.
‡ Research Assistant.
Department of Clinical Research, Royal Marsden Hospital and Institute of Cancer Research, London S.W.3.

described by Pentycross (1967) in which the final concentration of cells in culture is 10^6/ml. The phytohaemagglutinin cultures are harvested after 72 hours.

The chromosome and transformation studies were carried out on aliquots of the same blood samples. Microcultures using a slight modification of the method of Arakaki and Sparkes (1963) were often unsuccessful. Better results were obtained when suspensions of separated lymphocytes were used. The method was based on that of Moorhead *et al.* (1960), the polymorphs being removed by carbonyl iron (Carstairs, 1962). The preparations were fixed in 3 : 1 methyl alcohol and glacial acetic acid and the slides made by dropping a suspension in 45% acetic acid on to cold slides, which were then allowed to dry on a warm plate.

Results

Response to Phytohaemagglutinin

The percentage of transformed cells in the cultures from the patients ranged from less than 1 to 56 (transformation score). In our laboratory the score for normal people is 36–60%. Many workers quote a higher score than this for normal lymphocytes. In our laboratory at least 4,000 cells are counted from each culture by scanning the slides in systematic strips. This scoring method gives a result representative of the entire cell population in the culture.

In assessing the cultured lymphocytes *qualitatively,* two types of anomalous cell, which are only rarely seen in normal controls, were found to occur with increased frequency. (1) Large, probably transformed, cells having a bizarre nuclear pattern and ragged pale cytoplasm. The nucleoli (almost invariably present) were amorphous, basophilic, and completely circular. (2) Cells the size of small and medium lymphocytes with amorphous nuclei.

In some instances, moreover, the majority of transformed cells satisfied only the morphological criteria (stippling of nuclear chromatin, visible nucleoli, large size, and cytoplasmic basophilia) to a limited degree.

Anomalous cells and poorly transformed ones were found predominantly in association with transformation scores of less than 30%.

The patients have been arranged in the Table according to the transformation score. When a patient was tested a second time the higher score decided the position in the table.

The clinical staging (column 5 in table) was that of Peters (1950), modified by Kaplan (Karnofsky, 1966), as follows:

Stage 0: no detectable disease owing to excisional biopsy.

Stage I: disease localized to a single node and contiguous structures without systemic symptoms.

Stage II: disease limited by the diaphragm to the upper or lower half of the body, but at more than a single site.

Stage III: disease above and below the diaphragm.

Stage IV: disease demonstrated in any one of the following areas: bone marrow, pulmonary parenchyma, skin, gastrointestinal tract, or bone.

Stages II and III are subdivided into A and B, with or without symptoms of generalized disease respectively.

These stages depend, to a large extent on visible or palpable masses which do not necessarily relate to the total tumour bulk.

The information in the Table may be summarized as follows:

(*a*) There is some correlation between the percentage of transformed cells in the cultures of peripheral blood lymphocytes and the clinical staging. Thus the five patients in stages 0–I all had scores between 32 and 52%. On the other hand, the scores for the 15 patients in stages II–IV ranged from less than 1% to 56%, though all the patients with a score of less than 12% of transformed cells were staged at least as IIB.

(*b*) Age and length of history appear not to have influenced lymphocyte response to any significant degree.

(*c*) Of the two untreated patients, one (Case 1) had a transformation score within normal limits, and the other (Case 12) a score just below normal. However, chemotherapy and recent *local* irradiation do not appear to have contributed to any extent to the depression of the lymphocyte response in this series.

(*d*) Some of the patients with lymphopenia (less than 1,500/ml.) had low transformation scores. Virtually all those with transformation scores of 12% or less were lymphopenic. However, a normal lymphocyte count was not necessarily associated with scores in the normal range.

(*e*) With one exception (Case 9), there was no significant difference in transformation score when tests were performed twice on any one patient.

Chromosome Studies

The results of the chromosome studies are given in column 9 of the Table. Only those cells which did not show features suggesting radiation damage were analysed in detail, but all cells appearing in the Table were scored for the presence of secondary constrictions in the paracentric third of the long arms of chromosome C9.

Mitotic yields were poor in patients with a low score in the transformation test. Good mitotic yields were obtained in the cultures in Cases 6 (*b*) and 11, but only a few cells were of sufficient quality for analysis. This explains the discrepancy in these cases between the response of the lymphocytes to phytohaemagglutinin and the amount of data on the chromosomes.

In the series as a whole 19 cells out of 89 analysed were aneuploid. Twelve of these aneuploid cells were contributed by two patients (Cases 3 and 14). Rearranged modal cells were found in Case 3 but not in Case 14. Concurrently 89 cells were analysed from lymphocyte cultures of three normal individuals (covering the age range of patients in the study) and nine were found to be aneuploid.

In one untreated patient (Case 1) a hypomodal cell was found which contained a marker chromosome resembling a B-group chromosome with most of the short arms missing.

Some polyploid cells, not suitable for analysis, were seen in three patients (Cases 2, 3, and 11). The most likely cause of an increased number of polyploid cells is previous treatment with irradiation (Buckton *et al.*, 1962); it is unlikely that these cells represent circulating Sternberg–Reed cells.

The criteria for assessing radiation damage were based on the data of Buckton *et al.* The aberrations seen in our material were fragments, dicentrics, and chromosomal rearrangements. Cells showing features of radiation damage were seen in two patients (Cases 13 and 14) who had been treated with vinblastine sulphate but not by irradiation. The possibility arises that the damage was due to the action of vinblastine in vivo, but we have been unable to produce chromosome breakage in normal lymphocyte cultures in vitro with vinblastine even with concentrations as high as 100 μg./ml. of culture medium.

In two patients (Cases 3 and 13) an apparent dicentric chromosome formed by an end-to-end association of two chromosomes was observed. In Fig. 1 the D/F associated chromosome of Case 3 is shown; with this associated chromosome separated, the cell had a normal karyotype. In Case 13 (Fig. 2) the association was between A3 and G21-22, but the cell showed evidence of radiation damage. This type of association is not generally recognized as a radiation effect, but it has been described in cultures of cells infected with virus (Moorhead and Saksela, 1963). Marker chromosomes composed of two chromosomes in an end-to-end association have been observed in testicular tumours from untreated patients (Martineau, 1967).

Secondary constrictions were seen in 11% of C9 chromosomes in the normal controls previously mentioned. Among the patients, constrictions were present in 35% of available C9 chromosomes. An example of a constricted C9 chromosome

Details of Patients

Case No.	Sex	Age	Length of History (yrs.)	Stage When Tested	Treatment			Leucocyte Count	Transformed Cells %	Chromosome Studies				
					XRT	Yrs. Post XRT	Chem.			Secondary Constrictions in C9	Total Cells	Analysed Cells		Radiation Damaged Cells
												Chromosome Number		
												46	Others	
1	M	18	3/12	IIIA	0	0	0	T7000 L1470	56	13+2Ex.	16	15.N	1.n=45.D–1.M	0
2 (b) (31)	M	67	2.8/12	O–I	×1	2.3/12	0	T9000 L2520	52	12+6Ex.	18	11.N	0	7
2 (a) (31)	M	67	2.5/12	O–I	×1	2	0	T5500 L1820	42	8+3Ex.	11	6.N	1.n=45.C–1. 1.n=43.C–1:G–1:D–1	3
3 (a) (27)	M	18	2.5/12	I	×2	8/12	0	T4400 L1760	47	3+6Ex.	5	1.N 1.C+1:E–1.	1.n=45.F–1. 1.n=44.E–2 1.n=43.E–1:F–2.	0
3 (b) (27)	M	18	2.8/12	I	×2	1	0	T4400 L1890	47	7+3Ex.	10	4.N 1.C+1:E–1. 1.D/F Ass'n	2.n=45.F–1.	2
4 (a) (49)	M	64	8/12	IIIB	×1	2/12	CB VLB	T3200 L 500	44	0	1	0	1.n=47.C+1.	0
4 (b) (49)	M	64	9/12	IIIB	×1	3/12	CB VLB	T6800 L 270	42		N.A.			
5 (a) (10)	F	26	7.6/12	IV	×5	1.2/12	CB	T5000 L2200	44		N.M.			
5 (b) (10)	F	26	8	IV	×5	1.6/12	CB	T6000 L2400	40	0	2	1.N	0	1
6 (a) (18)	M	28	4.7/12	O–I	×1	4.7/12	0	T5000 L1960	40	1	4	2.N	1.n=45.G–1.	1
6 (b) (18)	M	28	5	O–I	×1	5	0	T7000 L1300	35		N.A.			
7 (19)	M	29	4.3/12	IIIB	×1	1.9/12	CP M	T5000 L1650	37		N.A.			
8	M	57	2	IIIB	×1	1.10/12	CP M	T4800 L1500	37		N.A.			
9 (b)	F	23	8.2/12	IIIB	×10	11/12	CB	T6000 L 660	36	1Ex.	6	4.N	0	2
9 (a)	F	23	8	IIIB	×10	9/12	CB	T6300 L 630	3		N.A.			
10 (23)	F	37	3.8/12	O–I	×1	3.1/12	0	T5000 L1400	33	6	5	2.N	1.n=47.E+1.	2
11	F	36	1.3/12	O–I	×3	7/12	0	T5500 L1020	32	0	4	0	0	4
12 (47)	F	83	9/12	IIIA	0	0	0	T18000 L?	31		N.M.			
13 (a)	M	50	3/12	IIB	0	0	VLB	T8500 L1780	28		N.A.			
13 (b)	M	50	5/12	IIB	0	0	VLB	T5400 L2700	22	2	6	4.N.	0	[2]
14	M	18	3/12	IIA	0	0	VLB	T4200 L1000	27	0	21	13.N	1.n=45.D–1. 1.n=45.C–1. 2.n=44.C–2. 1.n=44.D–1:F–1. 1.n=44.A+1:C–3. 1.n=44.B–1:C–1.	[1]
15	M	19	1	IIIB	×1	6/12	CB VLB	T8000 L1040	12	4+3Ex.	4	1.N	1.n=47.G+1	2
16 (a) (11)	M	35	6.7/12	IIB–IIIB	×2	3.2/12	CP M	T6000 L1440	12		N.M.			
16 (b) (11)	M	35	7.1/12	IIB–IIIB	×3	0	CP M	T4000 L 640	1	4+2Ex.	3	2.N	0	1
17 (a) (16)	F	65	5.5/12	II–IIIB	×1	1.2/12	0	T3500 L 805	8		N.M.			
17 (b) (16)	F	65	5.6/12	II–IIIB	×1	1.3/12	0	T3500 L 735	2		N.M.			
18 (44)	M	25	1	IV	×1	3/12	0	T5000 L1400	8		N.M.			
19 (b) (28)	M	51	2.10/12	III–IV	×2	8/12	Steroids	T6000 L1380	2		N.A.			
19 (a) (28)	M	51	2.6/12	III–IV	×2	4/12	Steroids	T6000 L1500	1	0	2	1.N	0	1
20 (24)	M	55	3.6/12	IIIB–IV	×3	0	0	T4000 L 440	1		N.M.			

Key to Table

Column 1.—( ) = Number in series of Goldman and Hobbs (1967). (a) = First test. (b) = Second test.
Column 5.—O-IV = Clinical staging of Peters (1950), modified by Kaplan (Karnofsky, 1966). A = No symptoms. B = Symptoms of generalized disease.
Column 6.—M = Mustine hydrochloride. CP = Cyclophosphamide. VLB = Vinblastine sulphate. CB = Chlorambucil.
Column 7.—T = Total W.B.C. L = Lymphocytes.
Column 9.—Ex. = Exaggerated or attenuated secondary constrictions. N = Normal diploid. N.M. = No mitoses. N.A. = No cells suitable for analysis. M = Marker chromosomes. [ ] = Damage of radiation type

from a lymphocyte culture of a normal control, when using the same technique of culture, is shown in Fig. 3. Some of the constrictions obtained in the cultures of the patients were exaggerated and sometimes markedly attenuated, and in the Table these are indicated by the abbreviation Ex. An example of an attenuated constriction is shown in Fig. 4, and the tendency for acrocentric chromosomes to associate with such regions (Ferguson-Smith and Handmaker, 1963) is shown in Fig. 5. No exaggerated constrictions were seen in normal controls.

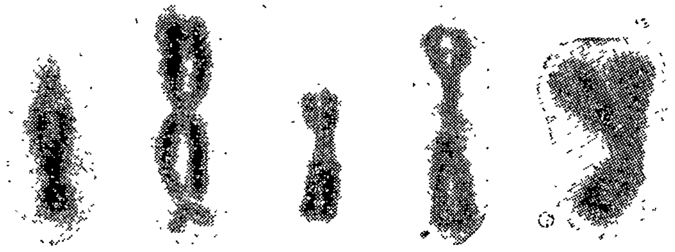


FIG. 1 FIG. 2 FIG. 3 FIG. 4 FIG. 5

FIG. 1.—D/F. Associated chromosome from Case 3. FIG. 2.—A3/G. Associated chromosome from Case 13. FIG. 3.—Constricted C9 chromosome from normal control lymphocyte culture. FIG. 4.—Attenuated constriction in a C9 chromosome from Case 3. FIG. 5.—D-chromosome associated with the exaggerated constriction in a C9 chromosome from Case 2.

Discussion

Response to Phytohaemagglutinin

There does seem to be a correlation between the clinical staging and the transformation scores. However, as noted already, the clinical staging may not precisely reflect the severity of the disease, since it depends on a visual assessment of the amount of disease present, which may bear no relation to total tumour bulk. A lymphangiogram, which is a useful test, especially for distinguishing stage II from stage III, was not always carried out on these patients.

The partial association between the lymphocyte count and the transformation score provides an interesting contrast to the situation existing in chronic lymphocyte leukaemia where there is a correlation between a high total lymphocyte count and a low transformation score (Hayhoe *et al.*, 1967). In the latter disease it would seem that there is a large population of lymphocytes which are unresponsive to phytohaemagglutinin, and therapy preferentially eliminates these. It is possible that in Hodgkin's disease there is a progressive reduction in both the numbers of lymphocytes and their responsiveness.

Local irradiation does not seem to have influenced the transformation score. Millard (1965) established that large doses of irradiation, not localized, may depress lymphocyte transformation for variable periods after cessation of therapy.

There may possibly be other (as yet unknown) factors. Case 7 was tested when in stage IIIB, and in fact died within three months, and yet his cells transformed moderately well. Case 9 differed in no way clinically or haematologically on the two occasions she was tested, but the transformation score varied between 3 and 36%.

Chromosome Studies

As might be expected when the response to phytohaemagglutinin is depressed, only few cells, if any, were available for analysis in patients with low scores in the transformation test. Suspension cultures proved more successful than microcultures. The failure of microcultures in lymphopenic patients can be attributed to the fact that an excessive number of red cells must be included in order to have an adequate number of lymphocytes.

In this series, more aneuploid cells were observed than were found in normal controls. This observation could be accounted for, at least in part, by radiation effects. There was no evidence for the circulation of a population of lymphocytes with abnormal chromosome complements. With the exception of the marker chromosome present in one cell of Case 1, no abnormal chromosomes resembling those observed in diploid cells obtained from lymph node material were seen.

In most cases the number of hypomodal cells was compatible with the assumption that they were randomly broken cells. The number of hypomodal cells in two patients (Cases 3 and 14) was significantly higher than in normal controls. This does not necessarily mean that a tendency to errors in division had produced the aneuploidy. Such a result could also be observed if the cells were more easily broken by the standard procedure than normal ones. The rearranged modal cells in Case 3 could not obviously be attributed to irradiation, but it is a possible cause, since Buckton *et al.* (1962) showed an increase in aneuploidy which continued for many years after *x*-ray treatment had been completed. In Case 14, treatment with vinblastine may have been the cause of increased aneuploidy. It is rare to find hypermodal cells in normal controls, but though one hypermodal cell was found in each of three patients the significance of this is difficult to assess because of the low mitotic yield.

The number of radiation-damaged cells observed was within the range described for lymphocytes in patients irradiated for other diseases.

The presence of prominent secondary constrictions in C9 chromosomes has been observed in lymph node material from patients with lymphomas (Miles *et al.*, 1966). In this laboratory, cells from a node of a patient with Hodgkin's disease, additional to those in the series, showed constrictions in 16 (38%) of the available C9 chromosomes when cultured with phytohaemagglutinin. Four of these constrictions were exaggerated.

This feature of increased frequency and prominence of secondary constrictions in the chromosomes of lymphoid cells is not restricted to Hodgkin's disease, since we have also observed it in patients with other malignant lymphomas and plasmocytoma. In assessing the significance of this observation certain facts have to be taken into account. These constrictions can be observed in lymphocyte cultures from normal individuals with a lower frequency, but it is extremely rare to find them in the attenuated form shown in Figs. 4 and 5. The frequency and the appearance of these constrictions can be altered in cultures of normal cells by varying the proportions of methyl alcohol and acetic acid in the fixative (Saksela and Moorhead, 1962), but in the present study the fixative was maintained throughout at the standard concentration. Cells treated with SV 40 virus in culture (Moorhead and Saksela, 1963) or with mitomycin C (Cohen and Shaw, 1964) or bromodeoxyuridine (Kaback *et al.*, 1964) also show an increased number of secondary constrictions. The appearances of the attenuated constrictions seen in the present study resemble the effect produced by the addition of mitomycin C to in-vitro cultures of lymphocytes. In this context it is interesting to note that mitomycin C, in causing chromosomal breakage in vitro, shows a preference for the areas of secondary constrictions. In this respect it differs from the other agents that have a random effect, though some of these may induce increased frequency of secondary constrictions.

The occurrence of secondary constrictions is not restricted to C9 chromosomes, but in this study it is the quantitative increase and attenuation in this particular chromosome that is most notable. The effect cannot be regarded as a specific one because it has been observed in patients with malignant lymphoma of different histological patterns and it is an exaggerated expression of a normal feature of the chromosomes. The enhancement of the secondary constriction in these diseased states is probably not due to treatment, since it can be observed in untreated cases. The association between lympho-proliferative disorders and the prominence of these regions of the chromosomes which are peculiarly sensitive to alteration by the action of certain chemical agents may have some relevance to the choice of drugs to be used in treatment.

Summary

The characteristics of the circulating lymphocytes in Hodgkin's disease have been investigated in 20 patients. The methods used were (1) in vitro response to phytohaemagglutinin and (2) chromosome analysis.

Transformation Studies.—The percentage of the lymphocytes that transformed morphologically after stimulation with phytohaemagglutinin varied between less than 1 and 56 (normal controls 36–60%). The depression of response was correlated to some extent with the severity of the disease. In some instances a low transformation score was associated with total lymphopenia. The depression of response did not appear to depend on current or previous treatment. It was concluded that the deficiency in response is one of the manifestations of the disease.

Chromosome Studies.—Mitotic yields were often low, but better results were obtained with suspension cultures than with microcultures. Most of the aneuploid cells, or cells with anomalous chromosomes, which we observed could be attributed to the effects of treatment. The frequency of radiation damage was within expected limits as compared with patients irradiated for other diseases. An increased frequency of constrictions in the C9 chromosome and the occasional exaggeration of this constriction was observed. This represents a modification of a feature present in normal cells and is by no means specific to Hodgkin's disease, since it has been observed in lymphoid cells in cases of other malignant lymphomas and in plasmocytoma.

The studies gave no indication of the circulation of a population of chromosomally abnormal lymphocytes, the majority of cells analysed having a normal chromosome complement.

We wish to thank Dr. L. Szur for permission to study his patients at the Hammersmith Hospital, and the consultant staff at the Royal Marsden Hospital for access to their patients; Dr. J. M. Goldman and Dr. J. R. Hobbs for their co-operation; and Dr. D. A. G. Galton for his valuable criticism of the manuscript.

C. R. P. gratefully acknowledges a grant from the Leukaemia Research Fund Ltd. in support of his work.

Requests for reprints should be addressed to Dr. S. D. Lawler, Department of Clinical Research, Royal Marsden Hospital, London S.W.3.

REFERENCES

Aisenberg, A. C. (1965). *Blood*, **25**, 1037.
Arakaki, D. T., and Sparkes, R. S. (1963). *Cytogenetics*, **2**, 57.
Baker, M. C., and Atkin, N.B. (1965). *Brit. med. J.*, **1**, 770.
Buckton, K. E., Jacobs, P. A., Court Brown, W. M., and Doll, R. (1962). *Lancet*, **2**, 676.
Carstairs, K. (1962). Ibid., **1**, 829.
Cohen, M. M., and Shaw, M. W. (1964). *J. Cell. Biol.*, **23**, 386.
Ferguson-Smith, M. A., and Handmaker, S. D. (1963). *Ann. hum. Genet.*, **27**, 143.
Galan, H. M., Lida, E. J., and Kleisner, E. H. (1963). *Lancet*, **1**, 335.
Goldman, J. M., and Hobbs, J. R. (1967). *Immunology*, **13**, 421.
Hayhoe, F. G. J., Sinks, L. F., and Flemans, R. J. (1967). In *The Lymphocyte in Immunology and Haemopoiesis*, edited by J. M. Yoffey, p. 66. London.
Hersh, E. M., and Oppenheim, J. J. (1965). *New Engl. J. Med.*, **273**, 1006.
Kaback, M. M., Saksela, E., and Mellman, W. J. (1964). *Exp. Cell Res.*, **34**, 182.
Karnofsky, D. A. (1966). *Cancer Res.*, **26**, 1091.
Martineau, M. (1967). *Lancet*, **1**, 386.
Miles, C. P., Geller, W., and O'Neill, F. (1966). *Cancer*, **19**, 1103.
Millard, R. E. (1965). *J. clin. Path.*, **18**, 783.
Moorhead, P. S., Nowell, P. C., Mellman, W. J., Battips, D. M., and Hungerford, D. A. (1960). *Exp. Cell. Res.*, **20**, 613.
—— and Saksela, E. (1963). *J. cell. comp. Physiol.*, **62**, 57.
Pentycross, C. R. (1967). *J. clin. Path.* In press.
Peters, M. V. (1950). *Amer. J. Roentgenol.*, **63**, 299.
Ricci, N., Punturieri, E., Bosi, L., and Castoldi, G. L. (1962). *Lancet*, **2**, 564.
Saksela, E., and Moorhead, P. S. (1962). *Cytogenetics*, **1**, 225.
Spiers, A. S. D., and Baikie, A. G. (1966). *Lancet*, **1**, 506.
Spriggs, A. I., and Boddington, M. M. (1962). Ibid., **2**, 153.

Mushroom-worker's Lung

ALEX SAKULA,* M.D., M.R.C.P.

[WITH SPECIAL PLATE BETWEEN PAGES 708 AND 709]

Brit. med. J., 1967, **3**, 708–710

In recent years the increased demand for mushrooms as a table delicacy has led to the development of intensive methods of cultivation in mushroom-growing farms. Many workers are at present involved in mushroom growing, and are therefore exposed to any potential hazard which might be associated with the process.

Mushroom growers have themselves been aware of the occasional development of various symptoms during the course of their work, but the only medical report of these was by Bringhurst *et al.* (1959), who described a respiratory disease among 16 immigrant Puerto Ricans working in the "Chester" County area of Pennsylvania, where 90% of the mushrooms consumed in the United States are cultivated. No special reports of similar cases have appeared since then.

In this paper four cases are described of mushroom workers in Sussex (where 50% of English mushrooms are cultivated) who developed respiratory disorders thought to be related directly to their occupation.

Mushroom Cultivation

The common edible mushroom, *Agaricus hortensis* (or *Psalliota bispora*), is grown on natural compost, consisting of a mixture of wheat straw and fresh horse manure, which is allowed to become partially decomposed or composted. This composting takes place in two phases.

In phase 1, carried on outdoors, stacks of compost are exposed to the atmosphere for three weeks. In phase 2 the compost is placed on to large wooden trays, introduced into closed chambers, and subjected for several days to a peak heat of 55–60° C., and 100% humidity, produced by blowing live steam into the chambers. This pasteurizing process kills off the pests and organisms which would interfere with the growth of the mushrooms. Various thermotolerant and thermophilic actinomycetes find the conditions of both phases of the composting process conducive to their growth.

The compost is then cooled to 25° C., and planted with specially prepared mushroom mycelium grown on manure or grain (known as spawn). This spawning process is usually

---

* Consultant Physician, Redhill General Hospital, Surrey.

ALEX SAKULA: MUSHROOM-WORKER'S LUNG

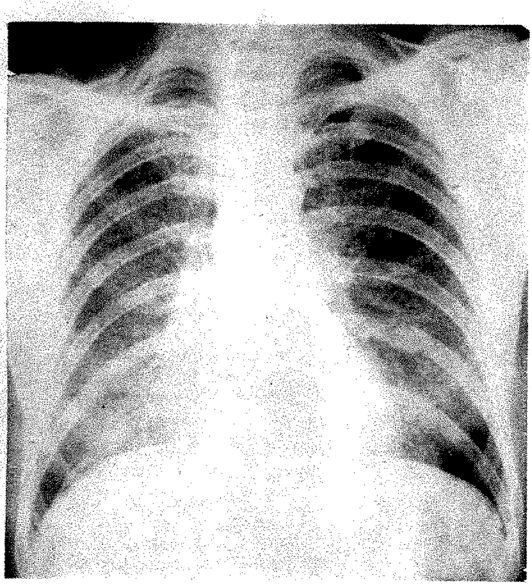


FIG. 1. — Case 1. Chest radiograph showing generalized mottling in both lungs and prominent hila.

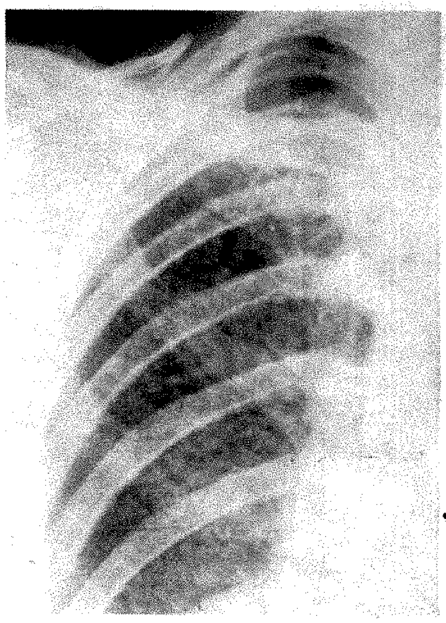


FIG. 2. — Case 1. Enlarged view of **right** upper zone of Fig. 1.

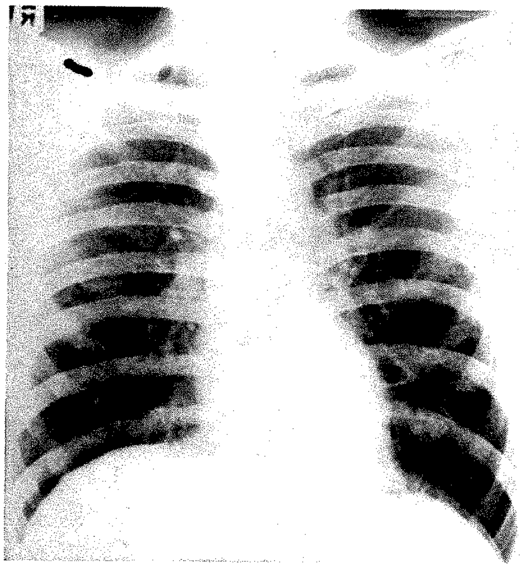


FIG. 3. — Case 2. Chest radiograph showing generalized mottling in both lungs.

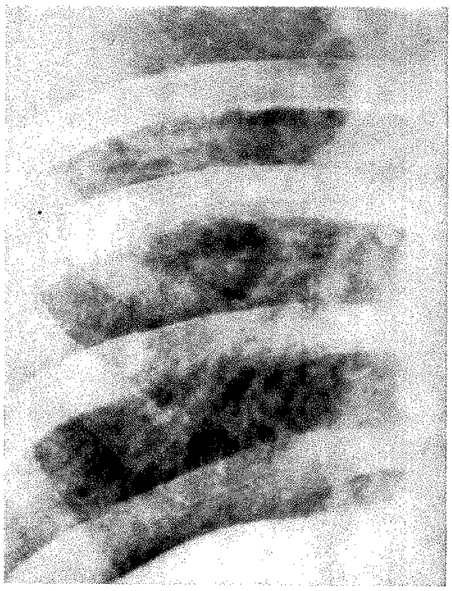


FIG. 4. — Case 2. Enlarged view of right lower zone of Fig. 3.

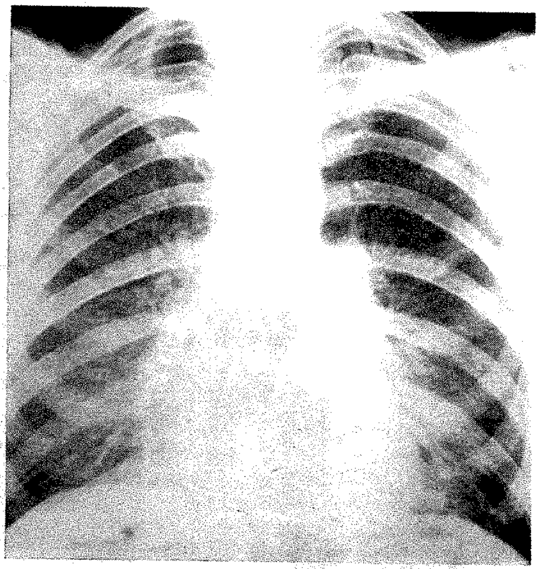


FIG. 5. — Case 3. Chest radiograph showing prominent hila and confluent mottling in both lungs, chiefly in lower zones.

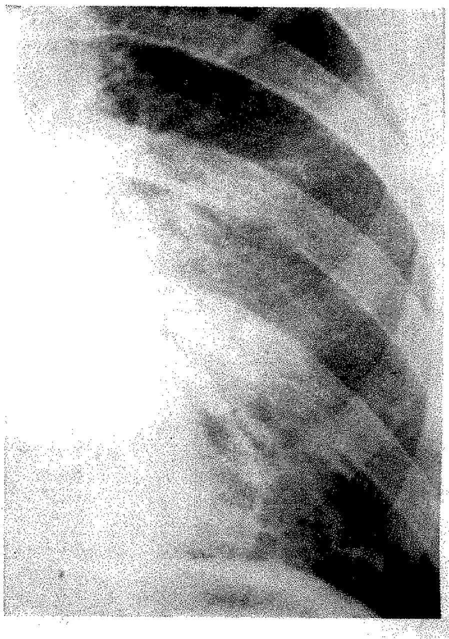


FIG. 6. — Case 3. Enlarged view of left lower zone of Fig. 5.

D. KENWIN HARRIS AND W. G. F. ADAMS: ACRO-OSTEOLYSIS FROM POLYMERIZATION OF VINYL CHLORIDE

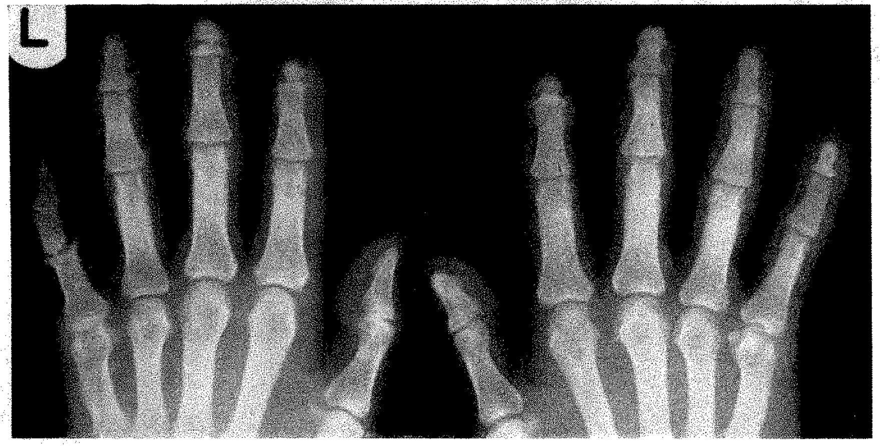


FIG. 1.—Case 1. Erosions of the terminal phalanges of index and middle fingers, both hands.

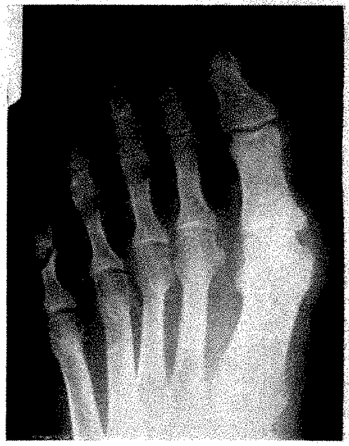


FIG. 2.—Case 1. Disorganization of the fifth proximal interphalangeal joint and erosions of the distal ends of the fifth proximal phalanges of both feet.

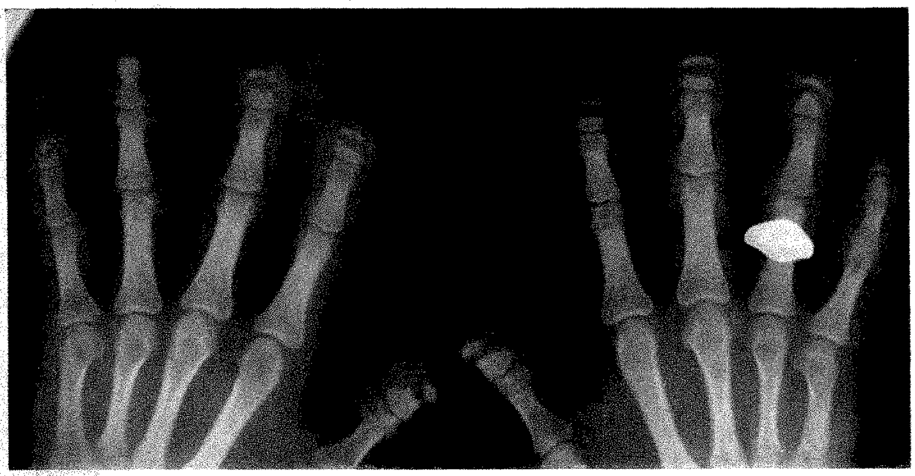


FIG. 3.—Case 2. Osteolysis is present in all the terminal phalanges except the left ring finger.

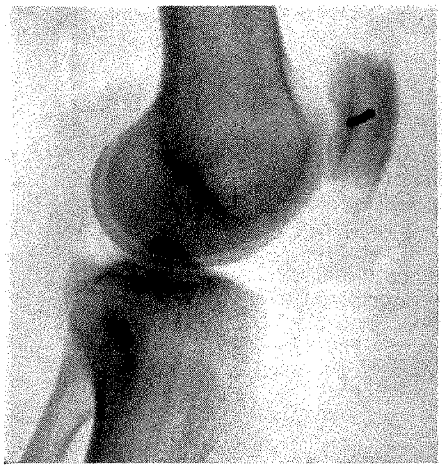


FIG. 4.—Case 2. Cortical erosion of posterior surface of the patella.

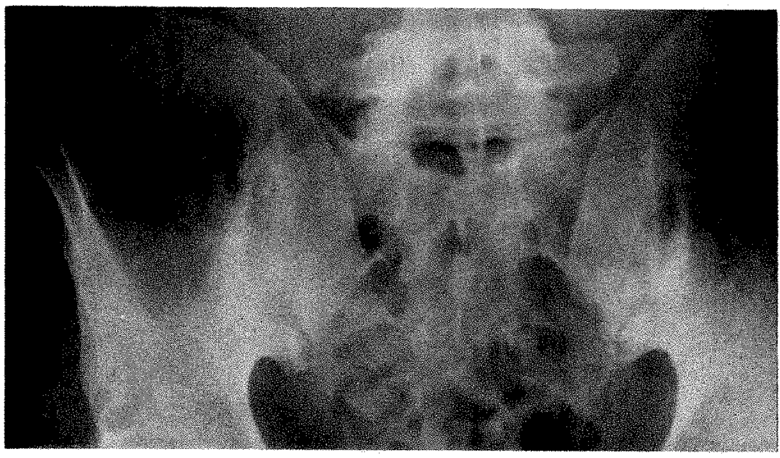
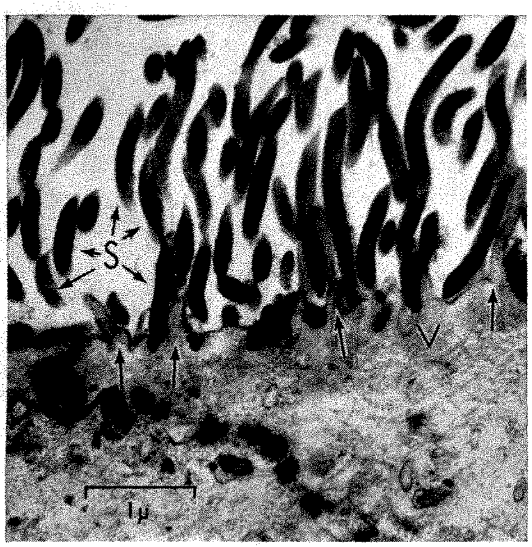


FIG. 5.—Case 2. Widening of the sacroiliac joint space, with cystic marginal sclerosis.

W. A. HARLAND AND F. D. LEE: INTESTINAL SPIROCHAETOSIS



Surface of two epithelial cells with numerous spirochaetes (S) orientated in the long axis of the cell. Arrows indicate microvilli. V is a reactive vacuole.

carried out by hand, either direct into the compost or by broadcasting the spawn on to the trays. The spawn is then mixed mechanically with the compost (through spawning), this process producing some disturbance of the compost with liberation of dust. Spawn running then occurs, the temperature being maintained at 20–25° C., with 90% humidity.

The compost in the trays is then covered or cased with a thin layer of peat-chalk mixture, which has previously been sterilized by heat or chemicals. This casing is necessary to encourage the fruiting of the mushrooms. The trays are then placed in the mushroom sheds, where the temperature is kept steady at 15° C. and the humidity at 80–90%, careful ventilation being maintained. The first growth or cropping will usually take place three weeks later, and the picking and packing of the mushrooms begins. Fresh flushes of mushrooms appear at weekly intervals, usually for six weeks. To prevent various parasitic diseases which might damage the mushrooms, various bactericides and fungicides—for example, formaldehyde—and pesticides and insecticides—for example, D.D.T. —are sprayed into the mushroom sheds. After the final picking the mushroom sheds are cooked out at 60° C., and the trays are emptied of the compost, which is dumped in a field.

It is during the spawning operation and when the mushroom sheds are emptied that most dust is liberated.

Case 1

A man aged 44 started work at a mushroom farm in November 1965 and was chiefly concerned with the spawning process. A month later he began to feel dizzy, developed headache and generalized muscle aches, and vomited. Cough and sputum ensued, and he became dyspnoeic on effort, with pain in the chest. When first seen in December 1965 he had ceased work, his symptoms were already subsiding, and there were no abnormal physical signs detectable in the chest. The chest radiograph showed a diffuse miliary mottling throughout both lung fields, the hilar shadows looking prominent (Special Plate, Figs. 1 and 2). Sputum culture produced a mixed growth of organisms; *Myobacterium tuberculosis* was not isolated. The tuberculin test was positive. W.B.C. was 8,000/cu. mm. (neutrophils 63%, lymphocytes 31%, monocytes 5%, eosinophils 1%); E.S.R. 8; serum proteins 6.4 g./100 ml. (albumin 4.1 g., globulin 2.3 g.). Skin allergy tests (including *Aspergillus fumigatus*) were negative. Serum precipitin tests were positive to *Micromonospora vulgaris* and negative to *Thermopolyspora polyspora* and to *A. fumigatus.*

During the ensuing month his symptoms cleared completely and the chest radiograph returned to normal. He ceased work on the mushroom farm, but when seen a year later, in April 1967, he was still bothered at times by undue dyspnoea and chest pain. A repeat of the serum precipitin test was negative to *T. polyspora.*

Case 2

A man aged 49 started work at a mushroom farm in February 1965. In December 1966 he became unduly dyspnoeic on effort, and developed cough and purulent sputum, these symptoms tending usually to be worse on Wednesdays, when he was engaged on spawning. The symptoms generally cleared by the week-end, only to return on the following Wesdnesday, when he needed to perform the spawning process again. His dyspnoea became so marked that he required to be admitted to hospital for one month, by the end of which time his condition had improved. On return to his former work, however, the respiratory symptoms at once occurred.

When first seen in February 1967 there were no abnormal physical signs in the chest. Chest radiographs showed a diffuse mottling in both lung fields, chiefly in the lower halves, but the hila were not prominent (Special Plate, Figs. 3 and 4). Sputum culture produced a light mixed normal growth. Culture for fungi was negative. *M. tuberculosis* was not isolated. The tuberculin test was negative. W.B.C. was 8,700/cu. mm. (neutrophils 67%, lymphocytes 29%, monocytes 4%); E.S.R. 13. Pulmonary function tests showed peak flow rate 415 litres per minute, forced vital capacity 4.05 litres, and forced expiratory volume in one second 3.25 litres (77% of F.V.C.). The serum precipitin test was positive to *T. polyspora.*

He remained away from his work and soon lost his respiratory symptoms; within two months the chest radiographs showed the lung mottling to have cleared completely.

Case 3

A man aged 47 was first seen in October 1960. He had been working at a mushroom farm for six months, being chiefly involved with the spawning process. He gave a six-weeks history of dyspnoea, this developing after what he had thought to be an "influenzal" illness. He was troubled by a spasmodic cough, little sputum, and attacks of dyspnoea several times daily. He felt weaker, had night sweats, and his weight dropped by 10 kg. Crepitations were audible over both lung bases. Chest radiographs showed a marked diffuse fine mottling, chiefly of the lung bases, to the extent that there was a "ground glass" effect, and the hilar shadows were prominent (Special Plate, Figs. 5 and 6). Sputum culture produced a mixed growth of organisms. *M. tuberculosis* was not isolated. W.B.C. was 4,500/cu. mm. (neutrophils 64%, lymphocytes 30%, monocytes 3%, eosinophils 3%); E.S.R. 18. The tuberculin test was positive. Skin allergy tests (including moulds and mushrooms) were negative.

After receiving penicillin and streptomycin by injection for one day he was remarkably improved. The antibiotics were discontinued, as it was thought that the rapid recovery suggested the subsidence of some sensitivity reaction rather than an infection. He returned to his former work, but was immediately troubled by bouts of dyspnoea, especially at night. Chest radiographs continued to show the mottled appearance at the lung bases. Treatment with prednisone was therefore started, and when seen a month later he had improved.

He returned to work at the mushroom farm, but was taken off the spawning process, though he remained in contact with the compost when emptying the trays and disposing of the used compost. When seen some years later, in April 1967, he was still bothered by undue dyspnoea and occasional chest tightness. Chest radiographs showed clearing of the mottling, though the right lung base looked fibrotic. Serum precipitin tests were negative to *T. polyspora* and *A. fumigatus.*

Case 4

A girl aged 17 was first seen in August 1960. She had been employed as a picker and packer in the mushroom sheds since leaving school at the age of 15. She had become subject to episodes of dizziness and cough for several months, but one week before being seen she developed anorexia and nausea, after which she became dizzy and more easily dyspnoeic, and chest pains developed. She had a cough, with purulent sputum, at times blood-stained. In addition, an irritating maculopapular rash appeared on the trunk and limbs. These symptoms developed within a few hours of entering the mushroom sheds, and cleared spontaneously after 48 hours' avoidance of the sheds. Clinical examination of the chest did not reveal any abnormal physical signs, and the chest radiograph looked normal. At first she was thought to have a simple bronchitis and and was treated with tetracycline, with improvement.

A month later she returned to her former work, but on re-entering the mushroom sheds she fainted on two occasions. Further investigation showed the chest radiograph to remain normal. Sputum culture grew normal flora. Culture for fungi was negative. *M. tuberculosis* was not isolated. The tuberculin test was negative. W.B.C. was 4,800/cu. mm. (neutrophils 62%, lymphocytes 31%, monocytes 7%). Bronchoscopy showed the bronchial mucosa to be pale and oedematous, and biopsy revealed normal histology. Skin allergy tests showed a positive reaction to moulds (including *A. fumigatus*), negative to mushrooms. Serum precipitin tests for moulds (including *A. fumigatus*) were negative. Cultures of specimens of the compost, the casing (peat and chalk), and sweepings of dust from the floor of the mushroom sheds all grew *A. fumigatus.* The serum precipitin test against *A. fumigatus* was negative.

The circumstantial evidence was strong enough to justify advising the girl to change her occupation. When seen six months later she had lost all her former symptoms. In April 1967 she was followed up, and was found to be quite fit; a chest radiograph appeared to be normal, and the serum precipitin test was negative to *T. polyspora.*

Discussion

In all four cases there was a definite occupational history of exposure to one of the mushroom-growing processes, the first three being definitely related to spawning. Usually some hours after exposure the initial symptoms of pyrexia, headache, dizziness, nausea, vomiting, or generalized muscle aches gave way to symptoms of acute respiratory distress, with cough, chest pain, dyspnoea, but not asthmatic wheezing. The radiological appearance of diffuse mottling seen in three of the cases could be easily confused with, for example, tuberculosis or sarcoidosis. In none of the cases was there a family or previous personal history of allergic illness, and skin tests were negative, with the exception of one case, which showed a positive test to moulds (including *A. fumigatus*). There was no eosinophilia. The symptoms cleared spontaneously on removal from the environment of the mushroom farm, but some degree of residual chest tightness persisted in two cases. A corticosteroid helped the symptoms of one case to clear. In two of the four cases the serum gave positive precipitin reactions to the actinomycetes *T. polyspora* or *M. vulgaris* respectively. In the other two cases the serological precipitin tests were not carried out at the time of the original illness but some years later, by which time the precipitin antibodies may well have disappeared.

Nature of Mushroom-worker's Lung

Respiratory disorders due to dusts of vegetable fibre origin were first described by Ramazzini (1700) in flaxworkers in Italy. Since then many similar conditions have been recognized, the best known being byssinosis from cotton, and bagassosis from sugar cane. The condition called farmer's lung was first described by Campbell (1932) in Westmorland. In recent years farmer's lung has come to be recognized as a not infrequent condition occurring in agricultural workers exposed to the dust arising from disturbing mouldy hay and other vegetable matter, and to be due to hypersensitivity to an antigen present in the dust of mouldy hay. The exact nature of this antigen was for long a subject of speculation, but the work of Pepys *et al.* (1963) showed that the antigens involved were the spores of thermophilic actinomycetes growing in the heated hay, chiefly *T. polyspora,* and rarely *M. vulgaris*. By means of agar-gel diffusion and immunoelectrophoresis it was demonstrated that the serum of the majority of patients suffering from farmer's lung contained precipitins to these organisms. In farmer's lung the subject develops constitutional and respiratory symptoms, usually three to six hours after exposure to the offending dust. The symptoms are unlike those of bronchial asthma ; thus there is no wheeze, there is no eosinophilia, skin allergy tests are negative, chest radiographs show a diffuse miliary mottling, pulmonary function tests demonstrate an "alveolar block" diffusion defect, and lung biopsy reveals granulomata resembling those of sarcoidosis (Dickie and Rankin, 1958).

The clinical and radiological features of the first three cases described above certainly bear a close resemblance to those seen in farmer's lung. The finding of precipitin antibodies in two of the four cases provides the final evidence that mushroom-worker's lung is merely a variant of farmer's lung. The heating of the compost to 60° C. favours the growth of the thermophilic actinomycetes, and the inhalation of their spores provides the antigenic stimulus for the sensitization process responsible for the symptoms of mushroom-worker's lung.

Other factors which might possibly have been concerned in the aetiology of mushroom-worker's lung may be considered. Sensitivity to the mushrooms themselves or their spores does not appear to be the cause. Though *A. fumigatus* was demonstrated in the dust from the mushroom sheds there was no evidence that inhalation of these contaminant spores was responsible for the respiratory symptoms in the four cases described above. These symptoms do not seem to be due to allergy to any of the pests or insects which plague the mushrooms. For example, the mushroom fly, *Aphiochaeta agaraci,* may produce a specific allergic asthma (Kern, 1938 ; Truitt, 1951), but this is a different condition from that described in the present paper. Nor can the fungicides or pesticides be held responsible.

Nitrogen dioxide emanating from the disturbed compost was suggested as a possible cause of mushroom-worker's lung by Bringhurst *et al.* (1959), as the condition was thought to bear a resemblance to silo-filler's disease. In silo-filler's disease (Delaney *et al.,* 1956 ; Lowry and Schuman, 1956) workers are overcome by the poisonous fumes of nitrogen dioxide arising from chemical changes in the decomposing grain stored in the silos. There is, however, no evidence that in the mushroom-growing process any significant concentration of nitrogen dioxide is produced which would be responsible for the symptoms of mushroom-worker's lung as described here.

Conclusion

It is not claimed that respiratory disorders are very common among workers at mushroom farms. Nevertheless, certain individuals do become sensitized to the organic dust containing actinomycetes arising from the compost in which the mushrooms are grown. Dust is liberated when the compost is disturbed, as in the spawning process or on emptying the mushroom sheds and trays. Every precaution should be taken to ensure that workers potentially exposed to these dusts are protected from them, either by personal masks being worn or by efficient ventilation being maintained. A rapid "cool down" after pasteurizing of the compost may also impede the growth of the offending actinomycetes.

Summary

Four cases are described of workers at mushroom-growing farms in Sussex who developed respiratory symptoms resembling those seen in farmer's lung. Chest radiographs in three showed a diffuse miliary mottling, which cleared on removal from the environment of the farm. The serum of one case contained precipitins to *Thermopolyspora polyspora,* and the serum of another case contained precipitins to *Micromonospora vulgaris*. Thermophilic actinomycetes play an important part in the causation of farmer's lung. The process of composting in mushroom-growing farms favours the growth of these thermophilic actinomycetes, and the inhalation of their spores is responsible for sensitizing certain mushroom workers and producing the condition described here as mushroom-worker's lung.

I am grateful to Dr. R. Pillman and Dr. E. C. T. Evans for allowing me to quote Cases 2 and 3. The serum precipitin tests were carried out in the laboratories of the London School of Hygiene and Tropical Medicine and the Brompton Hospital.

REFERENCES

Bringhurst, L. S., Byrne, R. N., and Gershon-Cohen, J. (1959). *J. Amer. med. Ass.,* 171. 15.
Campbell, J. M. (1932). *Brit. med. J.,* 2, 1143.
Delaney, L. T., jun., Schmidt, H. W., and Stroebel, C. F. (1956). *Proc. Mayo Clin.,* 31, 189.
Dickie, H. A., and Rankin, J. (1958). *J. Amer. med. Ass.,* 167, 1069.
Kern, R. A. (1938). *J. Allergy,* 9, 604.
Lowry, T., and Schuman, L. M. (1956). *J. Amer. med. Ass.,* 162, 153.
Pepys, J., Jenkins, P. A., Festenstein, G. N., Gregory, P. H., Lacey, M. E., and Skinner, F. A. (1963). *Lancet,* 2, 607.
Ramazzini, B. (1700). *De Morbis Artificium Diatriba.* English translation, *A Treatise of the Diseases of Tradesmen,* 1705. London.
Truitt, G. W. (1951). *Ann. Allergy,* 9, 513.

Dietary Iron and Haematological Status in Normal Subjects

R. H. DAVIS,* D.M.; A. JACOBS,† M.D., M.C.PATH.; ROSA RIVLIN,‡ M.R.C.S., L.R.C.P.

Brit. med. J., 1967, 3, 711–712

The maintenance of optimal haemoglobin concentration and red cell indices depends on an adequate supply of the nutrients necessary for haemopoiesis. The availability of iron depends on a positive balance between intestinal absorption and loss from the body. Iron deficiency is a common cause of anaemia (Kilpatrick, 1961) and in women is often associated with high levels of menstrual blood loss (Jacobs and Butler, 1965). When menstrual loss is increased iron balance must be maintained either by a diet with a high iron content or by an increase in the proportion absorbed by the intestine. Iron deficiency in men is most often associated with gastrointestinal blood loss and the same compensating mechanisms are necessary to maintain a normal haematological status. The relative importance of dietary iron content and increase in absorption for maintaining normal iron balance is not clear. The present study of apparently healthy individuals in a general practice shows that iron-deficiency anaemia may occur in subjects with a wide range of dietary iron intake.

Methods

Eighty-seven men and 100 women aged 20–69 were studied. They were healthy persons selected by a random process from a general practice population of approximately 7,000. The group consisted of approximately equal numbers in each 10-year age group and contained representatives of all the social classes. In men aged 20–29 years, and occasionally at other ages, it was sometimes necessary to add substitutes as their type of employment precluded an accurate dietary survey. One man completed the dietary survey but refused to allow a sample of blood to be taken. Two women were found to have a raised blood urea and their results have been excluded. In a few cases an inadequate blood sample did not allow all the haematological investigations to be completed. Each individual completed a prospective dietary survey covering seven consecutive days closely following the method described by Thomson (1958). All the food and drink consumed was weighed and recorded. The iron content of the diet was calculated by reference to the food tables of McCance and Widdowson (1960) and from data obtained from food manufacturers. Some food items were assayed by the Cardiff Public Analysts laboratory. The mean iron intake over seven days was calculated.

Before each individual survey was started the subject was visited, supplied with scales, and the procedure explained. A brief medical history was taken and an estimate for the weekly food budget obtained. The subject was also asked to supply an average daily menu. This information provided some check upon the accuracy of the weighed food items recorded. At least two additional visits were made during the survey in order to assess the standard of record-keeping. During the period of the survey a specimen of venous blood was taken either before breakfast or between midday and lunchtime. Standard haematological methods were used (Dacie and Lewis, 1963). Serum iron and iron-binding capacity was measured by the method of Ramsay (1957).

Results

Dietary iron intake in men was 8–27 mg./day (mean 17.52 ±0.47 mg.) and in women 6–24 mg./day (mean 14.10±0.34 mg.), a significant difference ($P<0.001$). Haematological values are shown in the Table. In both sexes there is a complete lack of correlation between the dietary iron intake and haemoglobin concentration, M.C.H.C., serum iron, total iron-binding capacity, and transferrin saturation. Daily iron intake and haemoglobin concentration for women is shown in the Chart. Haemoglobin concentration was below 12 g./100 ml. in 10 women and below 12.5g./100 ml. in one man. Nine of the anaemic women had not reached the menopause. Transferrin saturation was less than 16% in 11 women but in none of the men. The mean haemoglobin concentration of women aged 20–44 years (12.70±0.145 g./100 ml.) was lower than that of women aged 45–69 (13.30±0.049 g./100 ml.) ($P<0.001$). There was no significant difference in dietary iron intake between the younger women (13.96±0.037 mg./day) and the older women (14.25±0.185 mg./day). Fifty-seven of all the women for whom data are available were premenopausal and nine of these were anaemic. Forty-one women were postmenopausal and only one of these was anaemic.

Haematological Values in General Practice Patients

		No. of Cases	Range	Mean	S.E.
Haemoglobin (g./100 ml.)	Men	80	10·0–17·1	14·95	0·125
	Women	98	8·6–15·1	12·98	0·109
M.C.H.C. (%)	Men	80	30–36	33·61	0·151
	Women	98	27–36	32·31	0·143
Serum iron (µg./100 ml.)	Men	81	55–185	107·5	2·95
	Women	97	36–220	108·2	4·09
Serum iron-binding capacity (µg./100 ml.)	Men	73	210–600	326·2	3·0
	Women	88	250–492	359·2	6·4
Transferrin saturation (%)	Men	73	16·7–66·7	33·4	1·2
	Women	88	5·8–55·0	30·5	1·3

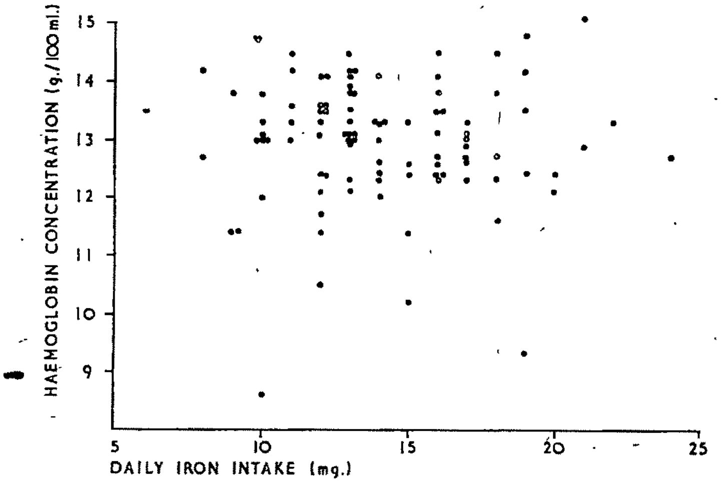
Discussion

The average daily dietary iron recorded in the present group of subjects is slightly higher than that of 14.1 mg. recorded by the National Food Survey (1966). This iron intake compares favourably with the recommendation of 12 mg. daily for adults over the age of 20 years made by the British Medical Association (1950) and would be adequate to sustain a daily iron loss from the body of 1.4 mg., assuming 10% iron absorption from food. Nineteen out of the 98 women in this survey had a daily iron intake of less than 12 mg. but the proportion of these with a haemoglobin concentration less than 12 g./100 ml. is not significantly greater than in those with a daily intake of 12 mg. or over. The Chart shows that anaemia can occur in women with different levels of dietary iron.

Normal blood values can be maintained in the presence of low iron intake only by an increase in absorption, and this presupposes that the food iron is in an available form. Absorption of ionizable iron is increased in response to anaemia except in some patients in whom achlorhydria is a limiting factor. Iron in meat and bread, which together provide 44% of the dietary iron (National Food Survey, 1966), also show this phenomenon, though not to the same degree as fully ionized iron (Hussain, Walker, Layrisse, Clark, and Finch, 1965). Elwood (1963) has shown that the iron normally added to white flour is very poorly utilized. The present data suggest that the iron content of food is not a limiting factor in maintaining iron balance in normal individuals, and it must be assumed that a considerable increase in absorption from dietary sources is possible under the stimulus of iron deficiency. The total amount of iron in the diet may be more important at levels of intake below 6 mg. daily and in individuals with impaired absorption.

---

* General Practitioner, Cardiff.
† Department of Pathology, Welsh National School of Medicine, Cardiff.
‡ Research Assistant, Cardiff.



Dietary iron intake and haemoglobin concentration in healthy women aged 20–69 years.

Mean iron intake and haemoglobin levels are both higher in men than in women, but there is no correlation between these two factors in either sex. In women anaemia is almost entirely confined to those still menstruating. Though haemoglobin levels are significantly lower under the age of 45 years there is no significant difference in iron intake between the younger and older women. These findings suggest that dietary iron intake may be a less important factor than menstrual blood loss in the aetiology of iron deficiency in women. They are in keeping with the observation of Hallberg, Hogdahl, Nilsson, and Rybo (1966) that there is a fall in haemoglobin concentration in women when menstrual loss exceeds 80 ml. (equal to 1.2 mg. of iron daily) and a fall in serum iron level when it exceeds 60 ml. (equal to 1 mg. of iron daily). Garby (1966) states that only a few individuals are in negative iron balance on a daily intake of 10–13 mg. It seems likely that in a normal population iron loss from the body is the most important determinant of iron status and that dietary iron is only limiting at very low levels or in individuals with a high iron loss.

Summary

A dietary survey in apparently healthy subjects showed no relation between iron intake and haematological status. It is suggested that iron loss from the body rather than dietary iron intake is the major determinant of iron status in normal individuals.

We should like to thank Professor H. Scarborough for his encouragement and the Medical Council for a grant to R.H.D.

References

British Medical Association (1950). *Report of the Committee on Nutrition*. London.
Dacie, J. V., and Lewis, S. M. (1963). *Practical Haematology*, 3rd ed. London.
Elwood, P. C. (1963). *Brit. med. J.*, **1**, 224.
Garby, L. (1966). *Acta med. scand.*, Suppl. No. 445, p. 264.
Hallberg, L., Hogdahl, A. M., Nilsson, L., and Rybo, G. (1966). *Acta obstet. gynec. scand.*, **45**, 320.
Hussain, R., Walker, R. B., Layrisse, M., Clark, P., and Finch, C. A. (1965). *Amer. J. clin. Nutr.*, **16**, 464.
Jacobs, A., and Butler, E. B. (1965). *Lancet*, **2**, 407.
Kilpatrick, G. S. (1961). *Brit. med. J.*, **2**, 1736.
McCance, R. A., and Widdowson, E. M. (1960). *Spec. Rep. Ser. med. Res. Coun. (Lond.)*, No. 297.
National Food Survey Committee (1966). *Domestic Food Consumption and Expenditure: 1964*. H.M.S.O., London.
Ramsay, W. N. M. (1957). *Clin. chim. Acta*, **2**, 214.
Thomson, A. M. (1958). *Brit. J. Nutr.*, **12**, 446.

Acro-osteolysis Occurring in Men Engaged in the Polymerization of Vinyl Chloride

D. KENWIN HARRIS,* M.B., B.S.; W. G. F. ADAMS,† M.B., CH.B.

[WITH SPECIAL PLATE BETWEEN PAGES 708 AND 709]

Brit. med. J., 1967, **3**, 712–714

The polymerization of vinyl chloride has been undertaken in this and other countries for over 20 years without apparent harm to the workers, apart from some accidental exposure to the vapour of vinyl chloride, the anaesthetic effects of which have been well known for years. The process consists, briefly, in submitting a mixture of liquid vinyl chloride and water in the presence of a catalyst to the effects of heat in large pressure vessels known as autoclaves. This produces polyvinyl chloride in slurry or latex form which is discharged from the vessel and conveyed elsewhere to be dried into a powder. When the autoclave is emptied at this final stage a deposit of white polymer is found on its inner wall. Air is then blown through the open vessel for at least a quarter of an hour, after which an atmosphere test for vinyl chloride is done inside it. If the autoclave is found to be clear of vinyl chloride vapour the cleaner enters it to scrape the wall with a small hand pallet.

An unusual condition affecting two men employed as autoclave cleaners in this process was first reported by Cordier *et al.* (1966). After doing this work for several months they developed symptoms resembling those of Raynaud's phenomenon and later a skin eruption of the hands, and in one case of the forearms, together with general asthenia and drowsiness. The most striking sign, however, was the radiological evidence of lysis of some terminal phalanges of the hands, and in one case of the feet. Most of these abnormalities disappeared and the bones showed signs of healing a year or two after the men had stopped work.

In view of that article, the hands of 588 men engaged in the manufacture of polyvinyl chloride were radiographed in

---

* Imperial Chemical Industries Limited, Plastics Division.
† Imperial Chemical Industries Limited, Mond Division.

April 1966; 150 of them were autoclave cleaners. Two cases with *x*-ray changes in the fingers similar to those described by Cordier *et al.* (1966) were found.

Case 1

A 44-year-old man who had worked on the autoclave section of the plant since 1950 had an interesting history in that he was diagnosed as a case of scleroderma by a consultant physician and dermatologist in 1957. The diagnosis was made on clinical grounds because of Raynaud's phenomenon, accompanied by puffiness of the face and thickening of the skin of the hands, fingers, and left forearm. The symptoms cannot have been very troublesome, because he had made no complaint, and the condition was noticed by his doctor only when he went to collect a prescription for his wife.

On being questioned about his condition during the present investigation he still made no complaints, and it was only with reticence that he admitted that his hands often felt unduly cold.

Examination revealed no evidence of the skin condition that had existed in 1957, and the only abnormalities were: (*a*) pseudoclubbing of all the fingers of both hands; this is not true clubbing, since the angle between the base of the nail and the adjacent skin was not obliterated; and (*b*) the liver was palpable on inspiration.

Radiological Reports.—"*Hands*: Periarticular erosions are present in the proximal interphalangeal joints. The proximal interphalangeal joint of the left little finger is disorganized. There are erosions of the terminal phalanges of index and middle fingers of both hands (Special Plate, Fig. 1). *Feet*: The fifth proximal phalanges of both feet show erosions on both their distal ends. The fifth proximal interphalangeal joint is disorganized on the left (Special Plate, Fig. 2). *Pelvis*: There is a widening of the joint space of the sacroiliac joint with cystic marginal sclerosis. *Chest*: Normal. *Skull*: Normal. *Cervical spine*: Normal. *Teeth*: Normal. *E.C.G.*: Normal."

Laboratory tests were carried out, and the only abnormality found was a persistently raised serum bilirubin.

Case 2

A 30-year-old man who had been an autoclave cleaner since 1960, having been self-employed as a window-cleaner before that date, recalled no previous serious illness, but had consulted his doctor in 1964 because of shortening of his finger-nails, which he thought to be due to biting them and "lack of calcium."

In April 1966 he had no symptoms, but radiologically he showed evidence of acro-osteolysis. Pseudoclubbing of the fingers was found to be present (Fig. I). Raised nodules in the skin, described as "xanthomatous-like" patches, were noted round his wrists.

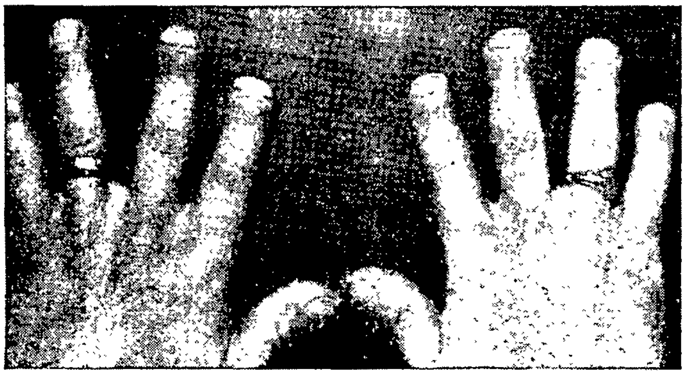


FIG. I.—Pseudoclubbing of the fingers.

Radiological Reports.—"*Hands*: Osteolysis is present in the shafts of all the terminal phalanges of the fingers and thumb, with the exception of the left ring finger" (Special Plate, Fig. 3). (Incidentally it is of interest to note that in most of the *x*-ray films of these cases seen by us here and in America the ring finger is unaffected.) "*Sacrum*: Widening of the joint spaces of the sacroiliac joint with cystic marginal sclerosis (Special Plate, Fig. 5). *Chest*: Normal."

The most notable feature was the comparative absence of abnormal findings, apart from those shown on the *x*-ray films. Laboratory tests showed nothing abnormal.

In July, however, he came to see one of us (W. G. F. A.) complaining of fairly persistent pain and frequent attacks of coldness in the fingers, accompanied by pallor. On examination at this time there was some tenderness of the finger-tips, more skin nodules were seen to be developing on the dorsum of his fingers, and some thickening and coarsening of the skin of the face was noted.

In the course of the next week or two the pains in the fingers and metacarpophalangeal joints increased, and Raynaud's phenomenon was troublesome even in warm weather. He was therefore admitted to hospital in August for further investigation.

The same tests as on the previous occasion were repeated, and once again the results were within normal limits, except in the case of the serum proteins. In this test the serum α2-globulin was 1 mg./100 ml. (normal 0.4–0.8 mg.). Hyland screening tests for rheumatoid arthritis and lupus erythematosus were normal. Serum transaminase was within normal limits. The E.S.R. had fallen to 4 mm. in one hour (Westergren). Blood pressure was 140/80.

Skin biopsy was performed on one of the nodules on the wrist, the histological report being as follows: "The full thickness of the dermis is incorporated in an interlacing acellular collagenous nodule, oedematous and partly hyalinized, enclosing normal sweat glands and covered by normal epidermis (Fig. II). The oedematous interstices contain a fine granular and filamentous material, metachromatic with toluidine blue, and staining faintly with alcian blue and periodic-acid Schiff, probably breaking up elastic (Fig. III). Two small dermal arteries are extremely thick-walled as a result of marked medial hypertrophy and intimal fibrous

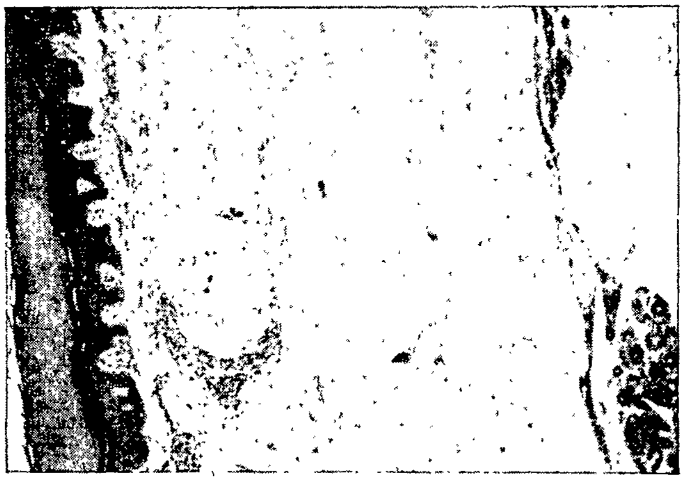


FIG. II.—Case 2. General appearance of thickened dermal collagen—also showing lymphocytic cuffing of small dermal blood vessel. (H. and E. ×55.)

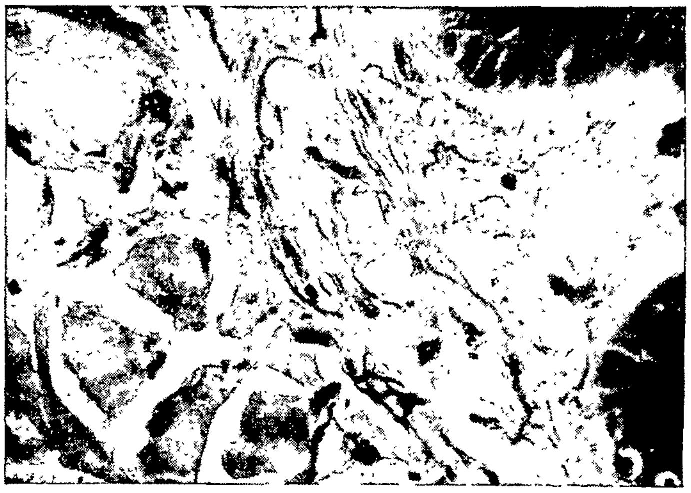


FIG. III.—Case 2. High-power view of fragmented elastic in upper dermis. (Verhoeff. ×270.)

thickening (Fig. IV). The appearances are similar to those described by Cordier *et al.* (1966)."

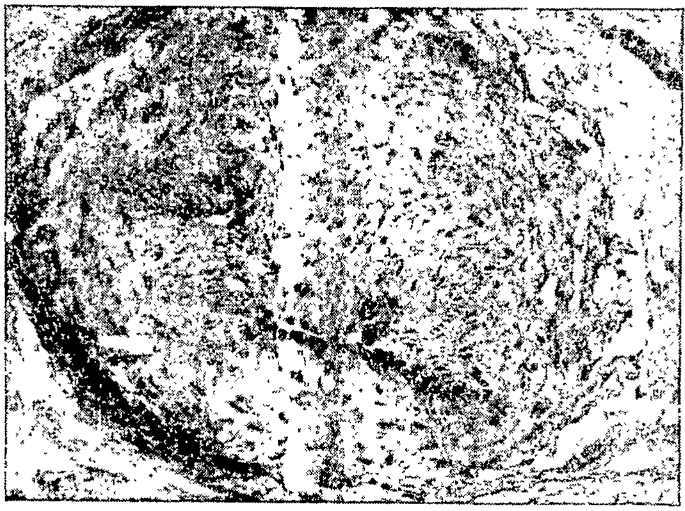


FIG. IV.—Case 2. High-power view of artery situated deeply within the zone of thickened dermal collagen. (H. and E. ×180.)

For a few months after his discharge from hospital he improved, and by the end of 1966 the Raynaud's phenomenon was less marked and the skin nodules were disappearing. About this time, however, he began to develop pain in the left knee and toes. *X*-ray examination of the left knee showed a cortical erosion on the posterior surface of the patella (Special Plate, Fig. 4). By June 1967 he felt reasonably well, though he still complained of pain in the left knee and stiffness of the hands, particularly at the metacarpophalangeal joints. The skin of the hands and face was practically normal.

Comment

No treatment was required in Case 1, and the treatment in Case 2 was directed towards relieving the symptoms, since no specific remedy is known for the condition.

Both men were removed from the job of autoclave cleaning as soon as the diagnosis was made, but it is not yet certain how this measure will affect the course of the illness. It would appear that Case 1 went through the acute stage while still doing his normal job, and the condition has become quiescent in spite of this.

Two more possible cases were found in our most recent survey. One of these is a 30-year-old autoclave cleaner who has had Raynaud's phenomenon for three years, but in whom no bony changes have been found. The other man is an ex-autoclave-cleaner in whom a suspicious appearance has been noted radiologically in the right thumb, which had, however, been recently subjected to injury.

Discussion

In view of the similarity of the findings in these men to the cases described in the paper of Cordier *et al.* (1966), it was thought that this condition was almost certainly linked with the men's occupation. Inquiries subsequently made in America and Europe revealed that similar cases had occurred there. In all cases the features appearing most consistently were Raynaud's phenomenon accompanied by osteolysis of the terminal phalanges of the fingers, occurring mainly in autoclave cleaners and not in those engaged in handling the finished product.

Many raw materials may be used in small quantities in manufacturing the polymer, but the only substance common to all cases is probably vinyl chloride. Though every autoclave is washed with water and has air blown through it at the end of each reaction, small quantities of vinyl chloride may remain and escape when the vessel lid is opened. It is also possible that very small pockets of gas may be trapped beneath the polymer adhering to the inner wall, and these can be liberated during the subsequent cleaning process. Vinyl chloride, however, has been manufactured and handled in this country for over 20 years without apparent harm apart from accidental exposure to its well-known anaesthetic action.

A point of general interest is the possible relationship of this condition to the collagen diseases. One patient (Case 1) had, in fact, been diagnosed as a case of scleroderma on clinical grounds 10 years previously. The histologist remarked on the superficial similarity of the biopsy taken in Case 2 to scleroderma, but a number of pathologists consider the appearance of the section to be unique. Cordier *et al.* (1966) mention an unusual skin condition seen in their cases. Suciu *et al.* (1963), in a paper describing conditions produced by vinyl chloride, referred to a skin lesion resembling scleroderma, but acro-osteolysis was not mentioned.

Finally, at a clinicopathological conference at the Royal Postgraduate Medical School (*B.M.J.*, 1966) it was stated that bony changes were commonly found in the terminal phalanges in scleroderma. It should be made quite clear, however, that the many radiologists who have looked at the films of our cases stated that they had not previously seen this particular lesion.

It would appear from our own and other cases that this condition is probably a self-limiting disease, which in spite of bone destruction leaves the patient with little disability. In *x*-ray films taken a year after the original diagnosis no further bony changes were noted in Case 1. In Case 2, however, there was evidence of partial ossification of the osteolytic bands in the terminal phalanges of both hands.

It is our intention to continue annual radiological examination of the hands of all men engaged on this work. Mechanical methods of cleaning new autoclaves have been introduced, and it is hoped in due course to extend this method to older vessels and thus eliminate the human factor.

Summary

Two cases of acro-osteolysis occurring in men engaged in the polymerization of vinyl chloride are described. The bones affected were the terminal phalanges of the fingers and the sacroiliac joints, but in one case the patella and in the other the phalanges of the feet were involved. The condition was accompanied by Raynaud's phenomenon and skin lesions.

It would seem that this condition is probably a self-limiting disease.

We acknowledge with gratitude the help given throughout this investigation by Dr. Thelwall Jones and other members of the medical staff of the David Lewis Northern Hospital, Liverpool, and by Dr. K. A. Rowley and his colleagues at Blackpool Victoria Hospital.

REFERENCES

Brit. med. J., 1966, **2**, 1642.
Cordier, J. M., Fievez, C., Lefevre, M. J., and Sevrin, A. (1966). *Cah. Med. Trav.*, **4**, 3.
Suciu, I., Drejman, I., and Valaskai, M. (1963). *Med. interna (Buc.)*, **15**, 967.

Sickle-cell Haemoglobin O Disease in a Sudanese Family

S. A. IBRAHIM,* D.K.S.M., PH.D.; DAOUD MUSTAFA,† D.K.S.M., F.R.C.P.

Brit. med. J., 1967, 3, 715–717

Besides sickle-cell anaemia, the finding of Hb S with other β-chain variants of adult haemoglobin was first demonstrated by Itano and Neel (1950) in the well-known discovery of sickle-cell Hb C disease. Since then Hb S has been observed with Hb D, E, G, J, and K (Itano, 1951; Aksoy and Lehmann, 1957; Schwartz and Spaet, 1955; Went and MacIver, 1959; O'Gorman *et al.*, 1963). In such circumstances there is a sickle-cell disease which, while of varying severity, is milder than the homozygous sickle-cell anaemia.

Hb S was first observed with Hb O in two children of an Arab family who were reported to be suffering from a sickle-cell Hb O trait condition. In those cases some Hb A was also found in addition to Hb S and O (Ramot *et al.*, 1960), and it was subsequently concluded that there must have been a previous blood transfusion (Baglioni and Lehmann, 1962). The clinical picture of sickle-cell Hb O disease has not yet been reported. The present report describes two cases which occurred in a Sudanese family.

Case 1

A Sudanese man aged 27 coming from the village of Abu Haraz, Gezira, was admitted into Khartoum Hospital on 1 September 1966 complaining of joint pains and malaise for one month and fever for seven days. Since early childhood he had suffered from similar attacks with occasional episodes of jaundice, which were often precipitated by exertion. During infancy he had bouts of screaming, and was once taken to a native healer, who manipulated the patient's upper limbs. It was thought that as a result of such manipulations he developed severe tenderness and swelling of the left shoulder. The swelling was later incised and pus was drained. The patient had had the last attack of joint pains about a month previously when he was admitted to a district hospital, and it was while there that severe pain developed, with swelling of the right shoulder. The condition was diagnosed as rheumatoid arthritis and he was given salicylates and corticosteroids without benefit. The pain and swelling in the right shoulder persisted till his admission into Khartoum Hospital. Four months previously he had been found to have intestinal schistosomiasis and was treated with stibophen (Fouadin).

On admission he was ill-looking, in pain, wasted, and anaemic but not jaundiced. He had a large skull and was running a temperature of 103° F. (39.4° C.). Heart, lungs, and abdomen were normal; liver and spleen were not palpable. He had brisk tendon reflexes, but otherwise the nervous system was normal. The fundus oculi showed slight engorgement of the retinal veins and arteriovenous nipping. The right shoulder was swollen, hot, and tender, with induration of the overlying deltoid and adjacent pectoralis major. Movements were restricted on account of pain. The left arm was smaller and 8 cm. shorter than the right.

TABLE I.—*Haematological Findings in Two Patients Suffering from Sickle-cell Hb O Disease*

Case No.	Age in Years	Sickling Test	Adult Haemoglobins	Hb F (%)	Haemoglobin (g./100 ml.)	P.C.V. (%)	M.C.H.C. (%)	Reticulocytes (%)
1	27	+	S+O	5·5	8·5	28	34	0·8
2	15	+	S+O	4·5	9	29	31	18

Investigations.—The haematological findings are given in Table I. A peripheral blood film showed many target cells, a few sickle cells, and some normoblasts. The erythrocytes showed anisocytosis and poikilocytosis. No malaria parasites were seen. Total W.B.C. 6,400/cu. mm. (polymorphs 61%, lymphocytes 35%, eosinophils 2%, and monocytes 2%). Bone marrow was predominantly normo-

TABLE II.—*Blood Chemistry in Two Patients Suffering from SO Disease*

Case No.	Serum Bilirubin (mg./100 ml.)	Alkaline Phosphatase (K.A. Units)	Thymol Turbidity	Plasma Proteins (g./100 ml.)			
				Total	Albumin	Globulin	γ-Globulin
1	0·8	18	1	7·6	2·4	5·2	2·9
2	2·2	21	8	7·8	1·9	5·9	3·2

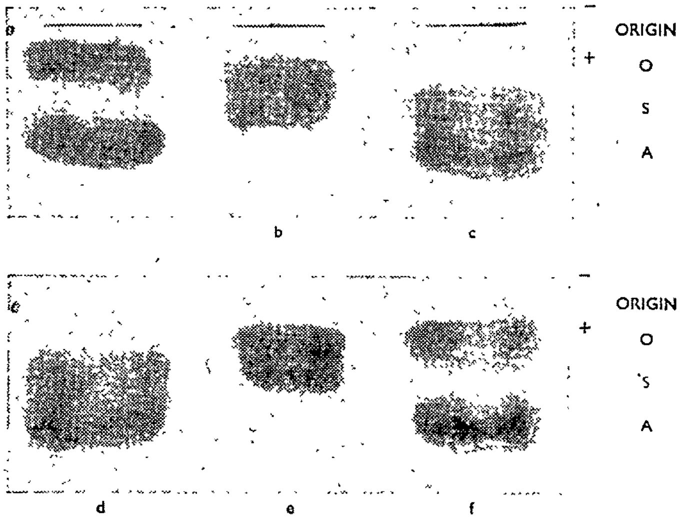


FIG. 1.—Paper electrophoresis in barbiturate buffer *p*H 8.6 of haemoglobins from two patients with SO disease and their parents. a and f, Mother's haemoglobin, showing Hb A+O. b: Haemoglobin of Case 1, showing Hb S+O. c and d: Father's haemoglobin, showing Hb A+S. e: Haemoglobin of Case 2, showing Hb S+O.

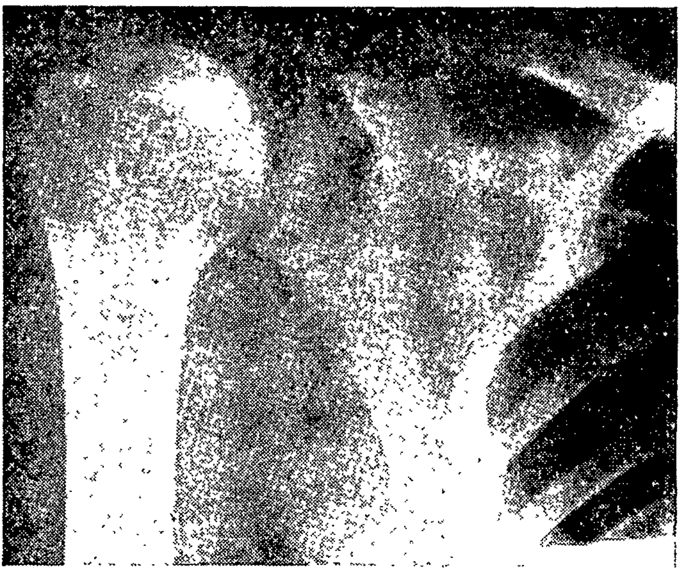


FIG. 2.—Case 1. *X*-ray film of right shoulder, showing osteoporosis of the head of the right humerus, thinning of cortex, and periosteal reaction in the humeral neck.

---

* Department of Biochemistry, Faculty of Medicine, University of Khartoum.
† Department of Medicine, Faculty of Medicine, University of Khartoum.

blastic with a fair number of megaloblasts and an increase of plasma cells. The blood chemistry is shown in Table II. Urine contained an excessive amount of urobilinogen, a trace of protein, but no R.B.C.s or bilirubin. Stools were repeatedly negative for schistosome ova. Haemoglobin electrophoresis showed Hb S+O (Fig. 1). This finding was confirmed by Dr. H. Lehmann at the M.R.C. Abnormal Haemoglobin Research Unit, Cambridge. Hb F constituted 5.5% of total haemoglobin. Electrophoresis of serum, using barbitone buffer, revealed a marked increase in the γ-globulin fraction. *X*-ray examination showed osteoporosis of the head of the right humerus, thinning of the cortex, and periosteal reaction in the humeral neck (Fig. 2). The skull was osteoporotic with opacities, and had a hair-on-end appearance. The left humerus was small, short, and had a very small remnant of a head (Fig. 3).

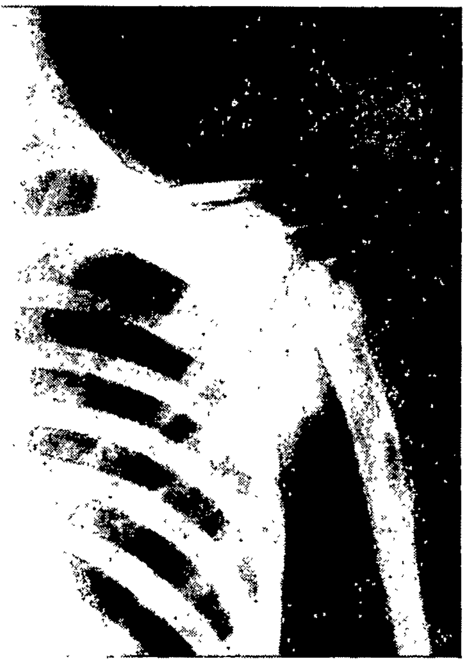


FIG. 3.—Case 1. *X*-ray film of left shoulder, showing a small remnant of left humeral head, thinning of cortex, and periosteal reaction in the shaft.

He ran a temperature of up to 102° F. (38.9° C.) for three weeks. The swelling in the right shoulder improved very slowly. On 25 October he complained of severe pain in the left loin and had microscopic haematuria, which cleared up in about a week. On 30 October a painful swelling appeared in the middle of his left femur which subsided in about a week. On 1 December the right shoulder swelling and pain got much worse. He was put on folic acid tablets, and this converted the marrow to normoblastic and resulted in haematological improvement.

Case 2

A Sudanese girl aged 15, sister of Case 1, was admitted to hospital on 1 October 1966, having had jaundice for two months, fever and cough for one month, and a painful swelling of the left shoulder for 10 days.

Since early childhood she had suffered from attacks of joint pains sometimes associated with swellings. At the age of 3 years she had a severe attack of measles accompanied by a painful swelling of both hands, including the fingers. Since then some fingers were noted to have become shorter. At the age of 6 she had jaundice, which lasted for one month.

On admission she had a temperature of 100° F. (37.8° C.) and was looking very ill, wasted, anaemic, and mildly jaundiced. Pulse was collapsing; B.P. 100/60; apex beat was in fourth space at the midclavicular line. No murmurs were heard. There were signs of right lower lobar pneumonia, and tender bony swellings were present on the seventh and eighth right ribs and on the sixth, eighth, and ninth left ribs at the midaxillary line. Liver and spleen were not palpable. Besides brisk tendon reflexes, the nervous system was normal. There was a moderately swollen left shoulder, which was hot and tender. The right middle finger was short and the proximal interphalangeal joint of the left index was ankylosed.

Investigations.—The haematological findings were as follows. A peripheral blood smear with many target cells, a few sickle cells, and erythrocytes showing anisocytosis and poikilocytosis. No malaria parasites were seen. Total W.B.C. 10,300/cu. mm. (polymorphs 69%, lymphocytes 24%, monocytes 5% and metamyelocytes 2%). The bone marrow was hyperactive, predominantly normoblastic, with a fair number of megaloblasts and an increase in plasma cells. E.S.R. 7 mm. in the first hour (Westergren). Serum calcium was 9.9 mg./100 ml. and phosphorus 3.8 mg./100 ml. The rest of the blood chemistry is shown in Table II. The urine contained a fair number of erythrocytes, urobilinogen in excess, but no bilirubin. Stools were normal. Electrophoresis of the haemoglobin revealed Hb S+O, a finding that was confirmed by Dr. H. Lehmann. Hb F constituted 4.5% of the total haemoglobin. Electrophoresis of serum showed a considerable increase in the γ-globulin fraction. *X*-ray examination of the chest showed right lower zone opacity and small areas of bone destruction in the right eighth and ninth ribs and to a less extent in the left sixth and eighth ribs at the sites corresponding to the tender swellings seen externally. An *x*-ray film of both hands (Fig. 4) showed that with the exception of the thumb the fingers of the left hand were all shorter than normal owing to reduction of the proximal and middle phalanges. The proximal phalanx of the right middle finger was also short. The ends of the affected phalanges showed osteoporosis, with cupping at the metacarpophalangeal and interphalangeal joints and reduction of joint spaces.

The patient maintained a low-grade fever for three weeks. The pneumonia and rib swellings subsided gradually. On 15 October she developed a painful swelling over the right radius; this subsided in a few days. On 8 November the old rib swellings subsided but two new non-tender swellings of the right eighth and ninth ribs appeared in the scapular line. On 30 November the left shoulder swelling and pain became worse. She was put on folic acid, and this converted the marrow to normoblastic with haematological improvement.

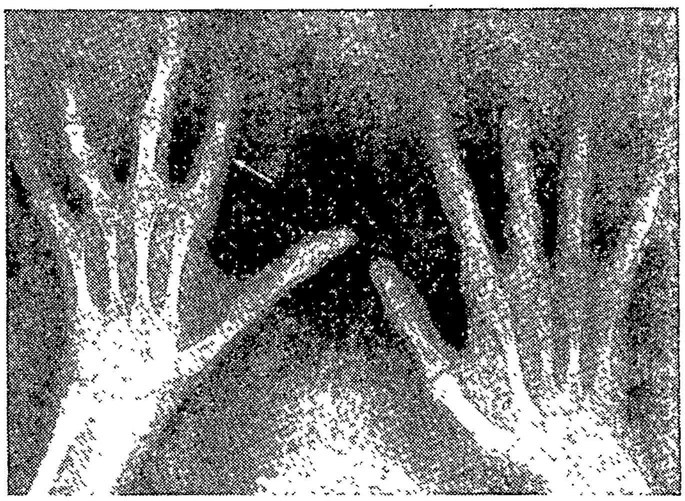


FIG. 4.—Case 2. *X*-ray film of both hands, showing shortening of the proximal and middle phalanges, osteoporosis, and cupping at the joints of the affected fingers. The proximal interphalangeal joint of the left index is ankylosed.

Family History

The parents are distant cousins; both are alive and well. They have eight more siblings—five daughters and three sons—who are reported to be well. One child died four days after birth.

Electrophoresis of haemoglobin showed that the father has Hb A+S while the mother has Hb A+O (see Fig. 1). The rest of the family have not yet been examined.

Discussion

The incidence of Hb S and O Arab in Northern Sudanese has been reported as 2 and 0.1% respectively (Vella *et al.*, 1966).

Examination of the peptides arising from tryptic digestion of the abnormal haemoglobin has shown that haemoglobin O Arab harbours the chemical abnormality in the β-polypeptide chains of the molecule (Baglioni and Lehmann, 1962). It has also been shown that Hb S differs from Hb A in the amino-acid composition of the β-polypeptide chains (Ingram, 1959). Since adult haemoglobins are genetically determined by allelomorphic genes inherited in a Mendelian fashion, then the inheritance of the genes for Hb S and O by an individual will result in the formation of only Hb S+O by that individual. No Hb A will therefore be formed, since the genes for Hb S and O both produce haemoglobins which are abnormal in the β-chains.

The clinical picture of sickle-cell Hb O disease has hitherto not been described. Both patients whose cases are reported here are Northern Sudanese of Arab ancestry in whom the onset of symptoms of the disease began early in life. The bony lesion of the left shoulder in Case 1 and of both hands in Case 2 are probably manifestations that had taken place in infancy and early childhood respectively. The onset of symptoms in sickle-cell disease is generally later than in sickle-cell anaemia, though it has been reported that in about 80% of the cases of SC disease the symptoms began in the first decade of life (Hook and Cooper, 1958).

The most prominent clinical features in these two cases of SO disease are the joint pains and bony lesions involving humeri, ribs, skull, hands, femur, and radius, and of particular prominence is the marked affliction of the head of the humerus. Aseptic necroses of the femoral and humeral epiphyses are very common in SC disease (Smith and Conley, 1954 ; Hook and Cooper, 1958 ; Ranney, 1958). Burchmore *et al.* (1962) suggested that arterial occlusion rather than capillary obstruction may be the main factor in the production of avascular necroses, multiple infarcts, and painful swellings seen in SC disease. Indeed, these authors provided unequivocal evidence of arterial occlusion in the case they reported.

Another prominent feature in our cases is the marked decrease of plasma albumin along with the considerable increase in γ-globulin. The common diseases which cause such a disturbance of plasma proteins in the Sudan are leishmaniasis, hepatosplenic schistosomiasis, chronic malaria, and hepatic cirrhosis. These two patients were not suffering from leishmaniasis and there was no evidence of chronic malaria. Though Case 1 gave a history of intestinal schistosomiasis for which he received treatment there was no clinical evidence of hepatosplenic involvement. Liver disease and disturbed liver function have been described in cases of sickle-cell anaemia. Thus decreased plasma albumin and increased γ-globulin were reported by Fenichel *et al.* (1950). Histological evidence of liver disease, together with disturbance in plasma proteins and liver function tests, was also given by Green *et al.* (1953). In the case of SC disease described by Burchmore *et al.* (1962) a considerable increase in the γ-globulin was also reported. It would seem probable that the disturbances in plasma proteins seen in our patients were due to hepatic disease. In both cases there was an increase in plasma cells in the bone marrow. Patients with liver disease who have very high serum globulin show plasmocytosis of the bone marrow (Sherlock, 1963).

In neither of our cases was there a palpable spleen. Splenomegaly occurs in the majority of cases of SC disease, in contrast to sickle-cell anaemia, in which a palpable spleen is detected in only a small proportion of cases (Wintrobe, 1961). However, Edington (1957) reported that in some cases of SC disease the spleen may be fibrosed and hence cannot be felt.

Though in both cases the anaemia has been severe, it is fairly well tolerated. Both had megaloblastic erythropoiesis. Haemolytic anaemia as a factor in the development of megaloblastic erythropoiesis has been demonstrated in the specific case of sickle-cell anaemia by Jonsson *et al.* (1959) and by Watson-Williams (1962). Megaloblastic anaemia complicating SC disease has been reported by Fullerton and Watson-Williams (1962), and the megaloblastosis has been attributed to excessive folic acid requirements.

It is of interest to note that one of our patients (Case 1) developed severe left loin pain which was associated with microscopic haematuria otherwise not observed in previous urine tests. Haematuria occurs in sickle-cell anaemia and in sickle-cell trait (Wintrobe, 1961). Massive haematuria that is probably the result of renal arterial occlusion (Burchmore *et al.*, 1962) often occurs in SC disease (Smith and Conley, 1954, 1958).

Summary

Two cases of a hitherto undescribed condition of sickle-cell Hb O disease are reported in detail and the relevant literature is reviewed. The prominent features of this condition (SO disease) are joint pains, bony lesions, anaemia, and marked disturbances of the plasma proteins. The occurrence of megaloblastic anaemia is also reported. Like other sickle-cell diseases, SO disease is relatively mild. The clinical picture bears some resemblance to that of SC disease.

We are grateful to Dr. H. Lehmann, Director, M.R.C. Abnormal Haemoglobin Research Unit, Cambridge, for confirming the finding of the abnormal haemoglobins and for valuable discussions while he was in Khartoum ; to Mr. T. R. Davis, Faculty of Pharmacy, Khartoum, for photographing the electrophoretograms ; to Professor K. R. Adam, of the Biochemistry Department, for advice ; and to Research Assistant Dr. El Daw Mokhtar for help.

References

Aksoy, M., and Lehmann, H. (1957). *Nature (Lond.)*, **179**, 1248.
Baglioni, C., and Lehmann, H. (1962). Ibid., **196**, 229.
Burchmore, J. W., Buckle, R. M., Lehmann, H., and Jenkins, W. J. (1962). *Lancet*, **2**, 1008.
Edington, G. M. (1957). *J. clin. Path.*, **10**, 182.
Fenichel, R. L., Watson, J., and Eirich, F. (1950). *J. clin. Invest.*, **29**, 1620.
Fullerton, W. T., and Watson-Williams, E. J. (1962). *J. Obstet. Gynaec. Brit. Cwlth*, **69**, 729.
Green, T. W., Conley, C. L., and Berthrong, M. (1953). *Bull. Johns Hopk. Hosp.*, **92**, 99.
Hook, E. W., and Cooper, G. R. (1958). *Sth. med. J. (Bgham, Ala.)*, **51**, 610.
Ingram, V. M. (1959). *Nature (Lond.)*, **183**, 1795.
Itano, H. A. (1951). *Proc. nat. Acad. Sci. (Wash.)*, **37**, 775.
—— and Neel, J. V. (1950). Ibid., **36**, 613.
Jonsson, U., Roath, O. S., and Kirkpatrick, C. I. F. (1959). *Blood*, **14**, 535.
O'Gorman, P., Allsopp, K. M., Lehmann, H., and Sukumaran, P. K. (1963). *Brit. med. J.*, **2**, 1381.
Ramot, B. *et al.* (1960). Ibid., **2**, 1262.
Ranney, H. N. (1958). *Nat. Res. Coun. Div. Med. Sci.*, Publ. No. 557, p. 287.
Schwartz, H., and Spaet, T. H. (1955). *Clin. Res. Proc.*, **3**, 51.
Sherlock, Sheila (1963). *Diseases of the Liver and Biliary System*, 3rd ed., p. 73. Oxford.
Smith, E. W., and Conley, C. L. (1954). *Bull. Johns Hopk. Hosp.*, **94**, 289.
—— —— (1958). *Nat. Res. Coun. Div. Med. Sci.*, Publ. No. 557, p. 276.
Vella, F., Beale, D., and Lehmann, H. (1966). *Nature (Lond.)*, **209**, 308.
Watson-Williams, E. J. (1962). *E. Afr. med. J.*, **39**, 213.
Went, L. N., and MacIver, J. E. (1959). *Brit. med. J.*, **2**, 138.
Wintrobe, M. M. (1961). *Clinical Haematology*, 5th ed., p. 669. London.

Preliminary Communications

Intestinal Spirochaetosis

[WITH SPECIAL PLATE BETWEEN PAGES 708 AND 709]

Brit. med. J., 1967, 3, 718–719

The purpose of this paper is to draw attention to a form of intestinal spirochaetosis that does not appear to have been previously described and yet would seem to be not infrequent. The condition was first noticed while the rectal mucus membrane was being viewed through the electron microscope.

INITIAL OBSERVATIONS

The patient, a man aged 64, had complained of persistent diarrhoea for three years. A rectal biopsy was taken as part of the clinical investigation, and on light microscopy nothing of note was seen. Small fragments of this biopsy specimen were fixed in 1% osmium tetroxide in phosphate buffer at *p*H 7.4 and embedded in Araldite, and thin sections were viewed in a Siemens Elmiskop 1A electron microscope.

Clinical Features of 10 Cases of Intestinal Spirochaetosis

Case No.	Sex	Age	Complaint	Duration of Symptoms	Clinical Diagnosis
1	M	64	Diarrhoea	3 years	?
2	M	52	Mucoid diarrhoea	2–3 days	Carcinoma of colon
3	M	49	Diarrhoea	4 weeks	?
4	F	19	Abdominal pain	1½ years	Appendicitis. Haemorrhoids
5	F	64	Constipation	5 ,,	Carcinoma of colon
6	M	56	Rectal bleeding	6 months	Haemorrhoids
7	M	56	,, ,,	8 ,,	Carcinoma of colon
8	M	60	Intermittent rectal bleeding	1 year	Multiple polyps Carcinoma of colon
9	M	61	Rectal bleeding	2 years	Haemorrhoids Polyps of colon
10	M	63	Diarrhoea	2 weeks	Carcinoma of colon

The electron microscopical findings are illustrated in the Fig. (Special Plate). Adherent to the surface of the epithelium was a forest of organisms, orientated in the long axis of the cells. The organisms were short and thin and had two or three short curves. They measured up to 3 μ in length and only 0.15 μ in average diameter. They were too short and thin for bacilli. Under high magnification occasional organisms, cut tangentially, showed bunches of spiral filaments. This finding, together with the shape and size of the organisms, indicated that they were spirochaetes.

The spirochaetes sometimes penetrated short distances into the epithelial cells, pushing the plasma membrane before them. Occasionally a vacuole could be seen forming in the cytoplasm of the cell at the tip of the organism. Some of the epithelial cells appeared to have an increased number of lysosomes, but no other reaction was noticed. There was no significant inflammation. Where the surface of the cells had been cut transversely each organism could be seen to be surrounded by a cluster of microvilli. This probably accounts for the consistent longitudinal orientation of the organisms.

Reappraisal of the routine histological sections in the light of the electron microscopical findings revealed a very faint blue haze on the surface of the mucosal cells.

SUBSEQUENT INVESTIGATIONS

It was soon realized that this basophil reaction had been seen histologically in other rectal biopsies but that it had been interpreted as an unusual staining of the brush border of no significance. A review of 100 consecutive rectal biopsies from the files of this department was then undertaken. In nine cases a faint blue haze, exactly as seen in the first biopsy, was present. It was clearly necessary to find out if all of these cases represented a single entity. Small blocks of tissue were excised from the paraffin wax in which they had been stored, the wax was removed in chloroform, and the tissue was post-fixed in osmium tetroxide, after rehydration through graded alcohols. Thin sections were then examined in the electron microscope.

Preservation of the tissue was naturally poor, but in all nine cases spiral organisms identical in size and shape to those seen in the original case were readily identified. As before, they were closely applied to the surface epithelium and in some places just penetrated the cell surface.

It was concluded that all these cases represent a single pathological entity, which we have called intestinal spirochaetosis. This condition can be readily diagnosed in rectal biopsies. It is recognized histologically, even with the low-power objective, as a distinct haematoxyphilic zone occupying the site of the normal brush border. This zone is about 3μ in width. It is not possible to resolve individual organisms in routine paraffin sections because of the thickness of the sections, but individual organisms can be resolved by the light microscope in very thin (1 μ) sections prepared from Araldite-embedded material.

CLINICAL OBSERVATIONS

The main clinical features of the 10 cases are shown in the Table. Both sexes are involved and there is a wide age distribution. All patients had symptoms referable to the bowel. In five cases carcinoma of the colon was definitely diagnosed either by the first biopsy or at a later date. It is of interest that in these cases only the normal mucosa, adjacent to the cancer, was infested by spirochaetes. In three cases haemorrhoids were thought to be the cause of symptoms.

There is evidence that intestinal spirochaetosis can persist for considerable periods. In Case 2, for example, the condition was diagnosed in two biopsies taken 17 days apart, but after preoperative antibiotic treatment spirochaetes were not identified in the resection specimen. In Case 1 two biopsies were both positive ; they were separated by a period of five months, during which the patient's symptoms persisted. Case 8 had five biopsies in six years and all showed clear evidence of spirochaetosis.

Case 4 is of special interest. This patient had had attacks of abdominal pain for one and a half years which led to appendicectomy. She still had symptoms, and haemorrhoids were injected. Spirochaetosis was present not only in the rectal biopsy specimen but also in the appendix removed two months earlier.

DISCUSSION

Since the last century spirochaetes have been known to be present in the intestinal tract, but have usually been regarded as harmless commensals. However, there are scattered reports in the literature that large numbers of spirochaetes can be found in the stool of patients with various forms of dysentery and cholera (Parr, 1923). In addition there are dysentery-like diseases, associated with spirochaetes, which have responded only to treatment with arsenicals (Sáenz, 1925). It is also claimed that spirochaetes are responsible for guinea-pig diarrhoea (Sanarelli, 1927).

Presumably because they have been considered to be non-pathogenic, there has been little attempt to culture and further classify these organisms. However, the morphological descriptions of the commonest organisms, the so-called *Spirochaeta eurygyrata* (Hogue, 1922), closely resemble the spirochaete found in this group of patients. Because these organisms stain with haematoxylin, we think that they would be best classified as Borrelia. In future publications further details will be presented.

It is not possible at the present time to decide the significance of our findings. All the patients had rectal biopsies performed because of symptoms of one sort or another referable to the bowel. Some were found to be suffering from carcinoma of the colon. On the other hand, others had dysenteric symptoms of unknown cause, and these might possibly be cases of "spirochaetal dysentery." Antibiotic treatment of some of these cases may provide an answer to this problem, since we have reason to believe that the spirochaetes disappeared in one case after preoperative antibiotic therapy. There is also the possibility that this form of spirochaetosis gives rise to vague abdominal symptoms simulating appendicitis. It remains quite possible, however, that this attachment of spirochaetes to the surface of the colonic mucous membrane has no clinical significance.

SUMMARY

Ten cases of a new and apparently common form of intestinal spirochaetosis are described. The condition was first recognized by electron microscopy, but diagnosis can be made on routine histological preparations. Short spirochaetes, tentatively classified as *Borrelia eurygyrata*, are attached to and penetrate short distances into the surface epithelial cells. They are characteristically orientated in the long axis of the cells. At present it is not possible to decide the significance of our findings.

We acknowledge the invaluable technical assistance of Mr. D. McSeveney, whose skill made this study possible; we thank Mr. D. H. Clark, who referred the first patient to us; and we acknowledge the financial assistance from the M.R.C., who provided the electron microscope.

W. A. HARLAND, M.B., PH.D., F.R.C.P.(C.) F.C.PATH.,
F. D. LEE, M.B., M.C.PATH.,
Pathology Department, Western Infirmary, Glasgow W.1.

REFERENCES

Hogue, M. J. (1922). *J. exp. Med.*, **36**, 617.
Parr, L. W. (1923). *J. infect. Dis.*, **33**, 369.
Sáenz, A. (1925). *An. Fac. Med. Montevideo*, **10**, 621. Abstract in *J. Amer. med. Ass.*, 1926, **86**, 916.
Sanarelli, G. (1927). *Ann. Inst. Pasteur*, **44**, 1.

Medical Memoranda

Volvulus of the Small Intestine after Herniorrhaphy

Brit. med. J., 1967, 3, 719–720

Primary volvulus of the small intestine is rare in Great Britain and its cause is usually obscure. Renton (1965) found five reported examples and added one of his own. Secondary volvulus is relatively common and its cause is better understood. The present case is reported in the hope that it may contribute to further understanding of the factors precipitating intestinal volvulus.

CASE REPORT

At 2 p.m. on 15 March 1966 a 68-year-old farmer developed lower abdominal pain after lifting a heavy weight while working in his fields. At the same time he noticed a tender swelling in his right groin. He was admitted to hospital at 6 p.m. For two years he had been aware of a small hernia in the right groin which previously had always been easily reduced. During the last seven years he had experienced attacks of abdominal distension, associated with flatulent discomfort, which lasted up to 10 days and resolved with the passage of watery diarrhoea. These attacks occurred two or three times a year and appeared to be unconnected with any disturbance in his hernia. He was not a vegetarian and ate a regular balanced diet.

On admission his general condition appeared satisfactory. His pulse was 72. The blood pressure was 160/80 mm. Hg. His chest showed signs of chronic bronchitis. A tender irreducible right inguinal hernia was present. The abdomen was not distended but bowel sounds were increased.

That evening the inguinal hernia was explored (N. H. V.) under general anaesthesia. It was found to be direct in type and to contain 6 in. (15 cm.) of gangrenous ileum, which was resected. End-to-end anastomosis was carried out and the hernia was repaired. Over the next few days his abdomen became painlessly distended and he was thought to have developed a paralytic ileus. On 19 March his bowels moved loosely and thereafter he had two or three loose motions daily, but the abdominal distension remained. He vomited 200 ml. of stomach contents on 22 March. When this was repeated on the 23rd an intravenous infusion of dextrose saline was started. On the 24th his abdomen suddenly became further distended, having increased 2 in. (5 cm.) in girth overnight. There was generalized abdominal tenderness and guarding. His pulse was 100. The blood pressure was 135/80. *X*-ray examination of the abdomen showed small-bowel distension, with fluid levels suggestive of obstruction in the distal ileum.

After the passage of an oesophageal tube and aspiration of the stomach, laparotomy was performed (C. J. C. R.). Blood-stained fluid was present in the peritoneal cavity. The small intestine was very distended, was dark purple in colour, and its viability appeared doubtful. The entire small intestine, except for the proximal 4 ft. (1.2 m.) of jejunum, had undergone a clockwise rotation of 720 degrees. There were no adhesions, and the previous anastomosis was patent and lying free in the right iliac fossa. No congenital or acquired abnormality was found to account for the volvulus. On reducing the volvulus the circulation to the intestine recovered. Because of the gross distension the bowel was deflated by a suction tube introduced through an enterotomy. The bowel was closed and the original anastomosis, which had leaked after handling, was oversewn. Later the same evening sputum retention and bronchospasm produced increasing dyspnoea, cyanosis, and carbon dioxide retention, leading to respiratory failure. Tracheostomy was performed (N. H. V.), allowing regular bronchial toilet. With physiotherapy, antispasmodics, and antibiotics respiratory function was improved. Gastric suction and intravenous infusions were continued until 28 March, when the abdominal distension started to resolve. His bowels thereafter moved once a day. Two episodes of vomiting on 2 and 6 April necessitated further gastric suction. By 8 April the vomiting and the abdominal distension had completely settled. The tracheostomy tube was removed and convalescence continued uneventfully.

COMMENT

In primary volvulus of the small intestine there is no obvious predisposing cause. It is commoner in Africa and India, where it is associated with a vegetarian diet of bulky indigestible food (Kerr and Kirkaldy-Willis, 1946 ; McWatters, 1945). Rose (1955), discussing the aetiology, mentioned hypermotility and bowel distension as exciting causes. In secondary volvulus there is usually an abnormal congenital or acquired fixation of the intestine.

In this case the past history is consistent with attacks of subacute volvulus recurring over seven years. Though no anatomical abnormality was obvious in the mesentery, a volvulus through 720 degrees suggests undue mobility and length of mesentery. This could have been the result of previous subacute attacks of volvulus or it could have predisposed to them. Bulky diets are said to cause an increase in length of bowel and mesentery as well as hypermotility (Dickson, 1950). There was no evidence of unusual dietary habits in this patient. The right inguinal hernia might have anchored a loop of small intestine and produced a secondary volvulus. However, this hernia was said to be easily reducible up to the final attack of strangulation and to have been present for only two years. If it was responsible its repair should have cured the tendency for the bowel to undergo volvulus.

The final attack of volvulus appeared to start only after the inguinal hernia had been repaired and the bowel resected. It is possible, though unlikely, that the anastomosis acted like the occasionally reported antimesenteric tumour by partly anchoring the bowel and predisposing to volvulus (Aird, 1957). Lulenski (1961) reported cases where volvulus was superimposed on small-bowel obstruction. In this case the anastomosis appeared widely patent without any evidence that it could have caused mechanical obstruction. After any abdominal operation, especially with intestinal resection, there occur transient ileus, gaseous and fluid distension of bowel, and later hypermotility. Sparkman (1952) and Cave (1953) reported cases of volvulus in the immediate postoperative period in which they thought that distension and hypermotility of the bowel were the exciting causes. It seems probable that this patient was subject to recurrent attacks of subacute primary volvulus and that the inguinal hernia was incidental. After the herniorrhaphy postoperative bowel distension and hypermotility were exciting causes in precipitating the final volvulus.

This case strengthens the view that postoperative distension can be an exciting factor precipitating volvulus, though a further predisposing cause is usually required. It emphasizes the necessity for observing carefully the progress of postoperative complications for any sudden deterioration that might call for urgent surgical treatment.

We are grateful to Mr. T. B. Field, who was in charge of this patient, for permission to publish this case.

C. J. C. RENTON, F.R.C.S., F.R.C.S.ED.
N. H. VELLANI, F.R.C.S.I.

Nottingham General Hospital.

REFERENCES

Aird, I. (1957). *A Companion in Surgical Studies*, p. 822. Edinburgh.
Cave, W. H. (1953). *Amer. J. Surg.*, 85, 142.
Dickson, P. R. (1950). *S. Afr. med. J.*, 24, 705.
Kerr, W. G., and Kirkaldy-Willis, W. H. (1946). *Brit. med. J.*, 1, 799.
Lulenski, C. R. (1961). *Amer. J. Surg.*, 102, 453.
McWatters, R. C. (1945). *Brit. med. J.*, 2, 626.
Renton, C. J. C. (1965). Ibid., 2, 743.
Rose, T. F. (1955). *Aust. N.Z. J. Surg.*, 25, 41.
Sparkman, R. S. (1952). *Ann. Surg.*, 135, 863.

Relation of Pregnancy Toxaemia to Trophoblastic Tumours

Brit. med. J., 1967, 3, 720

While the cause of pregnancy toxaemia remains obscure, the study of case histories of women with benign trophoblastic tumours (hydatidiform mole) serves to throw some light on this difficult subject.

The diagnosis of hydatidiform mole depends on four criteria: (1) a discrepancy between the expected and the actual size of the uterus, (2) the presence of pre-eclampsia before the 28th week of pregnancy, (3) a high urinary gonadotrophin excretion after the 16th week of pregnancy, and (4) the absence of foetal parts on radiology after the 16th week of pregnancy.

During 1958–64 250 cases of benign trophoblastic tumour were admitted to the General Hospital, Kuala Lumpur, and 66 (26.4%) of these had pre-eclampsia as defined by Dieckmann (1952), the disease being mild in 36 and severe in 30.

Size of the Uterus Related to Proportionate Incidence of Pre-eclampsia in Cases of Benign Trophoblastic Tumour

Size of Uterus	Total Cases	Pre-eclampsia	
		No.	%
Less than 12 weeks' pregnancy ..	8	0	0
12–15 „ „	17	1	6·0
16–19 „ „	75	10	13·3
20–23 „ „	78	22	28·2
24–27 „ „	55	22	40·0
28 or more „ „	17	11	64·7
	250	66	26·4

When the size of the uterus was related to the incidence of pre-eclampsia, it was noted that the greater the uterine size the more frequent was the associated finding of pre-eclampsia (see Table). But no correlation between the size of the uterus and the severity of toxaemia was noted.

COMMENT

That a higher proportionate incidence of pre-eclampsia was found in cases where the trophoblast was more active implies that abnormal trophoblastic activity rather than mechanical distension of the uterus is a precipitating cause of pre-eclampsia.

This opinion was further supported by the history of one of the patients who was admitted at 14 weeks' gestation with severe pre-eclampsia. She was Chinese, aged 24, gravida 2. Examination showed the uterus to be enlarged to the size of a 16-week gestation. A week after admission the uterus had enlarged to the size of a 20-week gestation, and the pre-eclampsia continued. Eight days after admission the signs of pre-eclampsia suddenly disappeared and no further uterine growth was noted. Intrauterine death was suspected, and as the uterus failed to expel the foetus spontaneously labour was induced with an oxytocin infusion on the 20th day after admission and a hydatidiform mole surrounded by fibrin and decidua was expelled.

DEREK LLEWELLYN-JONES, O.B.E., M.D., M.A.O., F.R.C.O.G.
Department of Obstetrics and Gynaecology,
University of Sydney,
Sydney, Australia.

REFERENCE

Dieckmann, W. J. (1952). *The Toxaemias of Pregnancy*, 2nd ed. St. Louis.

Death from Paraquat after Subcutaneous Injection

Brit. med. J., 1967, 3, 721

Gramoxone is a commercial formulation of a herbicide containing the di-metho sulphate salt of paraquat (1,1′-dimethyl-4, 4′-dipyridilium).

Bullivant (1966) reported that up to July 1964 one case of paraquat poisoning had occurred in a child in Ireland. He described two additional cases in men in 1966. The first was that of a 28-year-old man who drank half a glass of 20% paraquat solution; a day later gastrointestinal symptoms appeared, followed by signs of hepatorenal damage. He died of severe respiratory failure. The second case was that of a man aged 23 who drank a mouthful of paraquat and vomited immediately. In this case also signs of mild hepatorenal damage appeared, and he too died of respiratory failure.

The purpose of this paper is to present an additional case of paraquat poisoning, this time by subcutaneous injection. Suicide in such an unusual way has not to our knowledge been described in medical literature.

CASE REPORT

The patient was a 30-year-old Yemeni-born farmer, divorced, who emigrated to Israel 21 years ago. He was known from the records of a mental hospital to suffer from paranoid schizophrenia.

On 2 August 1966, by means of a syringe that was used for immunizing chickens, he injected himself with approximately 1 ml. of a 20% solution of Gramoxone. He was admitted to hospital a few hours later after vomiting and passing loose bloody stools. He was found to be in good general condition. His pupils were equal and reacted to light. His pulse was 76 and blood pressure 130/80. No other abnormal physical findings were observed. Two days after admission a right facial paresis occurred, abdominal reflexes were reduced on the right side, and Oppenheim's sign was present on the left side. On the fifth day after admission these findings were no longer elicited. Laboratory findings were not abnormal except that urinary sediment contained some erythrocytes and leucocytes. Blood urea varied from 69 to 140 mg./100 ml. and urinary output from 1,000 to 2,000 ml. a day. An E.C.G. was within normal limits.

For two days after admission he felt well, but on the third day he complained of anorexia and chest pain, and his temperature rose to 39° C. He had no dyspnoea at this time. *X*-ray examination during this phase showed a slight infiltrative shadow of the right lung base. After five days he again improved, his pain disappeared, and his temperature returned to normal. In spite of this his radiological changes persisted. On the eighth day in hospital jaundice appeared.

He was tender in the right hypochondrium and the liver was felt 6 cm. below the costal margin. Total serum bilirubin values were raised to 4.6 mg./100 ml., of which direct bilirubin was 3 mg./100 ml., and the serum S.G.O.T. rose to 250 units. Serum ammonia was 375 µg./100 ml. and leucine aminopeptidase was 364 units. All these findings disappeared by the 11th day. The patient felt well for the next three days, but on the 14th day he developed dyspnoea and tachycardia, both of which increased in severity. *X*-ray examination of the chest showed bilateral areas of opacity and deviation of the mediastinum to the left. The patient became oxygen-dependent, and his condition worsened steadily until he died in severe respiratory distress on the 18th day.

Necropsy Findings.—The kidneys did not show any macroscopic or microscopical pathological changes; the liver did not show macroscopic changes, but histological examination revealed some swollen periportal hepatic cells. The main findings were found in the lungs; the upper lung segments were swollen and emphysematous, and there was evidence of intrapulmonary haemorrhages as well as subpleural petechial haemorrhages, the lower segments were contracted and showed bilateral atelectasis.

Microscopical Findings.—The most striking change was proliferation of epithelium of the terminal bronchioles. In many places this proliferation partly or completely occluded the lumen at the prealveolar ducts. The epithelial cells were themselves cuboidal with nuclei rich in chromatin (Reif and Herzig, 1967).

DISCUSSION

There are some findings common to our case and the two cases published by Bullivant (1966). All began with gastrointestinal disturbances, though in our case poisoning followed a subcutaneous injection, and evidence of hepatorenal damage followed the gastrointestinal disorders. Death was due to progressive pulmonary failure. Transient general neurological signs which were seen in our case were not mentioned in the two other cases, but in laboratory animals Clark *et al.* (1966) showed that initial neurological symptoms did occur. If the animal did not die during this phase the deaths were due to respiratory failure. Histologically, an identical pulmonary proliferative process was found, especially in rats and mice, and less in rabbits.

Daniel and Gage (1966), working with laboratory animals, showed that 96% of paraquat labelled with ^{14}C was excreted unchanged in the urine within three days of its subcutaneous administration.

We could not find paraquat in the patient's urine and sputum three days after admission. It seems, therefore, that this substance initiates proliferative changes, which continue though it itself is no longer present.

Such a proliferative process is not unique and has been said to follow the administration of carcinogenic compounds to laboratory animals (Ackerman and Regato, 1954). It is interesting to note that, after subcutaneous injection of carcinogenic hydrocarbons in high-pulmonary-tumour strains of mice, diffuse proliferative changes could, as early as two weeks, be detected, partly projecting into the lumen of alveoli. In the fifth week pulmonary tumours were diagnosed in some strains (Ackerman and Regato, 1954). We felt that this similarity should not be overlooked, and we suggest that further work should be done with paraquat to clarify its mode of action and to show whether or not it, too, is a carcinogen.

The estimated fatal dose would be 4 mg./kg., which would explain why only a mouthful of it could also be fatal despite the poor absorption of this type of compound.

It may be mentioned that the liver and kidneys did not show anything gross pathologically in spite of the presence of clinical hepatorenal infection.

We are grateful for the help given by Dr. A. Reif, head of the Department of Pathology at Asaf Harofe Government Hospital, and Dr. E. Herzig, assistant in that department. We wish to express our thanks to Dr. E. Vure, head of Paediatric Department "B" at the above hospital, for his helpful advice.

CH. ALMOG, M.D.,
Head of Department.
E. TAL, M.D.,
Assistant.

Medical Department "C,"
Asaf Harofe Government Hospital.
Zrifin, Israel.

REFERENCES

Ackerman, L. V., and Regato, J. A. del (1954). *Cancer; Diagnosis, Treatment, and Prognosis*, 2nd ed., pp. 40, 45. St. Louis.

Bullivant, C. M. (1966). *Brit. med. J.*, 1, 1272.

Clark, D. G., McElligott, T. F., and Hurst, E. W. (1966). *Brit. J. industr., Med.*, 23, 126.

Daniel, J. W., and Gage, J. C. (1966). Ibid., 23, 133.

Reif, A., and Herzig, E. (1967). To be published.

Insulin Allergy Treated by Low-dosage Hydrocortisone

Brit. med. J., 1967, **3**, 722

Allergy to insulin was a common problem in the early days of treating diabetes mellitus (Lawrence, 1925 ; Marble, 1959), but introduction of purified preparations has made this less likely. Allergic patients can usually be treated by desensitization or by changing the type of insulin (Marble, 1959).

Today many patients needing only small doses of insulin have been prescribed oral hypoglycaemic agents instead. However, these may be inadequate during infections or operations, or if the diabetes becomes worse, and so insulin may be given again. A secondary immune response is then apt to occur, causing local or general allergy and sometimes fatal anaphylaxis (Hanauer and Batson, 1961 ; Michel, 1963 ; Aiken, 1964). We encountered this problem in the following case and used a different method of overcoming allergy.

CASE REPORT

A 49-year-old housewife developed diabetes mellitus in 1960 and was given insulin zinc suspension. A few days later she developed painful red swellings at the injection sites. As her diabetes was mild insulin was stopped and tolbutamide substituted.

Five years later oral hypoglycaemic drugs failed. Isophane insulin controlled the blood-sugar level, but local allergic reactions again occurred. Soluble, globin zinc, and Actrapid insulins produced similar reactions whether injected subcutaneously or intramuscularly. After 13 days she developed a widespread urticarial rash, angioneurotic oedema, and dyspnoea. Antihistamines provided no relief, and so, as symptoms were severe and potentially dangerous, prednisone 10 mg. was given by mouth ; remission occurred within one hour.

After this her diabetes was controlled by soluble insulin (28 i.u. morning and 32 i.u. evening) and the allergy suppressed with prednisone by mouth 10 mg. q.d.s. However, on reducing the dose of prednisone below 20 mg. daily allergic symptoms recurred. As this dose was undesirable it was decided to inject a corticosteroid drug with the insulin. Prednisolone 2 mg. failed, but hydrocortisone 10 mg. prevented both local and systemic reactions. The blood-sugar level was controlled, there being no insulin resistance, and the patient improved. Within two weeks as little as 2 mg. of hydrocortisone mixed with each injection of soluble insulin was satisfactory. Less than this allowed skin reactions of increasing severity to recur and the patient used 2 mg. again of her own accord.

A limited supply of insulin recrystallized six times was used. This, while superior to soluble insulin alone, was not entirely free of allergic properties, occasionally producing weals with induration up to 1 in. (2.5 cm.) in diameter. The mixture of soluble insulin with hydrocortisone was therefore restarted. Hydrocortisone was omitted from trial injections at approximately fortnightly intervals until after about six months soluble insulin could be used alone without adverse effect.

COMMENT

The occurrence of allergy to several different types of insulin of bovine and porcine origin suggests that the reaction is to either insulin itself or to a constant impurity. The latter seems more likely because recrystallization of insulin lowers the incidence of allergy greatly (Jorpes, 1949, 1950).

Desensitization is a lengthy and sometimes difficult procedure, whereas suppression of symptoms with corticosteroids is simple. The use of hydrocortisone, which mixes well with soluble insulin, allows less corticosteroid to be employed, with reduced risk of adverse side-effects. In this case the dose was within the range of endogenous cortisol production 16.2 ± 5.7 mg./24 hours (Cope, 1965). Presumably slow desensitization then occurs under corticosteroid cover. The only disadvantage is the need to mix drugs for injection.

This method is suggested (1) as an alternative in simple cases of insulin allergy, (2) when speed is important, (3) in cases resistant to the more usual methods of treatment, and (4) when recrystallized insulin is not available.

We wish to thank Dr. C. F. Hawkins for constant encouragement and for permission to publish this case, and Dr. R. A. Ellis, of the Medical Division, Boots Pure Drug Company Limited, Nottingham, for supplying the insulin recrystallized six times.

ROY COCKEL, M.A., M.B., M.R.C.P.
SHEILA MANN, M.B., CH.B.
Queen Elizabeth Hospital, Birmingham 15.

REFERENCES

Aiken, J. B. (1964). *Canad. med. Ass. J.*, 91, 660.
Cope, C. L. (1965). *Adrenal Steroids and Disease*, p. 160. London.
Hanauer, L., and Batson, J. M. (1961). *Diabetes*, **10**, 105.
Jorpes, J. E. (1949). *Arch. intern. Med.*, 83, 363.
—— (1950). *Acta med scand.*, 138, Suppl. No. 239, p. 313.
Lawrence, R. D. (1925). *Lancet*, 1, 1125.
Marble, A. (1959). In *Treatment of Diabetes Mellitus*, by E. P. Joslin, H. F. Root, P. White, and A. Marble, 10th ed., p. 401. London.
Michel, H. (1963). *Med. Welt (Stuttg.)*, 1, 909.

"Railroading" in Retinal Vessels

Brit. med. J., 1967, **3**, 722–723

Among the many problems involved in the treatment of cardiac arrest is that of deciding during the period of emergency whether the brain has been damaged irreversibly and when resuscitation should be abandoned. Widely dilated pupils and stagnant cyanosis do not necessarily mean that the patient is dead. Obviously it is undesirable to continue resuscitation if the brain is dead. Treatment should be abandoned as soon as this is clearly indicated.

"Railroading" or "cattle-trucking" seen during ophthalmoscopic examination of the retina is a well-known physical sign of death in traditional medicine in Britain, though it is not well known in some other countries. This physical sign is not described in many of the standard textbooks, though a brief description is given by Smith and Simpson (1956). It may develop as late as several minutes after cessation of the heartbeat and it may be seen until the cornea clouds over.

What one observes is a fragmentation of the column of blood within the retinal vessels. The fragments or aggregates of red cells move in either direction along the vessel at random and may collide with each other. This has been fancifully likened to the sequence of events that occur when a trainload of unbraked goods wagons stops. Accompanying the movement of the red cells, the diameter of the vessels alters rapidly, sometimes narrowing, sometimes dilating. The vessel itself may appear to be moving rapidly in and out of focus of the ophthalmoscope. This may be erroneously attributed to an inability to use the ophthalmoscope during the stress conditions of treating cardiac arrest by those making the examination.

What is not known is the significance of this sign in situations of cardiac arrest. The association of the time of its appearance to the known time of survival of the brain after circulatory arrest suggests that it appears at or after death of the brain rather than with cessation of the circulation. This physical sign could provide a good guide to prognosis, as shown in this case report.

CASE REPORT

A girl aged 10, a severe asthmatic, was admitted to hospital having "collapsed" approximately 15 minutes earlier during an asthmatic attack at home.

On arrival she was intensely cyanosed, pulseless, and apnoeic. Cardiac massage and intermittent positive-pressure ventilation were started immediately and the cardiac arrest team was summoned. Ophthalmoscopic examination at this time showed widespread "railroading" in the retinal vessels. An E.C.G. showed ventricular fibrillation against a background of severe electrical interference. In view of the doubt on how long she had been in circulatory arrest it was decided to defibrillate the heart. This was done externally with a single shock and was immediately followed by good heart action. A later examination of the fundi showed normal vessel architecture, though there was widespread oedema of the fundi.

Despite dehydration therapy with mannitol, hypothermia, artificial ventilation, etc., she did not regain consciousness. An E.E.G. taken the next day with a portable electroencephalograph showed widespread abnormal activity with high-voltage spikes alternating with slow waves every one to two seconds. Regular spontaneous respiration did not return until eight days after admission.

Fourteen days after admission she developed pneumonia and died. At necropsy there was widespread diffuse infarction of the cerebral cortex, hypothalamus, right caudate nucleus, and pons.

COMMENT

This case illustrates that despite an easy restoration of the circulation the brain may still be irreparably damaged. Had this patient survived she would have been decerebrate. The outcome suggests that the appearances of the fundi at the time of arrest provided a good indication of the state of the brain.

In a series of 70 personally attended cardiac arrests occurring in 61 patients "railroading" has been seen on 14 occasions during the time of active resuscitation. Of these, despite persistence of resuscitatory effort for up to 30 minutes after making observations, the only occasion when the circulation was adequately restored was in the case described above. This is a marked contrast to the results of the overall series, in which 33 times out of 70 the circulation was initially restored adequately. For technical reasons fundal examinations were not always carried out.

If "railroading" has no significance nearly half of the 14 patients showing this sign might have been expected to have their circulation restarted. Instead only one did. On statistical grounds this may be regarded as significant (χ^2 9.32 ; $P<0.01$).

Nevertheless, in dealing with individual patients suffering from cardiac arrest such statistics relating to a single physical sign should not influence management unless the clinical significance of the physical sign is absolute—that is, the brain is always dead. The chances of full recovery after cardiac arrest are limited and the aim of instituting treatment is to improve these against the statistical certainty of death.

The preliminary observations presented here suggest that the presence of "railroading" is of grave prognostic significance, and it would be useful to know of any cases where this physical sign has been observed (and recorded at the time) and the patient has made a full neurological recovery.

Early ophthalmoscopic examination of the fundi in cardiac arrest is extremely easy because the pupils are usually widely dilated (if they are not, then this too is useful information). It can be carried out quickly with very little practice. Cardiac massage need not be stopped until a retinal vessel is seen, and then it need only be stopped momentarily. The one difficulty in making the very rapid examination of the fundi required in these circumstances is the presence of lens opacities. These may be readily seen with the ophthalmoscope held some 2 feet (60 cm.) away from the eye being examined. A green filter makes the retinal vessels appear black, and then they stand out even more clearly. A routine search for this physical sign when taken in conjunction with other features of such cases should establish its prognostic value.

I should like to express my thanks to D. J. S. Wigglesworth, Institute of Child Health, for the necropsy report.

P. J. TOMLIN,* M.B., B.S., F.F.A. R.C.S.,
Senior Registrar, Department of Anaesthetics,
Hammersmith Hospital, London W.12.

---

* Present address: Department of Anaesthetics, University of Birmingham.

REFERENCE

Smith, S., and Simpson, K. (editors) (1956). *Taylor's Principles and Practice of Medical Jurisprudence*, 11th ed., p. 173. London.

Haemoperitoneum after Traumatic Avulsion of Uterine Fibroid

Brit. med. J., 1967, 3, 723–724

The causes of intra-abdominal haemorrhage can be divided into two main groups: those following traumatic injuries and those arising spontaneously.

In a review of 129 consecutive cases of haemoperitoneum, Ellis *et al.* (1958) noted that 68% were the result of gynaecological haemorrhage, 23% followed trauma, and the remainder resulted from a variety of causes. The gynaecological causes in their series were ruptured ectopic pregnancies and follicular cysts. Traumatic cases were usually the result of splenic, hepatic, or mesenteric injuries.

It is rare for haemoperitoneum to result from a gynaecological injury.

CASE REPORT

A woman aged 46 was admitted to Westminster Hospital on 14 January 1966 after a road accident in which she was knocked down by a car.

On admission she was concussed and shocked. Her blood pressure of 100/70 rapidly fell to unrecordable values. This was restored and maintained by blood transfusion. Her injuries included (*a*) a fractured pelvis, central dislocation of the right hip (Fig. 1), and a deep penetrating wound 3 in. (7.5 cm.) in diameter over the right greater trochanter; (*b*) a fractured neck of the left fibula with a lateral popliteal nerve palsy, and rupture of the lateral ligament of the knee; and (*c*) lacerations of the chin and buccal mucosa.

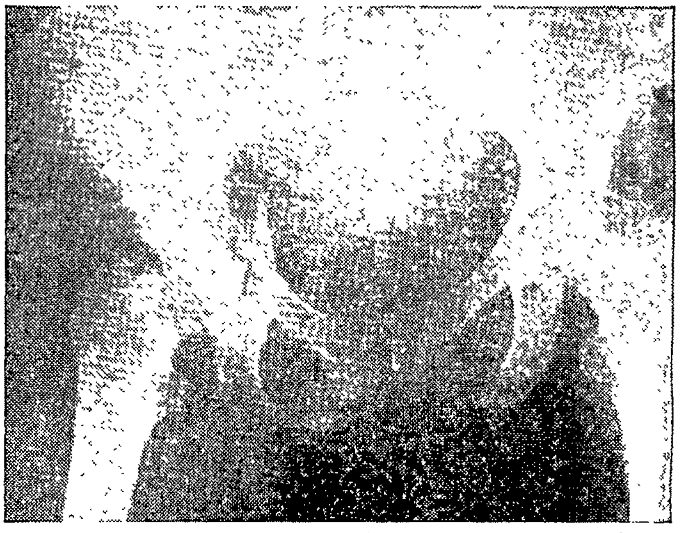


FIG. 1.—Radiograph of pelvis showing central dislocation of hip.

She complained of pain in her right shoulder—there was no external evidence of injury—and of lower abdominal tenderness. On abdominal examination there was tenderness and guarding over most of the lower abdomen which was maximal on the right near the pelvic brim. Rebound tenderness was elicited. Bowel sounds were present but diminished. The presence of free fluid was not detected clinically.

Chest *x*-ray examination showed a raised right diaphragm. A plain film of the abdomen did not demonstrate the presence of subdiaphragmatic gas. A catheter was passed to exclude any injury to the bladder or urethra and clear urine was obtained. It was thought that her symptoms and signs could be due to extraperitoneal haemorrhage alone, but as an intra-abdominal lesion could not be excluded laparotomy was undertaken.

Operation.—The findings were: (*a*) considerable intraperitoneal blood ; (*b*) an avulsed pedunculated fibroid measuring 8 by 7.5 by 5 cm. lying free in the peritoneal cavity (Fig. 2) ; (*c*) arterial bleeding from a raw area 2.5 cm. in diameter on the superior left surface of the uterus near the junction with the fallopian tube ; (*d*) a cyst of the right broad ligament 8 cm. in diameter ; and (*e*) extraperitoneal haemorrhage on the right side of the pelvis in relation to a central dislocation of the hip ; the peritoneum was intact. The raw bleeding area was oversewn and the broad-ligament cyst removed. Under the same anaesthetic the thigh wound was explored and found to be a deep penetrating wound with contamination. Debridement was performed and a Steinmann pin inserted into the right tibia.

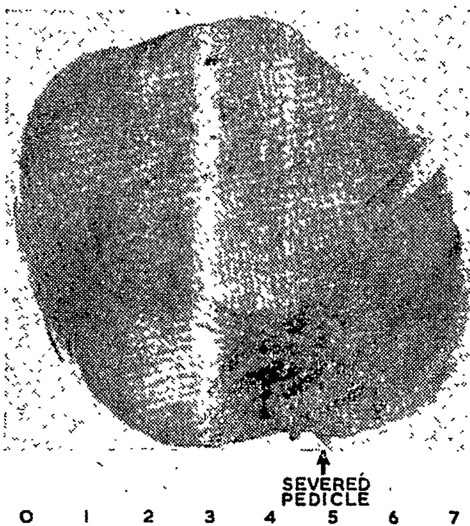


FIG. 2.—Avulsed fibroid with pedicle marked.

The patient was given a course of penicillin and streptomycin, and antitetanus and anti-gas-gangrene serum. The transfusion of 6 pints (3.4 litres) of blood was completed and continuous traction was begun.

Her recovery was uneventful until the fifth day after operation, when she became cyanosed, dyspnoeic, and disorientated. Signs of congestive cardiac failure were present. It was thought probable that this was due to fat embolism. She was treated with digitalis and diuretics and made a complete recovery.

Traction was maintained on her right leg for eight weeks and then gradual mobilization with increasing weight-bearing was begun. The movements of the right hip steadily improved and further *x*-ray examination of the pelvis showed consolidation of the fracture lines. The left lateral popliteal nerve palsy recovered and no abnormalities were detected on examination of the abdomen and of the cardiovascular system at follow-up.

COMMENT

The main feature of interest in this case was the presence of an avulsed fibroid and a fractured pelvis. We have been unable to find any previous report of this association.

It is known that fibroids may bleed spontaneously. Hasskarl (1949) collected 58 reports of cases where spontaneous bleeding occurred from dilated veins over the surface of fibromyomata. He excluded from his review those following torsion, though this does occur, as reported by Turel (1934).

We have traced only two cases where spontaneous separation of a fibroid caused intra-abdominal haemorrhage. The first (Shelley, 1931) was that of a woman aged 43 who complained of a sudden abdominal pain at rest. Laparotomy revealed haemorrhage from the pedicle of a separated fibroid lying free in the abdomen. The second (Cottalorda, 1935) was that of a patient who presented as a case of acute appendicitis. At operation the abdomen was filled with blood from the pedicle of a detached fibroid lying adherent to a gangrenous appendix in the pelvis.

We conclude that the most likely cause of the avulsion in our patient was a contrecoup type of injury, the uterus and fibroid moving at relatively different rates producing a sheering stress in the pedicle. There was no evidence to suggest torsion or direct injury.

We wish to thank Mr. David L. Evans for his permission to publish this case, Professor Ellis for his helpful advice, and the photographic department of Westminster Hospital.

C. W. VENABLES, F.R.C.S.
I. L. CRAFT, F.R.C.S.
Department of Surgery, Westminster Hospital, London S.W.1.

REFERENCES

Cottalorda, J. (1935). *Bull. Soc. Obstét. Gynéc. Paris*, **24**, 603.
Ellis, H., Griffiths, P. W. W., and MacIntyre, A. (1958). *Brit. J. Surg.*, **45**, 606.
Hasskarl, W. F. (1949). *Proc. Mayo Clin.*, **24**, 207.
Shelley, H. J. (1931). *Amer. J. Surg.*, **14**, 631.
Turel, S. J. (1934). *Int. J. Med.*, **47**, 240.

Current Practice

MEDICINE TODAY

One or Two Fits

"Medicine Today" is the television series for doctors produced by the B.B.C. Advice in the preparation of the programme is given by the Association for the Study of Medical Education.

The programme on B.B.C. 2 on 12 September was on the subject of fits. Printed below is an article prepared with the help of expert contributors to complement the television programme, which will be repeated on B.B.C. 1 on 19 September at about 11.20 p.m.

In "Medicine Today" the crucial importance of a carefully taken detailed history in the diagnosis of true epilepsy was stressed, and this remains true despite the many impressive advances that have been made in investigative and diagnostic techniques. The distinction of fits from faints, the recognition of major, minor, and focal epilepsy, and the appreciation of possible provocative factors such as fever, television flicker, and intoxication with alcohol or lead are almost entirely dependent on traditional clinical methods. Analysis of the events prior to an attack of loss of consciousness may point to micturition or cough syncope; prodromal symptoms may establish the diagnosis of basilar artery migraine or temporal epilepsy; cryptic injuries, incontinence of urine, stiff muscles, and dull headaches on getting up in the morning may suggest unrecognized nocturnal major fits. Few of these obiter dicta will ring new to the experienced general practitioner. He is more likely to have witnessed the circumstances of an attack than is a remote consultant; he knows who may have been drinking excessively; as for possible precipitating factors he is only too familiar with the plethora of tortuous explanations and bizarre theories often advanced by puzzled patients or anxious relatives to account for a catastrophic and unheralded fit.

When to Investigate

However, all too often the facts are unequivocal. The patient has suffered one or two definite fits. There are no abnormal physical signs or evidence of systemic disease and the doctor is placed in the exacting position of having to decide when to investigate, when to refer, and how to treat. There is no simple answer. The possible variables influencing clinical judgement include age of patient, type of fit, number of attacks, interseizure period, recognizable provocative factors, occupational hazards, and local facilities for investigation; and the doctor must take all of these into account when deciding what advice to give to his patient.

To be helpful, advice to doctors facing this problem must be dogmatic. One or two febrile convulsions in an infant do not merit investigation nor do they require long-term anticonvulsants; the post-seizure electroencephalogram is usually normal and cannot distinguish the unfortunate 5% of infants who will develop recurrent attacks. In an otherwise healthy child a solitary fit usually means idiopathic epilepsy and detailed investigation is unrewarding, unjustifiable, and usually impracticable. At all ages anticonvulsant drugs should be given in effective doses or not at all; homoeopathic drug regimens usually reflect the prescriber's anxiety and indecision. In this particular context—a child with one fit—anticonvulsant drugs should be withheld until further attacks occur.

Focal fits are usually symptomatic of cerebral disease and prompt investigation may reveal a local and perhaps treatable lesion. It is pertinent to recall that in patients presenting with focal epilepsy the most sensitive investigation may remain normal for long periods before a cerebral tumour can be identified. Gliomas have been suspected but unproved for ten years or more. Investigations should include *x*-rays of skull and chest, an E.E.G., serological tests for syphilis, and examination of cerebrospinal fluid. Brain scanning is a painless procedure and can be done as an outpatient investigation. Detailed neuroradiological tests may be required: in skilful hands cerebral arteriography can be practised without great distress to the patient but air-encephalography, admittedly often a valuable procedure, may be followed by severe headache for several days.

Fits in Adults

The older the patient, the more probable is the fit to be symptomatic and the more taxing is the task of management and treatment. When employment or driving licence may be in jeopardy knowledge of previous fits may be withheld or repressed and remote attacks are easily overlooked. When physical signs are absent there is no clinical guide other than the laws of chance to distinguish the patient who may have only one or two attacks of idiopathic epilepsy during a lifetime from the patient who may be harbouring a cerebral tumour. If a healthy adult appears to have had only one recent fit and *x*-rays of skull and chest and an E.E.G. are normal, many neurologists would prefer to leave the patient observed, undiagnosed and untreated. However, the patient's occupation—lorry driver, pilot, or steeplejack—or a second fit shortly after the first will enforce drug treatment and more stringent investigations. When the interval between the two fits is long, say a year or so, and the patient still appears to enjoy good health there is no uniformity of opinion concerning long-term drug treatment. An anxious professional man would probably require drugs while an elderly stoic benevolently contemplating a long and untreated remission might prefer to "wait and see." Assuming that the fits are not focal and that an adult patient who has had only one or two fits is otherwise well, detailed investigation is unlikely to be therapeutically rewarding. It is true that the possible symptomatic causes of epilepsy are legion, from uncommon cerebral tumours to intriguing but improbable biochemical disturbances such as hypocalcaemia, but it is manifestly unrealistic and unreasonable to investigate every patient intensively. Even the most erudite and obsessional of neurologists defers consideration of rare polyeponymous (and usually untreatable) systemic degenerations of the central nervous system until more than a couple of fits have occurred. *X*-rays of skull and chest should be done; if available an electroencephalograph might serve towards excluding a focal cerebral lesion. Most decisions in clinical medicine are still determined by common sense and probability and it is important to recall that idiopathic epilepsy is a much commoner cause of fits than is cerebral tumour, even when the first fit occurs after the age of 25 years.

ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Oral Contraceptives and Carbohydrate Metabolism

Q.—*Do oral contraceptives have any effect on carbohydrate metabolism and on the insulin requirements of diabetics? If so, what is the effect and what is its mechanism?*

A.—Wynn and Doar[1] reported minor abnormalities of glucose tolerance in approximately 20% of people taking a variety of oral contraceptive preparations. They suggested that the effect was similar to that found in corticosteroid diabetes and during pregnancy. The insulin requirements of a diabetic might therefore be increased on occasion, but the effect is not likely to be very great.

REFERENCE

[1] Wynn, V., and Doar, J. W. H., *Lancet*, 1966, 2, 715.

Scleroderma

Q.—*What is known about the aetiology and pathology of scleroderma, and is there any treatment?*

A.—The term scleroderma is used for two quite distinct clinical entities: morphoea, characterized by the transient appearance of sclerodermatous plaques without any evidence of systemic involvement, and systemic sclerosis, one of the major generalized collagen-vascular diseases with sclerodactyly and widespread sclerodermatous changes secondary to peripheral ischaemia.[1]

With the exception of linear morphoea, which may affect by direct extension the underlying tissues of the skull and limbs, morphoea is a benign and self-healing disorder. There is recent experimental and clinical evidence that the chelating agent penicillamine is of benefit in this condition by interfering with the excessive formation of dermal collagen.[2 3] An initial dose of two capsules (300 mg.) t.d.s. of penicillamine for one month with gradual reduction of the dose to one capsule (150 mg.) on alternate days is effective in most patients.

Treatment of systemic sclerosis should always be preceded by a full investigation of the renal, respiratory, and alimentary systems. Treatment with oral corticosteroids is disappointing unless they are given in high dosage during periods of rapid progression of the disease. Apart from clinical assessment, frequent repetition of pulmonary function tests is a useful guide to progress. The often grossly impaired peripheral blood flow, with digital ulcers, sclerodactyly, and widespread sclerodermatous changes, can be improved by infusions with low molecular dextran, two to six bottles being given at the rate of one bottle in 12 hours. This treatment has to be repeated every four to six weeks during the winter and every two to four months during the summer.[4]

REFERENCES

[1] Ingram, J. T., *Brit. J. Derm.*, 1964, 76, 238.
[2] Nimni, M. E., *Biochim. biophys. Acta (Amst.)*, 1965, **111**, 576.
[3] Harris, E. D., and Sjoerdsma, A., *Lancet*, 1966, 2, 996.
[4] Holti, G., *Brit. J. Derm.*, 1965, 77, 560.

Shampoos in Seborrhoea

Q.—*Is long-continued use of a shampoo of either cetrimide or a coal-tar preparation with hexachlorophane contraindicated in cases of seborrhoea?*

A.—The prolonged application of any chemical to the skin involves a risk of inducing allergic sensitization. Tar, hexachlorophane, and cetrimide are all potential sensitizers but relatively feeble ones. The use of these substances in scalp preparations can be regarded as safe. Used in this way they very rarely indeed induce allergic dermatitis.

Diphtheria Immunization of Nurses

Q.—*Does a prospective nurse require a full course of immunization against diphtheria if the Schick test is positive? If it is negative, what is the best method and preparation to use?*

A.—Schick-positive nurses should be given a full immunizing course of diphtheria toxoid consisting of either two injections of P.T.A.P., 0.2 ml. and 0.5 ml. respectively, or three 0.5-ml. doses of T.A.F. with an interval of not less than four weeks between injections. P.T.A.P. is a more potent antigen than T.A.F., and is therefore preferred despite its tendency to cause undesirable local reactions.

A negative Schick reaction is generally regarded as indicative of immunity to diphtheria, but this immunity is not always absolute and may be occasionally overcome by heavy infection of the gravis type. Prospective Schick-negative nurses should therefore be given a single booster injection of a diphtheria toxoid, preferably 0.2 ml. P.T.A.P.

Nurses with pseudo-positive Schick reaction are prone to react violently to diphtheria toxoids, but since they are immune to diphtheria they do not require further immunization.

Reaction of Triple Antigen

Q.—*Is it better to begin a course of triple antigen at the age of 3 months or of 6 months, when the risk of side-effects is less?*

A.—There is little evidence to support the view that side-effects to triple antigen are reduced by starting a course of immunization at 6 months instead of 3 months.

In a recent report on reactions to combined vaccines contained killed *B. pertussis*[1] it was stated that 23 of the 24 infants who had severe reactions to the first dose of *quadruple* vaccine (which included trial batches of vaccine) were under 6 months of age, though there were almost equal numbers of participants below or over 6 months. On studying the report further, it can be deduced that three of the six children who had severe reactions to second injections were over the age of 25 weeks, but the age distribution at the time of second injections is not known.

With regard to reactions following *triple* antigen, only two groups of sixty were immunized. The purpose of the study was to compare the incidence and severity of reactions produced by two manufacturers' vaccines. Six children aged 18 to 21 weeks had severe reactions, but it is possible that the study was confined to infants of this age.

These studies do not provide adequate evidence to justify changes in existing immunization schedules. Such changes should not be considered on the grounds of reactions until results are available on direct comparative trials in 3- and 6-months-old infants.

REFERENCE

[1] Haire, M., Dane, D. S., and Dick, G., *Med. Offr*, 1967, **117**, 55.

Stability of Hyoscine

Q.—*Do tablets of hyoscine keep their properties over long periods, and after, say, seven years could their strength and safety be relied on?*

A.—Hyoscine may be present in proprietary tablets either as the base or as a salt, usually the hydrobromide. In either case the substance is reasonably stable. Solutions of the salts can, for example, be sterilized by autoclaving.

If the tablets have been stored under the official conditions—protected from air and light in a cool place—they should retain their strength for several years, possibly as long as seven. Most pharmacists, however, regard about five years as the maximum shelf-life of any medicine.

There are unlikely to be any toxic products in tablets stored for seven years, but there may be some physical deterioration of the tablets.

Warmed Air and Asthma

Q.—*Is central heating by way of warmed air circulated through ducts likely to aggravate asthma and upper respiratory tract allergic conditions? Some asthmatics complain of this form of heating and think that dust and allergens may be circulated with the air.*

A.—I know of no evidence that central heating by warmed air circulated through ducts is likely to aggravate asthma or upper respiratory tract allergic conditions. It has been suggested that some asthmatics are better when the absolute level of moisture in the air is high, and it is possible that excessive drying of the air might lead to deterioration.

Treatment of Cataract

Q.—*Have injections of dilute hydrochloric acid any role in the treatment of cataract?*

A.—I know of no medical treatment which has been proved to have any value in the treatment of senile cataract, and I have no knowledge of the use of hydrochloric acid for this purpose.

Book Reviews

Autistic Children

Early Childhood Autism. Clinical, Educational and Social Aspects. Edited by J. K. Wing. (Pp. 333+xiii. 45s.) Oxford: Pergamon. 1967.

The Nature of Childhood Autism. By Gerald O'Gorman, M.R.C.P., D.P.M. (Pp. 134+vii. 30s.) London: Butterworth. 1967.

Most mentally retarded children are fairly uniformly backward in all their accomplishments. Those who are of trainable or imbecile level of intelligence are often cheerful, pleasant, and outgoing. The use of the term "idiot savant" was an early recognition that some patients are not uniformly retarded but are relatively advanced in some aspects of their performance while severely handicapped in others. It is probable that most patients who have previously been described as "idiot savant" would now be classed as autistic. With the passage of time more and more groups of handicapped children who present a special variety of problems have been recognized and attempts have been made to make special provision for them. This has happened in the case of autistic children, and there is now a voluntary body concerned with their interests. There is, however, a considerable lack of agreement about the precise nature of infantile autism or its definition; even the terminology is not agreed. Some authorities use "infantile schizophrenia" as covering much the same ground as "infantile autism," and still others prefer to use the term "infantile psychosis."

In view of the interest attaching to this subject at the present time it is fortunate that two volumes which should contribute to our knowledge of the problem have now appeared. The work edited by Dr. J. K. Wing is a composite effort by 11 contributors. Much of the material is derived from the Maudsley Hospital children's department, in particular Dr. M. L. Rutter's contribution. It is now well recognized that adequate provision for handicapped children requires a team approach, and this principle has been followed in Dr. Wing's book, which includes chapters by psychologists, a teacher, and a mother of an autistic child.

The chapter by V. Lotter deals with the survey carried out in the county of Middlesex on children aged 8, 9, and 10. On the basis of an extensive inquiry 61 children were selected as possibly autistic. Of these 35 were ultimately selected as being in fact autistic, giving a prevalence of 4.5 autistic children per 10,000 of the population. This is equivalent to 3,049 autistic children in England and Wales, of whom 1,287 would have an intelligence quotient of 55 or above on testing. On this estimate there are about as many autistic children as deaf children of school age, and about twice as many autistic as blind children. It should be emphasized, however, that in this survey and in other work on the subject no sharp cut-off point is found, and the 26 children who were excluded as not satisfying the criteria did in fact show some features of autism. Dr. Wing dislikes the use of the term infantile schizophrenia for this group of patients, preferring infantile autism or Kanner's syndrome. He says that none of the positive features of schizophrenia, such as specific kinds of delusions or hallucinations, occur in autistic children, and he also states that none of the well-documented series has demonstrated an increased risk of schizophrenia in the relatives.

Rutter points out that the prognosis for autistic children correlates fairly well with assessment of intelligence, as carried out by experienced psychologists, who usually have the opportunity of seeing the child on several occasions during the course of the stay in hospital. He emphasized that psychotic children are notoriously difficult to test and much patience and ingenuity are required. In spite of the bad prognosis with many such children, a number of successes have been recorded and it seems likely that with better educational facilities there would be more. O. I. Lovaas and other contributors to Dr. Wing's volume stress the need for a structured educational environment in teaching. A purely permissive attitude does not seem to be helpful with these children, who showed marked psychological rigidity or resistance to change. Dr. P. H. Connell's chapter mentions the many deficiencies in services. He points out that adequate numbers of comprehensive assessment units are not available and that there are very few day or residential schools. Despite this, however, he hopes that the needs of the autistic child will not be considered in isolation, but in relation to wider issues and other handicaps appearing during childhood.

The other new volume on the subject is by Dr. Gerald O'Gorman, whose work at Smith Hospital, Henley-on-Thames, in connexion with infantile psychosis is well known. He considers that the term childhood schizophrenia is appropriate for this group and points to examples of families with more than one case and with parents affected by schizophrenia. However, as he suggests, it is probable that arguments about terminology are not very appropriate, and most readers of these two volumes will be interested in the powerful plea made by all the writers for more research, more study, more objective appraisal, and more services for this group of very disturbed children.

B. KIRMAN.

Rheumatic Diseases

Modern Trends in Rheumatology. Vol. 1. Edited by Alan G. S. Hill, M.C., F.R.C.P.(Ed.), M.R.C.P. (Pp. 394+xii; illustrated. 95s.) London: Butterworth. 1966.

This is a well-illustrated and well-produced book. Most of the contributors are from Great Britain, but authorities from the United States are also represented. Daniel McCarty writes on calcium pyrophosphate crystal deposition disease, John H. Talbott on gout, Peter Kulka on vascular derangement in rheumatoid arthritis, Alan Cohen and Chang Kim on acute suppurative arthritis, and W. B. Reed on psoriatic arthritis. W. Hijmans, of Leiden, writes an interesting chapter on the L.E. cell phenomenon and the antinuclear factors. In an active growing subject such books as these are essential, and there is abundant room for this publication, even though *Progress in Clinical Rheumatology*, edited by A. St. J. Dixon, appeared less than two years ago, for the books do not cover the same ground, and have a different approach.

The present volume is well set out, and many of the chapters end in a summary or abbreviation of their contents. The syndrome "polymyalgia rheumatica" is shortly and adeptly discussed by F. M. Andrews, of Reading, who recommends a search for vascular tenderness, and a biopsy if it is found, so that the relationship of the syndrome to giant-cell arteritis can be finally elucidated. Gerald Rodnan contributes a useful chapter on diffuse scleroderma, and Carl M. Pearson on polymyositis and dermatomyositis. The chapter by Daniel J. McCarty on "pseudo-gout" due to deposition of crystalline material of different kinds is clear and informative. The opening chapter on epidemiology of the rheumatic diseases is ably done, as would be expected from such an acknowledged expert on the subject as J. S. Lawrence. The editor modestly does not contribute more than a foreword, but the whole work bears the stamp of his efficient selection and supervision. This is an essential book for anyone interested and working on this important and ever-growing subject.

F. DUDLEY HART.

Gynaecological Cancer

New Concepts in Gynecological Oncology. Edited by George C. Lewis, jun., M.D., W. Budd Wentz, M.D., and Ronald M. Jaffe, M.D. (Pp. 438+xxviii; illustrated. £8.) Oxford: Blackwell. 1967.

This book consists of 49 lectures and contributions to a symposium, with an introduction by S. L. Israel and R. J. Bolognese. In his preface the senior editor declares that its main purpose is "to provide a broad review of the present status of gynaecologic cancer." It does exactly this. The reader is presented with modern rather than new concepts, and these by eminent contributors, all except a few of whom work in the U.S.A.

There are two sections on squamous carcinoma of the cervix, two on adenocarcinoma of the endometrium, one each on ovarian tumours, carcinoma of the vulva, and trophoblastic tumours, with a final special lecture by Langdon Parsons on treatment centres and education of the physician. In addition to clear accounts of pathology, premalignant states, diagnosis, and treatment, attention is paid to the epidemiology of certain cancers, to fields in which research is active, and to the physician's responsibility for cancer control. Often one subject is dealt with by more than one authority, and this naturally reveals a few delightful differences of opinion and experience. Thus, a pathologist says that most chronic skin lesions of the vulva deserve conservative management, whereas a surgeon holds that all "leukoplakic" skin requires radical excision. Nevertheless, the work as a whole presents a concise and comprehensive picture with full details of surgical, radiotherapeutic, and chemotherapeutic techniques. The statements on results are balanced and fair.

Those who are at present concerned to encourage population screening with a view to detecting cancer at an early stage should study especially the relevant chapter, which includes the ten-point programme of the American Cancer Society. This makes it abundantly clear that all screening, including cervical cytodiagnosis, requires to be of the highest standard if it is to be valuable. This applies to both the clinical and laboratory aspects.

This book is expensive but it is worth the money, for it is beautifully produced and offers what must be one of the best available statements of present-day knowledge of the most common types of female pelvic cancer.

T. N. A. JEFFCOATE.

Statistics in Malaria Eradication

Statistical Methods in Malaria Eradication. By Satya Swaroop. (Pp. 164. £1 3s. 6d.) Geneva: W.H.O. 1966.

This monograph on statistical methodology is to help those engaged in malaria eradication. In 1956 Dr. Swaroop (then chief of the statistical studies section, W.H.O.) produced a cyclostyled document entitled "Statistical Notes for Malaria Workers." This was so well received that it was revised as "Statistical Methodology in Malaria Work." This was in two parts, yet a further version became necessary—this time called "Statistical Consideration and Methodology in Malaria Eradication."

The present volume is a revision started by Dr. Swaroop, interrupted by his untimely death in 1962, and completed by Dr. Gilroy. The chapters are devoted to: malariometric rates and population indices; collection and classification of statistical data; record cards: their design and uses; diagrams and their uses; the use of sampling in eradication programmes; sample size for field investigations; frequency distributions; the analysis of qualitative data; the analysis of ungrouped quantitative data; the analysis of grouped data; insecticide susceptibility tests; and the quantitative epidemiology of malaria. Annexes give a table of random numbers and tables of various statistical values.

The history and development of this monograph are a testimony to its usefulness and quality. In this increasingly noisy Tower of Babel in the communication of science it is brief, and by dint of careful selection in both inclusion and exclusion complete in itself.

WILLIAM KERSHAW.

Eye Disease

Modern Trends in Ophthalmology—4. Edited by Arnold Sorsby, C.B.E., M.D., F.R.C.S. (Pp. 272+ix; illustrated. £3 10s.) London: Butterworth. 1967.

This is a smaller book than its predecessors, and though published in London and compiled by Arnold Sorsby, emeritus research professor in ophthalmology at the Royal College of Surgeons, is an international product, eight of the authors being American, four British, one German, and one Swiss. It aims not to cover the whole field of ophthalmology or even all the section under discussion but rather to highlight the growing points in which there have been recent developments. The technique and more accurate diagnosis which can result from fluorescein retinal photography and the potential value of ultrasonography are discussed. Recent work on some of the rarer types of glaucoma and on infections, nutritional, and vascular diseases involving the retina and choroid are described, and the final chapters deal with modern methods of treatment of corneal opacities and cataract surgery and contain a concise account of the present methods of replacing detached retina employed at one noted American clinic.

There must be many thousands of ophthalmic surgeons the world over who, under the pressure of heavy work, are unable to keep pace with the exceptionally voluminous literature which pours forth on the eye and its relations with systemic disease, for there is scarcely a part of the body with which ocular disease may not be in some way connected. To these this book, which can be read in a week-end, provides the opportunity of a brief but authoritative home refresher course.

HAROLD RIDLEY.

Symposium on Steroids

Research on Steroids. Transactions of 2nd Meeting of International Study Group for Steroid Hormones. Vol. 2. Edited by Cataldo Cassano. (Pp. 553+xv; illustrated. No price given.) Rome: Il Pensiero Scientifico. 1966.

In recent years an ever-increasing proportion of published work has appeared in book form as the proceedings of an international conference of some highly specialized group of scientists. This has the advantage that a large number of related papers are collected together in the confines of one volume. It also means that many interested specialists who were unable to attend the conference can share in the fruits of the meeting. There are, however, a number of disadvantages and dangers. Work published in this way may not be so generally available as if it had appeared in regular journals. More serious, perhaps, is the criticism that such work is not subjected to the normal editorial process, so that experimental details may be inadequate.

Lack of experimental detail and failure to give adequate references are to be found in some of the contributions to this report of an International Study Group which met in Rome in December 1965. The book is divided into three parts. The first part consists of four lectures and 11 communications on the general subject of "Oestrogens in Pregnancy." The second part contains four lectures and 16 communications on "Methodology in Steroid Estimation." The last part is a round-table conference on "Steroidal Antifertility Agents."

A notable feature of the first section is an excellent review by E. Diczfalusy and G. Benagiano on "Oestriol Metabolism in Mid-pregnancy." This lecture emphasizes the important role of the foetus in the placental synthesis and conjugation of oestriol. Practical applications of these concepts are dealt with by A. Klopper, who describes the value of estimations of urinary oestriol in the assessment of placental function and foetal viability. A number of short communications to this section are also concerned with this subject.

The second section, on methodology, begins with a lecture by E. C. Horning and W. L. Gardiner on the "Estimation of Human Steroids by Gas Liquid Chromatography." Many of the communications in this section describe specific methods for the determination of oestrogens, androgens, or corticosteroids in body fluids. There is also an excellent lecture by R. De Hertogh on "Isotopic Methods in the Study of Steroid Hormone Metabolism in vivo." This reviews the calculation of secretion rates using both urinary and blood methods and also the complications which ensue when there is interconversion of hormones within the body.

The final and largest section of the book contains 30 contributions on steroidal antifertility agents. Most of these papers are followed by some discussion. A number of the earlier contributions, especially those by L. Martini, J. Haller, and E. Diczfalusy, deal with the mechanism of action of antiovulatory steroids. The greatest number of papers report the effects of these steroids on the female genital tract and the menstrual cycle. The remaining papers are concerned with effects on other organs—for example, the adrenal cortex (G. Sala), thyroid (I. De Salcedo), liver (D. Bayot) and on the coagulation of blood (H. L. Krüskemper). The volume is completed by an excellent list of 114 antifertility preparations with structural formulae of their component steroids.

In summary this book is a valuable source of information for anyone concerned with either the biochemistry of steroids or the endocrinology of reproduction.

R. V. BROOKS.

Nurses' Progress

The Lamp and the Book. The Story of the R.C.N. 1916-1966. By Gerald Bowman. (Pp. 206; illustrated. 21s.) London: Queen Anne Press. 1967.

In 1966 the Royal College of Nursing celebrated its jubilee. To commemorate this its history has now been published, the College retaining the copyright. The writing of it was entrusted not to a nurse but to an author of distinction, who received help and assistance from members and the staff of the College.

The College is concerned with promoting the science and art of nursing, looks after the interests of nurses, holds educational courses, and grants certificates. Since 1916 more than 120,000 nurses have been admitted to its membership.

Florence Nightingale made nursing a profession; and Dame Alicia Lloyd Still, successively matron of Brompton Hospital, the Middlesex Hospital, and St. Thomas's Hospital, a woman of outstanding administrative ability, sympathy, and knowledge, continued her noble work. Dame Alicia had also a large share in the founding of the College. Other founders recorded here were: Miss Cox-Davies, matron of the Royal Free Hospital, who persuaded Lady Cowdray to give the College its present building in Henrietta Place, Cavendish Square, at the cost of some half-million pounds; Dame Sarah Swift, matron-in-chief of the British Red Cross; Sir Arthur Stanley, treasurer of St. Thomas's Hospital; Sir Cooper Perry, consulting physician to Guy's Hospital; and Sir Comyns Berkeley, consulting obstetrician to the Middlesex Hospital.

Mr. Bowman also gives an account of the general progress of nursing in the nineteenth and present centuries, including State registration of nurses; the General Nursing Council; nursing legislation; and the Athlone, Horder, and Rushcliffe Committees, sponsored by the Ministry of Health. Possibly, through exigencies of space, his account of the Government's preparations for nursing in wartime is a little incomplete; and, while paying due tribute to Mrs. Bedford Fenwick's zeal and work for nurses, he dwells at too great length on the defects of her qualities. These are minor criticisms of an excellent book, which deserves many readers.

ARTHUR S. MACNALTY.

Books Received

Review is not precluded by notice here of books recently received.

Emergencies in Medical Practice. 8th edition. Edited by C. Allan Birch, M.D., F.R.C.P. (Pp. 852+xvi; illustrated. 60s.) Edinburgh and London: E. & S. Livingstone. 1967.

Nursing Emergencies. By P. S. London, M.B.E., F.R.C.S. Foreword by Mary Powell, S.R.N., M.C.S.P. (Pp. 262+x; illustrated. 30s.) Oxford: Blackwell. 1967.

Transactions of the International Chest and Heart Conference. Eastbourne, 1967. (Pp. 219 + Supplement 202 pp. £2 2s.) London: Chest and Heart Association. 1967.

Studies of Rheumatoid Disease. Proceedings of 3rd Canadian Conference on Research in the Rheumatic Diseases. Toronto, 1965. (Pp. 322+xi; illustrated. £7.) Toronto: University Press. London: Oxford University Press. 1967.

Radiobiological Factors in Manned Space Flight. Edited by Wright H. Langham. (Pp. 274+xvii. $7.50.) Washington: National Academy of Sciences–National Research Council. 1967.

Symposium on Shock. Report of the Proceedings held in Dublin, 1966. Edited by Professor Patrick FitzGerald, M.Sc., M.D., M.Ch., F.R.C.S.I. (Pp. 71. No price given.) Uppsala, Sweden: Pharmacia International. 1967.

Replacement of Renal Function. Proceedings of the European Dialysis and Transplant Association. 1966. Vol. 3. Edited by David N. S. Kerr. (Pp. 400+xxiii; illustrated. £7 10s. 9d.) Amsterdam: Excerpta Medica. 1967.

Danni da Sport Agonistico nell'Età Evolutiva. By Professor Enrico Tatafiore. (Pp. 93. No price given.) Naples: Ospedale "Santobono." 1967.

Reading and Health. Papers given at the Hospital Libraries and Handicapped Readers Group Conference. (Pp. 51. 12s. 6d.) London: The Hospital Libraries and Handicapped Readers Group, Library Association. 1967.

A Surgeon's Guide to Cardiac Diagnosis. Part 2. The Clinical Picture. By Donald N. Ross, B.Sc., M.B., Ch.B., F.R.C.S. (Pp. 88+viii; illustrated. $6.00.) Berlin, Heidelberg, and New York: Springer. 1967.

Practical Cytology. By R. G. W. Taylor. (Pp. 148+xi; illustrated. 39s. 6d.) London: Academic Press. 1967.

Ultrastructure of the Kidney. Ultrastructure in Biological Systems. Vol. 2. Edited by Albert J. Dalton and Françoise Haguenau. (Pp. 240 +x; illustrated. £5 12s.) London and New York: Academic Press. 1967.

Mathematical Challenges to the Neo-Darwinian Interpretation of Evolution. Wistar Institute Symposium Monograph No. 5. Edited by Paul S. Moorhead and Martin M. Kaplan. (Pp. 140 +xi. $5.00.) Philadelphia: Wistar Institute of Anatomy and Biology. 1967.

Obstetrics and Gynaecology in the Tropics and Developing Countries. By J. B. Lawson, M.A., M.B., B.Chir., F.R.C.O.G., and D. B. Stewart, M.B.E., B.Sc., M.D., F.R.C.S.(C.), F.R.C.O.G. (Pp. 630; illustrated. £8.) London: Edward Arnold. 1967.

Lipid Metabolism in Tissue Culture Cells. Symposium held at the Wistar Institute of Anatomy and Biology. Edited by George H. Rothblat and David Kritchevsky. (Pp. 164+vii; illustrated. $5.00.) Philadelphia: Wistar Institute. 1967.

Through Youth to Age. Proceedings of the Fourth International Congress of the World Federation of Occupational Therapists, London. Edited by R. L. Kleinman. (Pp. 431; illustrated. $15.60.) Amsterdam: Excerpta Medica. 1967.

The Connective Tissue. International Academy of Pathology Monograph. By 30 authors. Edited by Bernard M. Wagner, M.D., and David E. Smith, M.D. (Pp. 408+xi; illustrated. £7.) Edinburgh and London: E. & S. Livingstone. 1967.

Scientiae Pharmaceuticae. Vol. 1—Symposium: Cardioglucosides. Vol. 2—Symposium: Identification of Drugs. Edited by Dr. Oldrich Hanc and Dr. Josef Hubik. (Pp. 496+xiii. Pp. 639 +ix; illustrated. £10 10s. per set of two volumes.) London: Butterworth. 1967.

Pathology. 3rd edition. By Stanley L. Robbins, M.D. (Pp. 1434+x+xxvi; illustrated. £7 3s. 6d. Two-volume set £8 15s. 6d.) London: W. B. Saunders. 1967.

Manual of Preoperative and Postoperative Care. By the Committee on Pre- and Post-operative Care, American College of Surgeons. Editorial Subcommittee: Henry T. Randall, M.D., James D. Hardy, M.D., and Francis D. Moore, M.D. (Pp. 506+xiv; illustrated. £2 19s. 6d.) London: W. B. Saunders. 1967.

Novak's Gynecologic and Obstetric Pathology. With Clinical and Endocrine Relations. 6th edition. By Edmund R. Novak, A.B., M.D., and J. Donald Woodruff, B.S., M.D. (Pp. 696 +xvi; illustrated. £7.) London: W. B. Saunders. 1967.

Radiation Therapy. 2nd edition. By Walter T. Murphy, M.D. (Pp. 1030+xiii; illustrated. £15 15s.) London: W. B. Saunders. 1967.

Structure of the Human Body. By Weston D. Gardner, M.D., and William A. Osburn, M.M.A. (Pp. 417+xiii; illustrated. £3 1s.) London: W. B. Saunders. 1967.

Grundprobleme der neuen Hämodynamik und Therapeutische Konsequenzen. Edited by Professor P. Volger and Dr. J. C. Cordes. (Pp. 260; illustrated. £1 11s. 8d.) Leipzig: Georg Thieme. 1967.

Portraits from a Shooting Gallery. Life Styles from the Drug Addict World. By Seymour Fiddle. (Pp. 360+xvii. 60s.) New York: Harper & Row. 1967.

Biology in Action. By N. J. Berrill, F.R.S. (Pp. 878+xvi; illustrated. 50s.) London: Heinemann. 1967.

The Thin Book by a Formerly Fat Psychiatrist. By Theodore Isaac Rubin. (Pp. 112+viii. 18s.) London: Heinemann. 1967.

Textbook of Organic Medicinal and Pharmaceutical Chemistry. 5th edition. Edited by Charles O. Wilson, Ph.D., Ole Gisvold, Ph.D., and Robert F. Doerge, Ph.D. (Pp. 956+xviii. £6 10s.) London: Pitman. 1967.

Clinical Orthopaedics and Related Research. Vol. 48. Edited by Marshall R. Urist. (Pp. 306 +ix; illustrated. 60s.) London: Pitman. 1967.

The Basal Ganglia and Posture. By James Purdon Martin, M.A., M.D., F.R.C.P. (Pp. 152 +xiii; illustrated. 80s.) London: Pitman. 1967.

The Gross Anatomy of the Human Brain. A Manual of Dissection. (By W. Hewitt, M.B., B.S. (Pp. 170; illustrated. 30s.) London: Pitman. 1967.

A New Look at Industrial Medicine. By Ray L. Luffingham, M.B., B.S., D.I.H. (Pp. 103. 12s. 6d.) London: Pitman. 1967.

A Clinical Study of Intestinal Bilharziasis (Schistosoma mansoni) in Africa. By Michael Gelfand. (Pp. 230+x; illustrated. 65s.) London: Edward Arnold. 1967.

Hypertension. Vol. 15. Proceedings of the Council for High Blood Pressure Research, Cleveland, 1966. Edited by J. Edwin Wood, M.D. (Pp. 226; $2.50.) New York: American Heart Association. 1967.

The Year Book of Dentistry. 1966–1967. Edited by Morton Amsterdam, B.A., D.D.S., *et al.* (Pp. 480; illustrated. 60s.) London: Lloyd-Luke. 1967.

Advances in Gerontological Research. Vol. 2. Edited by Bernard L. Strehler. (Pp. 431+xi; illustrated. £7 8s.) New York and London: Academic Press. 1967.

Current Perspectives in Gastroenterology. Edited by William S. Blakemore, M.D., and L. Kraeer Ferguson, M.D. (Pp. 319+xiv; illustrated. £5 8s.) New York: Harper & Row. 1967.

Middle Articles

Collection of Unwanted Drugs from Private Homes

W. A. NICHOLSON,* M.D.

Brit. med. J., 1967, 3, 730–731

It is not uncommon to find that the unused portions of medicines and tablets prescribed are left on shelves in private houses long after the need for them has ended. It was suspected that this stock might be quite large, and in March 1967 a week's collection was arranged in the Hartlepools, designed to fit in with the normal period of spring cleaning. The then West Hartlepool† Health Department provided posters to be displayed in their departments, the local pharmacies, doctors' waiting-rooms, and the local hospitals. The pharmacists agreed to act as collecting-points from which the Health Department brought the results to the General Hospital, West Hartlepool.† for counting and identification. The collection went on from 13 to 18 March. Considerable local publicity was given by the press and television services. The numbers collected are shown in Table I.

TABLE I

Tablets and capsules ..	43,554	Ear-drops (bottles)	13
Ampoules	194	Nasal drops (bottles)	17
Bottles of medicine ..	83	Lozenges	131
Liniments	16	Powders and cachets	123
Ointments and lotions ..	56	Pessaries and suppositories ..	178
Eye-drops and ointments ..	17	Miscellaneous	46

The number of separate items was 1,395.

TABLE II.—*Tablets, Capsules, and Ampoules Identified*

	Tablets and Capsules	Ampoules
Antacids	755	
Gastric sedatives and antispasmodics	2.679	
Laxatives	1,331	
Anticoagulants	39	1
Cardiac and cardiovascular reactants	1,674	2
Vasoconstrictors	871	
Antimigraine agents	146	
Analgesics	4,571	
Anti-inflammatory agents	392	1
Hypnotics	2,179	
Anticonvulsants	303	
Sedatives and tranquillizers	4,719	11
Thymoleptics	423	
M.A.O. inhibitors	338	
C.N.S stimulants	552	
Antihistamines	648	1
Antiemetics	341	
Muscle relaxants	221	8
Endocrines	1,615	30
Hypoglycaemics	188	
Urinary antiseptics	361	
Diuretics	1,192	38
Antibiotics	1,523	41
Sulphonamides	587	4
Antituberculosis agents	418	
Antiamoebics, antileprotics, and antitrichomonal agents	266	
Antianaemic agents	2,689	45
Vitamin and mineral additions	1,510	6
Anabolics	235	
Carcinochemotherapeutic agents	107	
Cough suppressants and bronchial spasm relaxants	2,197	2
Antiobesity agents	541	
Miscellaneous	631	4
Total	36,242	194

62 packets of Inpasade were also handed in.

Tablets were identified by determining their diameter by passing them through slots ranging from 5/32 to 22/32 in. (4 to 17.5 mm.) in a specially made steel disc. The references used in identification were: (1) *The Chemist and Druggist* tablet and capsule identification guide; (2) *Medindex*; (3) the punch-card system devised by Mr. C. M. McArdle, chief pharmacist at Birmingham General Hospital; (4) information provided in the literature of some drug firms.

The general findings are shown in Table II and details of some of these are given in Table III.

TABLE III.—*Numbers of Tablets Over* 200 *in Certain Sections of Table II*

Gastric sedatives and antispasmodics:	
Tabs Bellergal	870
„ Nacton	276
„ Paminal	296
Cardiac and cardiovascular reactants:	
Tabs digitalis folia	243
„ Praenitrona	233
„ Peritrate	203
Analgesics	
Tabs Panadeine	259
„ Panadol	216
„ pethidine	628
„ Tanderil	636
Hypnotics, tranquillizers, etc.:	
Caps Sodium Amytal	234
Tabs Seconal	559
„ Soneryl	213
„ Insidon	268
„ Largactil	1,336
Caps Librium	885
Tabs Mornidine	417
„ Stemetil	284
„ Taractan	242
„ Valium	405
„ Tofranil	295
„ Niamid	270
Antihistamines:	
Tabs Phenergan	239
Diuretics:	
Tabs Hydrosaluric	253
„ Hydrosaluric-K	432
„ Lasix	374
Antibiotics:	
Caps Achromycin	249
„ Chloromycetin	396
Sulphonamides:	
Sulphamethazine	253
Antituberculosis agents:	
Tabs isoniazid	393
Antianaemic agents:	
Tabs Ferraplex	238
„ Fersamal	545
„ Sidros	376
Anabolics:	
Tabs Anabolex	212
Cough suppressants, etc.:	
Tabs asthmaco	442
„ Brovonite	502
„ Cardophylin	324
Antiobesity agents:	
Duromine	219
Miscellaneous:	
Penicillamine	200

It was not possible to state accurately the number of households involved, but it is thought to be no more than 500. There are about 30,000 households in the area, with a population of 100,000. If the same pattern obtained in the remaining households we might have collected over 2,500,000 tablets and capsules. The identified finds were priced roughly on the basis of N.H.S. costs per 100, and a cost of £220 was obtained. Given a total clear-out for the area, this would represent about £13,200. On a United Kingdom basis the numbers and cost would be staggering.

Some of the "hoards" were probably "left-overs" from houses where there had been a death. The biggest hoard was 1,200 tablets from a house where an elderly woman had died just before the collection started. It included Guy's pills 179, Blaud's pills 85, calomel 1 gr. (65 mg.) 78, calomel ½ gr. (32 mg.) 85, Bellergal 234, various analgesics, laxatives, and a tin of rat poison; it seemed to represent a lifetime of discarded treatment. The hoards of pethidine were no doubt left-overs from deaths from cancer. But doctors cannot be acquitted of some overprescribing. The pethidine hoards were 10 in number, and two contained over 100. There were other large single hoards—Largactil 576, Seconal 209, Librium 170, Monidine 302, Valium 159, Chloromycetin 300, Fersamal 261, Lasix 190. Against the accusation of overprescribing, it must be remembered that a patient may be given a course of treatment and the treatment may be changed, or the patient comes into hospital or dies or may decide not to continue the treatment. The remnants of the prescription usually then go on to a shelf in case they may be needed again. In time the original use is forgotten or the drugs may cease to be effective. They may be offered to relatives or friends on the basis of "these did me good, they may help you." I have seen a case of glaucoma precipitated by the misuse of an atropine-containing ointment, and combinations of tablets can be very dangerous. There is the risk of distraught persons taking any tablets available in an act of self-poisoning. In 1965 a man was admitted here with thalidomide poisoning. If the patient had been a pregnant woman the results would have been disastrous. Also there is the risk to children, for drugs in homes are seldom properly guarded and so many tablets look like sweets.

---

* Consultant Physician, the General Hospital, Hartlepool.

† The County Borough of West Hartlepool and the Borough of Hartlepool amalgamated on 1 April 1967 to form the County Borough of Hartlepool.

It is difficult to know how to deal with the situation. Established hypochromic anaemia may need several months' treatment with iron. Patients with depression may need a long course of antidepressive drugs. Nevertheless, the patient will have to be seen at intervals to check progress, and the prescriptions should cover no more than these intervals. Patients should be encouraged to hand to their doctors or pharmacists all the unused portions of prescriptions, and when there is a death all the drugs left over should be handed in. It would help if doctors would ask for this to be done. Similarly, hospitals could help where death has occurred in hospital by offering to dispose of drugs still at home.

The National Health Service is not likely to benefit financially by the handing back of unused drugs. Apart from administrative difficulties it would hardly be possible to make use of them again, in view of the limited shelf life of many. Some waste is inevitable under any form of service, private or public. There are a large number of drugs marketed with only minor variations. Selling pressure causes them to be prescribed, and for a short time there are runs on this or that drug. If demand fails they may be left on the hands of the retail pharmacist. One pharmacist handed in for disposal 6,328 tablets and capsules, out-of-date stock (these are not included in the collection described above). In few homes are there not bits of this and that put aside in case they might be useful at some time, and the dustbins proclaim the great quantity of waste food from plates and left-overs. But if unwanted drugs were handed in there would not be this frightening load of poisons lying on the shelves.

Summary

A collection of unwanted drugs was made in the Hartlepools area from 13 to 18 March. A total of 43,554 tablets and capsules were handed in, of which 36,242 were identified.

The counting and identification were done mainly by Miss E. Irvine. I should like to thank Dr. H. C. Milligan, Medical Officer of Health for Hartlepool, his staff, the local pharmacists, and the press and T.V. services for their help in the collection. I should like to thank Mr. W. Ryder, hospital group engineer, and his staff for their help in designing and cutting the prototype disc; the pharmacists and pharmaceutical firms for assistance in identification; and the Hartlepool Hospitals Management Committee for the use of a room for counting and identification.

This work was supported by a grant from the Newcastle Regional Hospital Board, which is gratefully acknowledged.

NEW APPLIANCES

Roto-rest

Dr. F. X. KEANE, of the National Medical Rehabilitation Centre, Dun Laoghaire, County Dublin, Eire, writes: The Roto-rest has been designed to introduce automation into the nursing of severely disabled patients. It makes improved nursing care possible which hitherto was not practical or economical, and facilitates medical examination and specific therapy of these patients. This bed is primarily intended for use in the treatment of spinal injuries, with or without the complication of paraplegia or quadriplegia, and also for head injuries and orthopaedic cases. It may also be used to great advantage for the chronic patient at home.

The standard Roto-rest is remarkably simple in construction, and is no longer than the standard hospital bed fitted with skull-traction equipment; it is 3 ft. (91 cm.) overall in width and 8 ft. (244 cm.) in length. In the horizontal position the patient is at a convenient height, being 41 in. (104 cm.) above floor level. This size of bed will take a patient varying in stature from 4 ft. 10 in. to 6 ft. 3 in. (147 to 190 cm.), including the distance required to accommodate conventional skull-traction tongs and special traction assembly.

The bed consists basically of three parts. A ground frame with four braked 6 in. (15 cm.) castors. This frame has two upright pillars on which a U frame rocks longitudinally to provide varying degrees of head and foot inclination. The foot of the U frame may be clamped in bearings on the ground frame at the foot end, and by activating a jack, mounted between the ground frame and this U frame, the U frame may be raised so that the patient can be put in a standing position if desired. The bed proper is pivoted at either end in the U frame, so that rotation about the longitudinal axis is achieved (Figs. 1–3).

The surface of the bed is divided into hatches which may be opened independently. These are situated under the patient's legs, arms, and centrally under his head and neck, thorax, and buttocks. The hatch situated in the thoracic region carries a spring steel section which permits adjustment, so that the lumbar and thoracic spine may be supported or extended at any position along its length (Fig. 4). In place of a conventional mattress plastic-covered removable foam-plastic sections are used. Upright removable members are fitted which extend from the axilla to the foot of the bed, and may be contoured to the individual patient by the surgeon to afford lateral support. Adjustable head, shoulder, knee, and foot supports are also provided. Skull traction is available, from 0 to 56 lb. (25.4 kg.), by a constant-tension spring system, which is concealed within a frame member of the bed. Conventional bedclothes are dispensed with, and an air blower in the foot of the bed may be provided.

The patient is placed on the bed, all parts of which can be adjusted to the surgeon's satisfaction. This usually takes about five to ten minutes. The patient never again has to be manually lifted for the full duration of his treatment. Nursing care may be carried out by one person alone through the

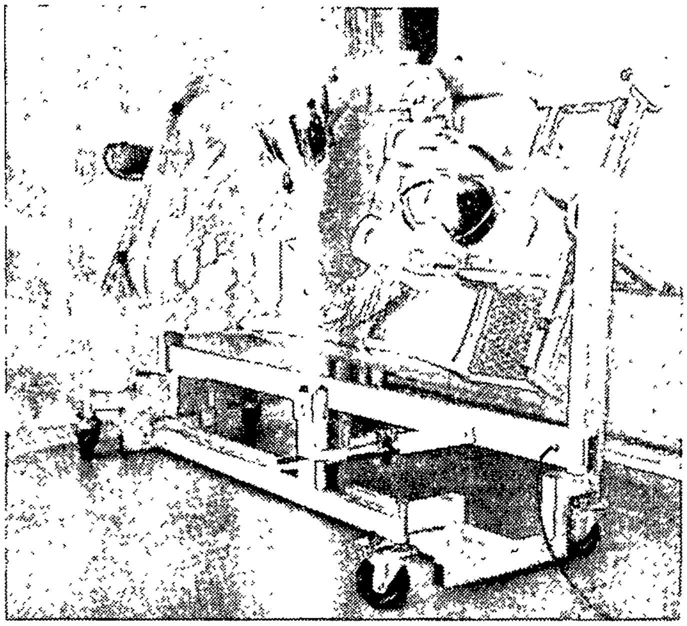


FIG. 1

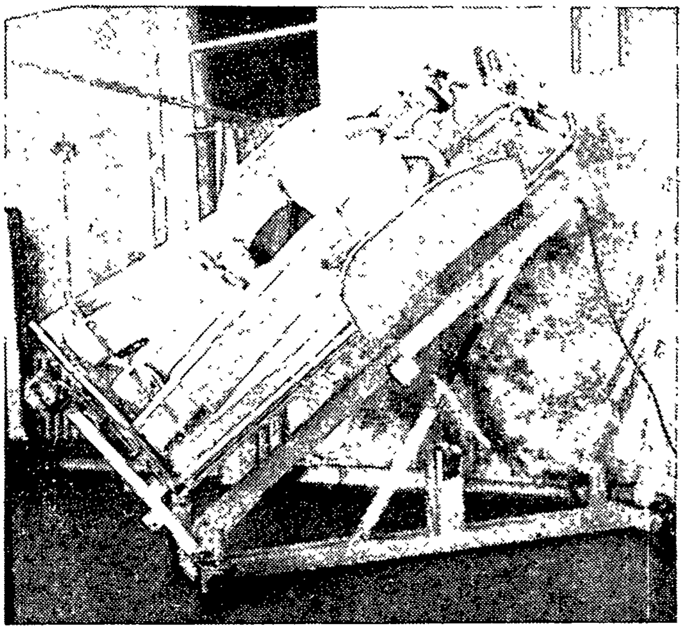


FIG. 3

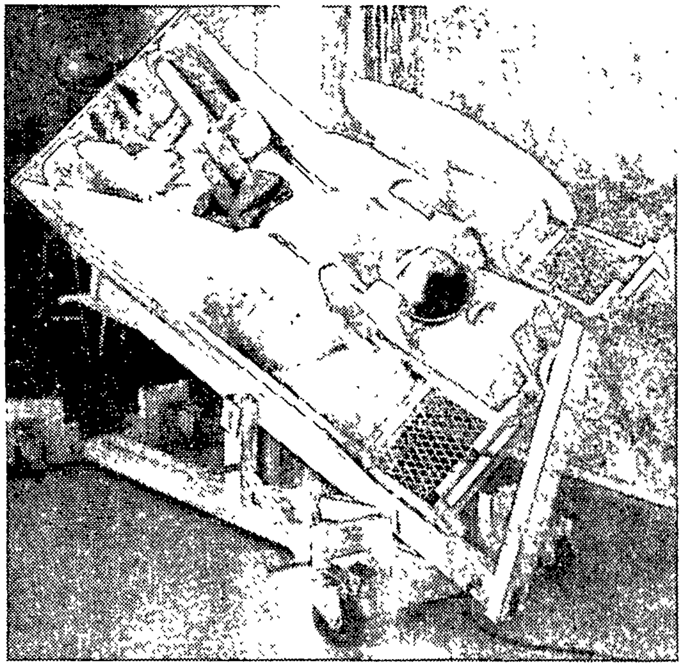


FIG. 2

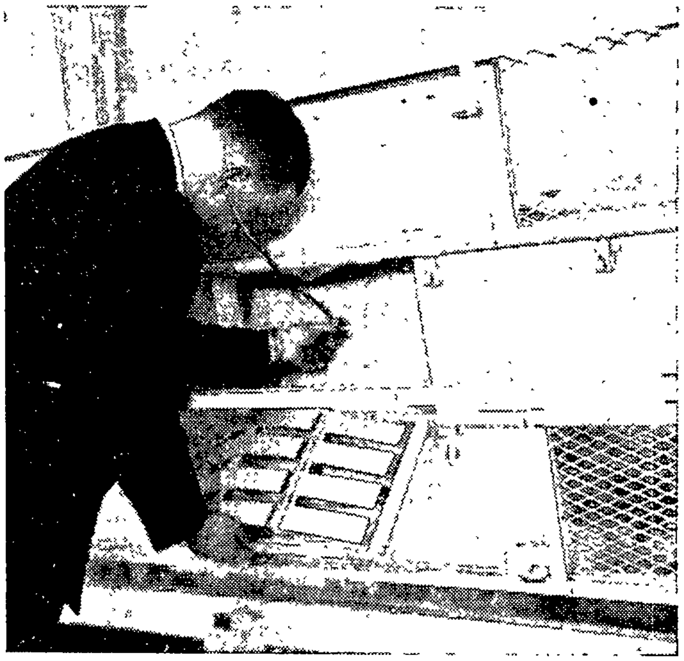


FIG. 4

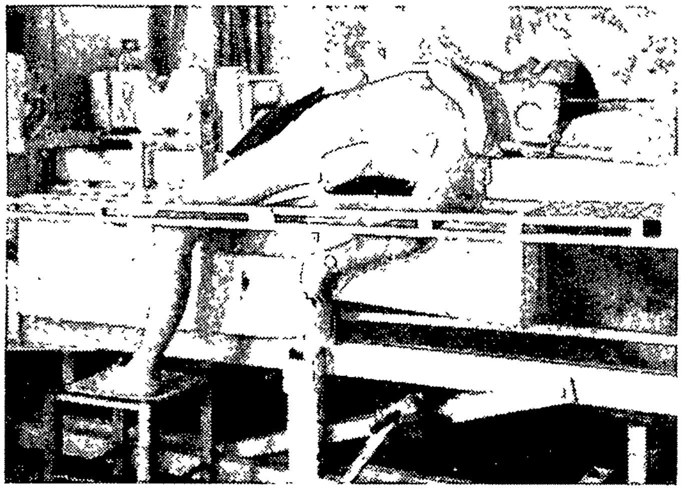


FIG. 5

FIG. 1.—The patient is capable of moving his arms freely to hold a book, etc., while the bed is on the automatic turning control.

FIG. 2.—Elevation of foot of bed, showing positioning of patient.

FIG. 3.—Bed elevated to about 45 degrees.

FIG. 4.—Accessibility to patient's thorax, etc., through back of bed.

FIG. 5.—How extension of hip and shoulder is achieved.

hatch system and removable sections of the bed. The functions of the bed are described below in order of their importance:

(1) *Automatic Turning of the Patient.*—The bed may be programmed to carry out turning of the patient through a preselected number of degrees up to 160 as a continuous motion or executing one turn at 10-, 15-, or 30-minute intervals. The optimum speed of rotation has been established at 35 degrees a minute. In the event of electrical failure the patient may be turned by one person without effort through 160 degrees in six seconds. The patient may turn himself through any desired number of degrees and stop the bed in a required position by a press-button provided for his use, and may switch on to "auto control" for hours of sleep. In the event of electrical failure the patient, if he has the use of his arms, may turn the bed manually himself.

(2) Correct alignment of the spinal column and continuous skull traction are provided at all times for the full duration of treatment, even when the bed is working on the auto control.

(3) A continuous venous blood flow, particularly in the lower limbs, is maintained to avoid the complication of venous thrombosis.

(4) A full range of joint movements of the upper and lower limbs can be achieved by the physiotherapist with the patient in the horizontal recumbent position by the use of the hatches, which means that she does not have to turn the patient to complete a full treatment, and gravity may be used to assist in achieving extension of the hip joint (Fig. 5).

(5) The placing of a patient with head or foot raised through 15 degrees is carried out by activating the jack.

(6) The patient may be placed in a standing posture for re-education of the vascular system at 80 degrees with the horizontal, and when in this position his weight is taken on the foot supports.

(7) The Roto-rest may continue to execute automatic turns, and traction may be maintained while operations 4 and 5 are executed.

(8) Toilet care is carried out through the rectal hatch, and continuous catheter drainage, or the use of the Urovac, is facilitated through an opening in the hatch. Reflux of urine into the bladder is discouraged owing to the position of the drainage tube and urine container when the full container is being replaced.

(9) Conventional bedclothes are not used, and the bed is washed and dried at the same time as the patient's bathing is carried out. This avoids all laundry expense and bedmaking, and tends towards better hygiene in the ward. Disposable paper sheets are placed only under the patient's head, thorax, and buttocks without manual movement of him, as all areas of the body are easily accessible for this purpose. Conventional bedclothes may be used as a top cover if desired, and if so are held by clips.

(10) The patient is retained in the bed by the removable shoulder and knee clamps only, thus avoiding any embarrassment of respiration. These clamps also serve to maintain proper posture of the lower limbs and control involuntary spastic movements.

(11) The clamps prevent a confused or agitated patient injuring himself by movement or climbing, or by falling out of bed.

(12) A patient, while secure in bed, is able to move his hands and arms freely to feed himself, read, etc., but owing to the design of the shoulder clamps he cannot interfere with the head-traction assembly.

(13) While the patient has a desirable freedom of movement of his upper limbs, he is prevented from reaching and removing his catheter, if one is in situ, owing to the height of the side-supporting members.

(14) Ventilation of the skin is achieved as the bed is usually turning in continuous motion, thus avoiding constant skin contact with the weight-bearing surfaces.

(15) Control of the patient's temperature is possible by a variable-speed air blower situated in the foot of the bed. As the patient turns, practically all areas of his body become exposed to the air-flow which it produces, thus avoiding the use of hypothermic drugs, ice drips, etc.

(16) Continuous intravenous infusion is more easily maintained, because accidents caused by handling of the patient for turning are obviated, and the tendency to thrombosis in the veins is reduced.

(17) A red warning light indicates to the nursing staff that the bed is in motion. If this light is not visible the cause must be investigated. If desired, a no-volt alarm may be fitted which will alert the staff or awaken the patient if an electrical failure results; this is important, particularly where the bed is intended for home use.

(18) Variable abduction of the patient's legs is possible to enhance the venous return when rotating, as each leg is alternately elevated and depressed.

(19) Facility for positioning *x*-ray plates is incorporated so that films may be taken in any posture of the head, neck, and trunk without lifting the patient.

(20) Spring leg traction may be fitted up for treatment of fractures of lower limbs.

ADVANTAGES FOUND ON CLINICAL TRIAL

The medical officer's time is saved, as any part of the patient's body is immediately accessible for examination and treatment. The physiotherapist can carry out a full range of joint movement of the limbs while the patient is in the recumbent position, and can make use of gravity to effect extension of the hip joints. Patients can be put in any posture for chest physiotherapy, etc. Nursing is reduced to bed-bathing, toilet care, and administering drugs. Bed-making is not required. Bedsores do not occur.

Venous thrombosis in the lower limbs has not occurred in any patient nursed in the bed so far. Flexion contractures from spasticity are prevented. Clinical trial has shown that practical immobilization of spinal fracture is achieved and correct alignment traction is possible during continuous automatic turning. Marked relief of pain at fracture site has been observed. Chest complications in susceptible patients have not appeared, and patients who already have contracted chest infections improved rapidly when put on the bed. This is an outstanding advantage to paraplegics and quadriplegics, who may suffer greatly from respiratory embarrassment.

It has been noted, when carrying out intermittent catheterization, that sediment has not been allowed to form, or, if so, is minimal. Prolonged intravenous infusion has been easier to maintain, as clotting tendency and accidents are reduced. Urinary reflux cannot occur, as the orderly cannot lift the bottle higher than the patient because the drainage tube comes out through the hatch under the middle of the bed, and not over the side, which is the case in standard practice. It has been noted in some patients that constipation and nausea have set in when they were transferred to conventional beds. Noise in the ward at night-time caused by personnel is eliminated, and the patients may have an undisturbed night's rest.

At a turning speed of 35 degrees a minute the patient is unaware of the turning motion, and yet it is fast enough to ensure adequate blood flow in the limbs. Another minor advantage is that the patient does not suffer from sore ears, which may be a problem on conventional beds. He also has a changing field of vision as he turns. Embarrassment to him is avoided when having to use a bed-pan, as stripping of the bed is not required. There is a possibility that with this bed a device could be used to handle faecal incontinence; this is under consideration.

FINANCIAL ASPECT

The use of the bed has reduced the doctor's, physiotherapist's, and nurse's time considerably in carrying out their treatments. It takes 35 minutes for one nurse to wash and dry the patient and bed, which is carried out once in 24 hours. Apart from this the nurse has to attend only to the administration of drugs and toilet care. No bed-making is necessary. Orderlies for turning and lifting the patients are entirely dispensed with during treatment. Since virtually no laundry is required, each bed has represented a saving of 42s. a week in this respect. Cost of drugs is also reduced owing to the reduction in chest complications. The bed is powered by a single one-tenth h.p. motor. The cost of running the motor is equivalent to that of a 50-watt bulb. The bed is extremely robust in construction and requires no maintenance. Independent sections replace the normal mattress; therefore at the most only the three sections under the patient's trunk may require replacement at intervals of about two years, which is an extra saving.

Proposed Legislation on Drugs

Last week the Government issued a White Paper (Cmnd. 3395, H.M.S.O., London, 1s. 9d.) on forthcoming legislation on the safety, quality, and description of drugs and medicines. A summary of the proposals is printed below. (See leader p. 689).

Reasons for Legislation

The White Paper reviews the action taken by the Government in 1962 as a result of the disquiet caused by the teratogenetic actions of thalidomide. A committee under the chairmanship of Lord Cohen of Birkenhead recommended that legislation on the safety and efficacy of drugs was urgently required and that meantime a voluntary system should be set up to screen drugs for toxicity and adverse reactions. This led to the appointment of the Committee on Safety of Drugs under the chairmanship of Sir Derrick Dunlop.

The Paper goes on, "The voluntary system has had the full support of the pharmaceutical industry and the medical and pharmaceutical professions, but the Government considers that the provision of statutory backing for these safeguards would give greater reassurance and should not be further delayed," and draws attention to the recommendation made by the Committee on Safety of Drugs in 1965 that its arrangements should be made permanent by legislation.

The Paper points out that controls similar to those which it proposes have already been introduced in Commonwealth countries, the U.S.A., and elsewhere, and that in the event of Britain joining the European Economic Community legislation of this kind may become necessary.

The responsibility for the proposed controls will lie with the Health and Agriculture Ministers of the United Kingdom. The Home Office will no longer be concerned with medicinal aspects of substances in the poisons lists.

Medicines Commission

A commission, known as the Medicines Commission, is to be appointed by the Ministers after consultation with professional bodies representing medicine, dentistry, and veterinary surgery. The Commission will advise the Ministers on matters of policy and make recommendations about the terms of reference of expert committees. The Commission will also act as an appeal body for applicants for licences (see below).

The Commission will take over from the General Medical Council the responsibility for the production of the *British Pharmacopoeia*. It will not deal with non-medical aspects of substances controlled as poisons.

The new measures will control drugs and preparations for use in diagnosis, treatment, and prevention of ailments in men and animals, or in modifying physiological functions.

They will also control medical devices having a mechanical or physical action, including shunts, valves, pacemakers, syringes, catheters, and dressings.

The controls will not automatically apply to substances marketed for non-medical use, such as cosmetics or disinfectants; but the Ministers will have power to list substances of this kind as subject to control.

Licensing

A licence, for which there will be a fee, will be required for the marketing, importation, or manufacture of or wholesale dealing in drugs, with appropriate requirements for each activity, and in the case of sale or supply for the purpose of clinical or field trial a certificate or some similar form of authority will be required, in order to ensure that appropriate toxicity testing has taken place before the trial begins.

A manufacturing licence will, however, not be required by a doctor or dentist to make up a preparation for one of his patients.

The particulars to be supplied to the licensing authority in support of applications for marketing and importing licences, or for clinical or field trial certificates, are expected to be on the lines of those now requested by the Committee on Safety of Drugs. Conditions of manufacture, storage, and distribution will also be considered. Temporary provision will be made for existing drugs to be marketed without licence until they can be brought into the scheme.

A licence may be refused, revoked, or suspended if the Minister is advised by the Commission or the appropriate expert committee that the drug no longer conforms with the requirements for safety or efficacy imposed at the time that the licence was given. Provision is made for appeal to the Commission against revocation of a licence or refusal to grant one. There is also a right to be heard by the licensing authority and to appeal to the High Court on a point of law.

Retail sale of drugs to the public will, with some exceptions, be limited to registered pharmacies. The exceptions will permit prepacked drugs for human use listed by the Ministers for general sale to be sold at any shop. Doctors and dentists will be able to sell or supply drugs to their patients or to a person having the care of such patients.

Labelling and Advertising

The sale, supply, or possession of any drug (including samples) bearing a label which falsely describes the drug or is likely to mislead as to its nature, substance, quality, effects, or the purposes for which it is intended to be used or ought not to be used will be prohibited. Similar provisions will apply to any leaflet intended to accompany a drug.

The publication, or display by any means, including radio or television, of advertisements which falsely describe a drug or are likely to mislead will be prohibited.

The Ministers will be able to make regulations specifying drugs or classes of drugs all advertising of which will (subject to stated exceptions) be prohibited.

Requirements could also be made, the Paper states, with respect to the content, format, and manner of presentation of advertisements for drugs, to ensure that those to whom the advertisement is directed are given adequate information about the drug.

Before a drug is promoted to a doctor, dentist, or veterinarian by direct mailing or by medical representatives he must be provided by the promoter within a specified period beforehand with an objective summary, probably in the form of a standard size of data sheet, of essential reference particulars about the drug conforming to provisions in the licence, and the promotional matter will have to be consistent with these.

Consultation

The Paper concludes by stating that before making regulations (other than those broadly reproducing existing regulations) the Ministers will be obliged to consult such organizations as appear to them appropriate as being representative of the interests substantially affected, and that it is the Government's expectation, judging by the general tenor of the observations received on the earlier proposals, that legislation on the lines now to be introduced will command widespread support.

Correspondence

Letters to the Editor should not exceed 500 words.

Consultants' Views of General Practitioners

Sir,—Mr. Cecil W. Flemming writes (26 August, p. 561) that my statement in a General Medical Services Committee debate "Teaching hospital consultants saw only the worst side of general practice; they did not see the successes" (*Supplement*, 12 August, p. 115) is in his experience complete nonsense. In his experience no doubt it was so, but perhaps my words could be described as an overstatement provoked in the heat of debate by an exposition of the consultants' case against some general practitioners. The most provoking sentence was "there were many general practitioners who were only too delighted to dump the whole of their work on to the hospital service."

Sadly there seems to be a great lack of contact and understanding between general practitioners and consultants in these days. Pre-war, I am told, most consultants became so after a spell in general practice and continued their contacts with general practitioners in consultations. Consequently, each group understood each other's problems and had respect for one another. Nowadays the vast majority of consultants have done no general practice in the Health Service and apart from domiciliary consultations have very little contact with those who give primary medical care.

Part of the trouble arises, as I tried to say in the debate, from the fact that in hospital outpatients in general and in medical outpatients in particular general practitioners' mistakes are likely to stick out like sore thumbs. Those patients whose problems have been fully coped with by the family doctor will never reach outpatients and the consultant is never aware of them. As a result of seeing an unbalanced picture he may well tend to be critical of general practice in his dealings with his juniors. As was said earlier in the same debate "students were getting the 'vitriolic drip, drip' from consultants who continually drew attention to what was wrong with general practice."

Measures are needed to resolve these misunderstandings. Perhaps the most effective would be to make a period of general practice compulsory for all doctors and for refresher courses to take place at regular intervals.—I am, etc.,

B. D. Morgan Williams.

Claverdon, Warwick.

Sir,—Mr. Cecil W. Flemming (26 August, p. 561) describes as nonsense the remark of Dr. B. D. Morgan Williams to the effect that "teaching-hospital consultants saw only the worst side of general practice; they did not see the successes." Perhaps the remark would be more literally true if the words "comment on" were substituted for "saw" and "see." Mr. Flemming thinks the remark is to be deplored, but, as reported, it seems to me pretty harmless. However, if he wants a remark to which the term deplorable is flattering, he should look up again the same *Supplement* (12 August, p. 114), where Dr. H. Glyn Jones is reported to have said that "there were many general practitioners who were only too delighted to dump the whole of their work on to the hospital service."

It is an unfortunate fact of modern medical life that teaching hospitals—and indeed most non-teaching hospitals—indoctrinate students and young graduates with the idea that general practitioners are largely skrimshanking medical morons. This is one reason why young doctors opt for hospital work or emigrate instead of going into general practice in the N.H.S. Other reasons are that these young men can see for themselves what a relatively important and privileged life is led by senior hospital staff in the N.H.S., and they are very conscious of the excessive moaning about their lot by a small proportion of general practitioners. These are not the only reasons for the unpopularity of general practice but they are important ones.

Most doctors, whether in specialist—modern euphemism consultant—or general practice will deplore and question the motive of blanket attacks by members of one section of the profession or another. Criticisms should be made face to face or by personal letter in individual cases and not, as is too frequently done, by general innuendo; so far general practitioners have specialized in turning the other cheek in spite of a superabundance of material for attack by them. Perhaps the sturdy defence of general practice by Dr. H. N. Rose and Dr. B. D. Morgan Williams is the first sign that the worm is beginning to turn.—I am, etc.,

Bath.

W. B. S. Crawford.

Place of the Mentally Retarded

Sir,—I was dismayed to read in your leading article, "Place of the Mentally Retarded" (2 September, p. 567), that you advocate that no special search should be made to "ascertain" or to make special provision for the large proportion of mentally subnormals who are not known to hospitals or local authorities, because there is not enough provision for those who are already known. As at the present time already 77 inborn errors of metabolism are known and an ever-increasing number of these are becoming treatable, it would be disastrous if no arrangements were made for systematic screening and for regular follow-up treatment of the afflicted.

Furthermore, a number of mentally retarded of all ages have somatic handicaps which can be treated, and the expert assessment of their training and employment potential would increase their usefulness to society. It is therefore of the utmost importance that a special search should be undertaken for the half a million subnormals in our midst.—I am, etc.,

Rudolph Payne.

Little Plumstead Hospital,
Norwich, Norfolk.

Sir,—Your leading article (2 September, p. 567) gives an interesting review of the position of the mentally retarded in hospital in parts of England, but in some respects the figures quoted are very different from this area in Scotland.

In the period 1959 to 1964 the proportion of feeble-minded patients in our hospital group of 1,731 patients had fallen from 41.2% to 33.9%.[1] In 1964 the average I.Q. for the feeble-minded females was 50 on the Terman–Merrill L–M Scale (males 57.5).[1] Thus two-thirds of all the patients were in the imbecile and idiot groups with an I.Q. below 45. The proportion who could be discharged for useful work in the community is much less than you suggest, but I would heartily endorse your remarks about the dearth of open hostels.—I am, etc.,

D. Primrose.

Lennox Castle,
Lennoxtown, Glasgow.

Reference

[1] Primrose, D. A. A., *J. Ment. Defic. Res.*, 1966, **10**, 168.

S.T.P. and the Law

Sir,—The Food and Drug Administration has now positively identified S.T.P. as 4-methyl-2,5-dimethoxy alpha-methyl phenylethylamine,[1] and so has confirmed the first of the speculations in your leading article (2 September, p. 570). This substance, also called D.O.M., was developed by the Dow Chemical Co., which published no information about it, made no supplies of it available, and did not ask for permission to conduct clinical investigations with it. The mode of its entry into illegal channels is unclear.

On facts, such as they are, you were helpful; on positive suggestions for action much less so. It is inadequate, if not meaningless, to suggest that the statutory measures relating to such substances be made more flexible. Laws must be workable as well as flexible, and it is abundantly clear that the existing law on soft drugs is neither, while the law on hard drugs may well soon cease to be both. Young people are beginning to try any drug. I understand that antidepressives, tranquillizers, and appetite suppressants are already available in the usual quarters. Is the law to be sufficiently "flexible" for it to be an offence to possess any centrally active drugs without a prescription? Abuse of other therapeutic substances not primarily used for their mind-altering properties, which for obvious reasons I shall not name, may well follow, since they certainly can induce sensory or perceptual changes. Will a flexible "law" forbid the possession of any drugs at all without a prescription? There might be something to be said for this, whereas for the present policy of changing the law, or designating secret and in fact non-existent treatment centres, there is absolutely nothing to be said.

It is time to examine comprehensively the attitude of our society to the flood of new chemicals that it is itself calling into existence. What new kinds of drug action do we need? If we will only specify them, our inventive and resourceful pharmaceutical industry is very likely to produce them. Meanwhile, it is apparent that we need hallucinogens, for they are what we are getting. Why? We need scientific answers, not guesses themselves based on fantasies. Perhaps we should begin by asking that our legislators recognize this as the kind of question that matters, and that not until we have tried to answer it scientifically can there be any reasonable basis for changing the law, whether in the direction of increased flexibility or the reverse.—I am, etc.,

C. R. B. JOYCE.

Department of Pharmacology,
London Hospital Medical College,
London E.1.

REFERENCE

[1] F.D.A. Press Release No. 67–90, August 1967. Washington.

Experiments on Man

SIR,—I hope that Dr. M. H. Pappworth, whose clinical ethics, to judge from his book and now from his letter (2 September, p. 616), appear to him to be so impeccable, will not lose time in writing his code for clinical investigation. He must also list the punishments that are, as he pleads, to be "meted out to those who flagrantly disregard" him. Presumably the penalty for an unnecessary I.V.P. will be less than for an unnecessary retrograde pyelogram. It will be interesting to see how he defines the precise indications for such things. We shall certainly all need a large reference book on our clinic desks. Will the penalties be fines graded by offence and income? Who will exact them?

Life will be simpler in some ways, since no new methods could get on to the list, for all are potentially risky and of unproved value when first done, so none of us will have to bother with any advance of techniques.

Does Dr. Pappworth really believe that his fantasy is preferable to the judgement of senior members of a profession whose ethical standards have always been its pride? Let us have no more of this petty nonsense, and let men of knowledge and probity ensure that the difficult ethical problems of clinical research are handled helpfully and sensibly, to ensure that the evil things to which Dr. Pappworth has rightly drawn our attention are stopped, while the stream of medical research flows on unimpeded.—I am, etc.,

London S.W.10. CHARLES FLETCHER

Training for Obstetrics and Gynaecology

SIR,—Your leading article "Training for Obstetrics and Gynaecology" (2 September, p. 568) seems to have failed to grasp the real meaning of what the select committee of the Royal College of Obstetricians and Gynaecologists was trying to do. The objects of the report are laid out in the last paragraph of the foreword[1] and I feel that the R.C.O.G. should have been given credit for having the courage to initiate such an investigation. The results of a similar investigation by other bodies might make interesting reading.

In the leading article it is stated: "If they had had enthusiasm, dreamed dreams, and seen visions, the medical world would not have such a drab view of what obstetrics and gynaecology is." One would have thought that this is exactly what the founders of the R.C.O.G. were doing, and what their successors have been doing for years with such excellent results. The R.C.O.G. pioneered training before examination, and much of what has been common practice in the College examinations is now being copied by other examining bodies.

The College, however, is not content to stand still, and the Report is an attempt to initiate the improvements deemed necessary to meet the changed conditions of today and the challenge of the future.—I am, etc.,

C. H. G. MACAFEE.

Royal College of
Obstetricians and Gynaecologists,
London N.W.1.

REFERENCE

[1] Royal College of Obstetricians and Gynaecologists, *The Training of Obstetricians and Gynaecologists in Britain, and Matters Related Thereto*, The Report of a Select Committee to the Council of the College, 1967. London.

Summer and Death from Neuroblastoma

SIR,—Dr. J. A. H. Lee (13 May, p. 404) has reported that neuroblastoma deaths were more common in summer than in winter among children under 15 years of age in England and Wales in 1958–64; the quarterly totals starting in January were 84, 112, 105, and 84 (total 385). In a similar but much larger study (n=1,362) of neuroblastoma deaths among white children in the U.S.A., 1960–4, we have found no corresponding seasonal variation over the entire country or for the colder north-eastern and north-central States (see Table).

Numbers of Neuroblastoma Deaths Among U.S. Whites Under 15 *Years of Age by Season,* 1960–4

Area	Season of Death, 1960–64				P*
	Jan.–Mar.	Apr.–June	July–Sept.	Oct.–Dec.	
Total U.S. ..	339	328	346	349	0·14
N. East and N. Central ..	203	187	194	201	0·15
Other ..	136	141	152	148	0·25

* Probability that annual variation was due to chance based on χ^2 value, 1 d.f., in a one-tailed test.[1]

An adaptation of the Ederer–Myers–Mantel statistical procedure[1] for detecting clusters of rare events was applied to three- and four-month seasons and to months within seasons, beginning alternately in January, February, March, or April. Only 3 of the 42 tests performed were significant at the 5% level, which is consistent with normal expectation. Study was then made of neuroblastoma mortality by State of usual residence, including the District of Columbia, and five one-year periods. In a summation across all 255 time-space intervals no excessive cluttering was found. Summation across the nine geographical divisions of the United States, however, revealed clustering significant at the 5% level, an effect due to an excess of neuroblastoma deaths in certain years in the middle Atlantic, west-south-central, and mountain divisions. To illustrate, the annual totals for the mountain States were 7, 9, 23, 9, and 13. When the States were considered individually only Texas (a west-south-central State) displayed year-to-year fluctuations which were significantly different from normal expectation. No explanation for this variability could be found.

Finally, the sex ratio (M/F) for neuroblastoma deaths under 5 years of age decreased progressively from 1.7 in 1960 to 1.1 in 1964, a change which was statistically significant at the 2% level. Thus, though neuroblastoma deaths did not vary seasonally in the United States, there appeared to be other irregularities in the distribution of the disease in time and space. A fuller description of our observations will be published elsewhere.—We are, etc.,

ROBERT W. MILLER.
JUDITH A. HILL.

Epidemiology Branch,
National Institutes of Health,
National Cancer Institute,
Bethesda 14, Maryland, U.S.A.

REFERENCE

[1] Stark, C. S., and Mantel, N., *Amer. J. Epid.*, 1967, 86, 199.

Speed Control

SIR,—Speed does not necessarily cause accidents, but "unrecognized" speed and high speed by any other than the comparatively few highly experienced drivers does. The disproportionately high serious injury and fatality rates in teenage drivers are evidence of this. When crashes occur at speed the injuries are correspondingly more severe and multiple. On motorways the accident rates are, by comparison, lower, but the fatality rates significantly higher, and 50% of those who die do so before reaching hospital, and this is double the early death rates on other roads.

From research experience, one of the more difficult assessments to make is the speed of a car at the time of its crash. The estimates of roadside witnesses are notoriously fallacious, but, much more important, so are those who have the speedometer in front of them. This is not so much a matter of speedometer design, though some are better than others. Drivers are reluctant to take their eyes off the road, and they give their next priority to their rear view and side mirrors with occasional glances only at the speedometer. Then they may be horrified, surprised, or pleasantly conditioned by such things as the sound of a police siren, the recognition of having been caught in a radar trap, or the considerable difficulties experienced in negotiating a roundabout after leaving a motorway, or in coping with any dangerous situation.

There are two devices, both American, that help in such situations. One is a radar detector that slips on the sun visor and peers through the windscreen, useful to drivers who have fully developed the art of police detection, and perfectly legal in the States, but frowned upon in Britain. The other should be more widely known, though not yet available in Britain. It allows the driver to give his full attention to the road and its environment and relieves him of the impossible task of judging his speed by instinct. Any desired speed is set by the flick of a switch on the steering column from a chosen speedometer reading. The foot is taken away from the accelerator pedal and placed over the brake pedal. The chosen speed is then precisely maintained apart from easing off slightly up a gradient and gaining an insignificant amount when going downhill. The set speed can be instantly overriden by pressure on the accelerator pedal—a useful aid when entering a road with a higher speed limit—and a downward flick of the switch again sets the device to conform to that limit. The merest touch of the brake or clutch pedals puts the device out of action.

After four months use of this speed control no faults have developed, but it has given me a new sense of speed and safety. The instinctive feeling at first was of moving too slowly; a glance at the speedometer corrected that impression. Next I developed a greater confidence in judging braking distance and eliminated my hitherto frequent use of accelerator and brake pedals, which resulted in a smoother performance of my car and economies in engine and tyre wear and in petrol consumption.

The commonly held objections to speed limits may rest in great part on the inability of most drivers to conform to them. Something more than a speedometer would seem essential with the smooth performance of modern cars on good road surfaces and the crowded traffic conditions. The available research evidence on speed indicates that there is a need for minimal as well as maximal speed limits—the former has particular reference to heavy freight transporters on open roads.

It is estimated that the device would sell in Britain at around the price of a car's radio, and one wonders why manufacturers are so hesitant to offer it to the public. Perhaps it is yet another example of the repetition of the old dilemma—research evidence was not good enough in the United States for voluntary action by the Detroit manufacturers on safer car design. Finally, it became a matter for legislation. It seems that safer car design is on the way in, and the indications are that in future battles for car sales worthwhile safety features will outsell useless stylists' gimmicks.—I am, etc.,

WILLIAM GISSANE.

Birmingham Accident Hospital,
Birmingham.

Hetacillin and Ampicillin

SIR,—With reference to a recent letter entitled "Hetacillin and Ampicillin" (5 August, p. 367) we would like to draw attention to further independent absorption and excretion studies of hetacillin and ampicillin. In a series of studies on the stability, absorption, and excretion of hetacillin[1] the following results were obtained.

Hetacillin, which is a condensation product of ampicillin with acetone, is rapidly hydrolysed in aqueous solution to ampicillin and acetone with a half-life time of about 30 minutes between pH 3 and 8.

The absorption and excretion characteristics of hetacillin were defined in comparison with ampicillin by crossover studies. Hetacillin gave marginally higher blood concentrations than ampicillin at 6 and 8 hours. In this respect our results are in agreement with those of Bunn *et al.*[2] and Kirby *et al.*[3] However, the peak level of hetacillin was only about half that of ampicillin. Furthermore, the urinary excretion of hetacillin was again only about half that of ampicillin, indicating poorer absorption of hetacillin.

These studies were carried out on hetacillin prepared by Bristol and ampicillin prepared by Beecham, both products obtained commercially. Our results are thus in much better agreement with those reported by the Beecham investigators (24 June, p. 804) and also with those of Ridley[4] than with those of the two American groups.[2 3]—I am, etc.,

BERNDT SJÖBERG,
Research Director,
Astra Research Laboratories.

Södertälje,
Sweden.

REFERENCES

[1] Magni, L., Örtengren, B., Sjöberg, B., and Wahlqvist, S., in press.
[2] Bunn, P. A., Milicich, S., and Lunn, J. S., *Antimicrobial Agents and Chemotherapy, 1965*, 1966, 947.
[3] Kirby, W. M. M., and Kind, A. C., *Proc. N.Y. Acad. Sci.*, 1967, in press.
[4] Ridley, M., *Brit. med. J.*, 1967, 3, 305.

Hypernatraemic Dehydration

SIR,—Dr. H. Simpson and Dr. J. O'Duffy's warning about overstrong infant feeds (26 August, p. 536) is timely. Hypernatraemia may also occur in small babies on normal feeds if extra water is not given when they are hot, feverish, or panting; and clinical dehydration is not necessarily present.

A two-week-old boy was admitted because of a staphylococcal infection of the scalp. This responded well to cloxacillin, but after a heat wave shortly before discharge he became torpid with no specific signs or weight change. His cerebrospinal fluid contained no cells and a normal amount of glucose. The serum sodium concentration was 212 mEq/l., chloride 180 and urea level 102 mg./100 ml.; potassium and bicarbonate levels were normal. He recovered uneventfully on half strength feeds and a slow infusion of half normal saline (77 mEq/l.). Three years ago a month-old baby was admitted in a similar state and is well.

The greatest peril of hypernatraemia is its treatment. If the osmotic pressure of the cells or of the cerebrospinal fluid lags behind that of the blood because of too rapid treatment with dilute liquid, fits or anuria from cerebral or renal oedema may occur, and demand hypertonic mannitol or frusemide. I have discussed this elsewhere in a different setting.[1] —I am, etc.,

T. H. HUGHES-DAVIES.

Downton, Wiltshire.

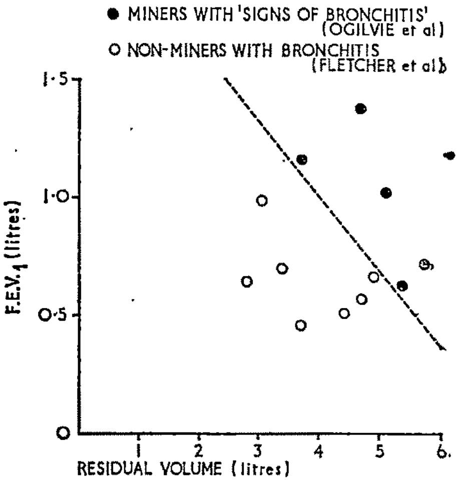
REFERENCE

[1] Hughes-Davies, T. H., *Lancet*, 1966, 1, 822. 4, 376.

Overinflation of the Lungs of Coal Miners

SIR,—Drs. G. B. Field and J. E. Cotes (19 August, p. 493) have compared five of our seven miners having "signs of bronchitis" with six of the ten without such signs. They apparently conclude that disability is mainly due to chronic non-industrial lung disease in the first group and compensation neurosis in the second. The remaining six miners are also placed in one or other of these two categories.

The argument presented in favour of non-industrial lung disease as the cause of the increased lung volumes in the five miners with signs of bronchitis depends upon their similarity to Fletcher's patients with chronic bronchitis.[1] This resemblance is superficial, for when they are actually compared with Fletcher's patients the five still display the pattern shown by the group of miners as a whole—that is, an increase in lung volume disproportionate to the degree of airways obstruction (see Fig.). A separation of the two groups similar to that shown in the Figure can also be obtained when the five bronchitic miners are compared with our own patients having non-industrial lung disease, and when F.R.C. or T.L.C. is substituted for R.V. The distinction is even more definite when (as seems reasonable) the other two miners with signs of bronchitis are also included.



Forced expiratory volume (1 second) plotted against residual volume for miners "with signs of bronchitis" (Ogilvie *et al.*[5]) and non-miners with bronchitis (Fletcher *et al.*)

The argument presented in favour of compensation neurosis as a cause of the large residual volumes in the six "non-bronchitic" miners rests largely upon their "remarkably low expiratory reserve volumes"—that is, failure to expel the vital capacity. But in fact the expiratory reserve volumes are "remarkably" low only by the prediction formula of Cotes and Meade.[2] The mean E.R.V. of these six miners is 79% of the value obtained in our normal subjects, 73% of the value predicted from the formula of Needham *et al.*,[3] but only 46% according to the formula of Cotes and Meade. (Baldwin *et al.*[4] do not have a formula for E.R.V.) Drs. Field and Cotes claim that the Cotes and Meade formula is in some way "more appropriate" than the formula of Baldwin

	Cotes and Meade	Baldwin *et al.*
Vital capacity	90%	100%
Vital capacity	90%	100%
Residual volume ..	77%	106%
Total lung capacity ..	80%	102%
Expiratory reserve volume	60%	82%*

The lung volumes of the normal subjects reported by Ogilvie *et al.*[5] shown as percentage of predicted normal according to the formulae of Cotes and Meade and of Baldwin *et al.*

* E.R.V. predicted from the formula of Needham *et al.* (not available in Baldwin's formula).

et al. which we used. It may well be more appropriate to the inhabitants of South Wales (upon whom it was presumably based), but it compares unfavourably with Baldwin's formula when applied to the healthy Lancastrians who served as our normal controls.

It is on this evidence that Drs. Field and Cotes have attributed the disability of our miners either to non-industrial lung disease or to psychological factors. In doing so they appear to have ignored one of their own subgroups of our miners (those with neither *x*-ray changes nor signs of bronchitis). As a group these men have relatively little evidence of airways obstruction, but their average total lung capacity is larger than in either of the other groups considered by the writers and nearly 2½ litres greater than for our normal subjects. This cannot be attributed to bronchitis, in which the total lung capacity is usually normal even when there is gross airways obstruction.[1] Nor indeed to psychological factors—for what man, by taking thought, can add 2½ litres to his total lung capacity ?

We agree (and indeed admitted in our paper)[5] that we have not made a "good case" for the existence of focal emphysema among our miners because, to achieve this, we must wait until they are dead. What we do claim to have shown is that the great majority of the miners have a degree of lung overinflation which is greater in relation to airways obstruction than in any published series of patients with chronic non-industrial lung disease—including our own.—We are, etc.,

COLIN OGILVIE.
KEITH BROWN.
W. E. KEARNS.

Liverpool Cardio-Thoracic
Surgical Centre,
Liverpool, 14.

REFERENCES

[1] Fletcher, C. M., Hugh-Jones, P., McNicol, M. W., and Pride, N. B., *Quart. J. Med.*, 1963, **32**, 33.

[2] Cotes, J. E., *Lung Function, Assessment and Application in Medicine*, 1965, Oxford.

[3] Needham, C. D., Rogan, M. C., and McDonald, I., *Thorax*, 1954, **9**, 313.

[4] Baldwin, E. de F., Cournand, A., and Richards, D. W., jun., *Medicine (Baltimore)*, 1948, **27**, 243.

[5] Ogilvie, C., Brown, K., and Kearns, W. E., *Brit. med. J.*, 1967, **3**, 10.

Oxygen Therapy Equipment

SIR,—In your leading article (26 August, p. 511) you refer to our paper,[1] and state that we found that the M.C. mask had a significant dead space. However, you do not make clear what you consider to be a significant dead space, and, while we reported a small one, we did not say that this was significant. Testing the M.C. mask, Bethune and Collis[2] found that the subject's physiological dead space increased by 75 ml. breathing oxygen at 2 l./min.

In our paper we showed that, while breathing room air through the vents in the M.C. mask, with no oxygen flowing in, the CO_2 concentration inside the mouth fell to zero between each respiration as rapidly as when the subject was wearing no mask. We therefore consider it unlikely that the small dead space is of clinical significance.

The Edinburgh mask was not tested for dead space, and so we do not think comparisons should be made with this. In their original description of the Edinburgh mask the authors[3] described it as being designed to give controlled oxygen at low concentrations (23–40%) and for this reason we were surprised that it was recommended by you as being the best mask for general purposes.—We are, etc.,

MARY CATTERALL.
GEORGE KAZANTZIS

Respiratory Function Laboratory,
Middlesex Hospital,
London W.1.

[1] Catterall, M., Kazantzis, G., and Hodges, M., *Lancet*, 1967, **1**, 415.

[2] Bethune. D. W., and Collis, J. M., *Thorax*, 1967, **22**, 221.

[3] Flenley, D. C., Hutchison, D. C. S., and Donald, K. W., *Brit. med. J.*, 1963, **2**, 1081.

Advertising Arthritis

SIR,—With what justification does the Arthritis and Rheumatism Council put up posters with the headline "Arthritis Means Crippling, Pain" ? Is not the *raison d'être* of rheumatology to refute this sort of statement, or should doctors now use the word "arthritis" with great circumspection in view of its new sinister connotation "crippling pain" ?—We are, etc.,

K. E. BRITTON.

Middlesex Hospital,
London W.1.

HEATHER SUCKLING.

London N.1.

Oculogyric Crises Due to Phenothiazines

SIR,—Recent correspondence on the subject of oculogyric crises due to phenothiazines (22 July, p. 241, and 12 August, p. 438) prompts us to report two recent cases of acute extrapyrimidal attacks in which oculogyric crises were a prominent feature. Both patients were children who had been prescribed dehydrobenzperidine (Droperidol) as sedation to permit positioning for radiotherapy.

The first case was a 6-year-old girl under treatment for a pontine glioma which had caused a spastic left hemiparesis. She was given dehydrobenzperidine 7.5 mg. orally each day one hour before treatment. Two minor episodes of spasm were witnessed by nurses (approximately six hours after administration) during the first two weeks of treatment. A third episode was witnessed by one of us and the details recorded. It occurred three and a half hours after ingestion, and consisted of generalized rigidity of the trunk and limbs, the neck being extended and the arms flexed. The paretic leg became acutely hyperextended and the unaffected leg was flexed. There was also a fine tremor of the limbs. The eyes were rolled upwards and maintained in a position of elevation, and this condition persisted for 30 minutes before gradually subsiding.

The second case, a 2-year-old girl with acute lymphoblastic leukaemia in complete haematological remission, was given a course of prophylactic radiotherapy to the brain. Dehydrobenzperidine 2.5 mg. was given by mouth, and three hours later her eyes rolled upwards and the neck became hyperextended. The upper limbs were rigidly extended and there was a fine tremor of the hands. These attacks came in spasms for the next three hours. Next day a similar but more severe episode was repeated after the same dose of dehydrobenzperidine.

Acute parkinsonism may occur with large doses of dehydrobenzperidine. In both these cases, however, the doses used were within the recommended range, and it may be that the threshold is lowered by pre-existing brain disease.

We are grateful to Dr. P. E. Thompson Hancock and Dr. H. J. Bloom for allowing us to publish these cases.

—We are, etc.,

J. E. FREEMAN.
A. C. ROBERTSON.
H. NGAN.

Royal Marsden Hospital,
Sutton, Surrey.

Multiple Sclerosis in South Africa

SIR,—Dr. G. Dean's important study (17 June, p. 724) of multiple sclerosis (M.S.) in South Africa has been long awaited. Especially noteworthy are the differential frequencies by the country of origin of the patients. The crude prevalence rates for probable M.S. for all groups except the English-speaking natives are within the ranges expected for their homelands in accordance with the general distribution of M.S. within three broad frequency zones: high (30–60/100,000) in Europe from Switzerland northward, medium (circa 10) in southern Europe, and low (0–4) in Asia and Africa ; with similar high and medium zones in the United States and Canada.[1]

Thus immigrants retain the M.S. prevalence of their land of origin when moving into low frequency areas, as is also attested to by the studies of Alter in Israel,[2] Saint (recalculated) in Australia,[3] and Moffie in the Dutch Antilles,[4] although their progeny in these other studies at least acquire the disease at the rate appropriate to their new home. This certainly bespeaks an exogenous disease rather than one genetically determined.

Since there is some evidence[5 6] that the critical period in the lives of M.S. patients may be that up to about age 15, it would be most helpful if, for the 72 Europeans who first developed symptoms in South Africa, Dr. Dean could provide us with a table listing the ages at immigration, at onset of symptoms, and at prevalence day. This might provide further information on the hypothetical "incubation" or latent period[5 7] between presumed disease-onset and symptom-onset.

The English-speaking natives of South Africa showed a relatively high prevalence rate of 11 M.S. per 100,000 population. Dr. Dean noted that 46 of these 101 individuals had visited Europe before prevalence day, while 41 controls "matched by sex, birthplace, language, and age group, and with the same birthplace of parents, had visited Europe." I believe the fallacy here lies in matching on variables related to the variable in question. Birthplace, language, and birthplace of parents would all seem related to the chances of a person visiting Europe, especially in childhood. Dr. Dean *did* note that 40 of the 101 (twice expectation) had parents both of whom were born in Europe, and 22 had one such parent. Indeed, it may not be possible to devise a proper control group here, but this need not militate against the attempt to measure age and duration of visits and the period to clinical onset in the patients. That people pass through an endemic area unscathed does not lessen validity of considering those who do become ill after such a visit. If we can assume that most or all of these 46 travellers had been to Europe before symptoms began, as well as before prevalence day, there would then be left some 55 English-speaking homebound natives of South Africa to provide a prevalence of about 6 per 100,000, not too dissimilar from the rate of 3 found for the Afrikaners.

Dr. Dean's hypothesis, which is also Poskanzer's,[8] is that early exposure to infection in low risk areas prevents the later development of M.S. If this were true, however, the "unexposed" immigrants should show a much higher attack rate than is found in their native lands, which seems not to be the case in Australia, Dutch Antilles, Israel, or South Africa. Further, the native-born English-speaking South Africans, as well as the Israelis, are recent arrivals, and from neither land do the current prevalence studies indicate any appreciable rate of M.S. in the parents of the subjects. Thus the evidence suggests that M.S. is "caught" in the high risk areas and brought by the migrants in a latent form into these low risk regions which provide such an invaluable human laboratory for M.S. What is the latent period can perhaps be better defined from the points raised here with the data available to Dr. Dean.—I am, etc.,

J. F. KURTZKE.

Neurology Service,
Veterans Administration Hospital,
Washington, D.C., U.S.A.

REFERENCES

[1] Kurtzke, J. F., *J. Indian Med. Prof.*, 1964, **11**, 4896.
[2] Alter, M., Halpern, L., Kurland, L. T., Bornstein, B., Leibowitz, U., and Silberstein, J., *Arch. Neurol. (Chic.)*, 1962, 7, 253.
[3] Saint, E. G., and Sadka, M., *Med. J. Austral.*, 1962, **2**, 249.
[4] Moffie, D., *Ned. T. Geneesk.*, 1966, **110**, 1454.
[5] Kurtzke, J. F., *Acta Neurol. Scand.*, 1965, **41**, 140.
[6] Alter, M., Leibowitz, U., and Speer, J., *Arch. Neurol.*, 1966, **15**, 234.
[7] Schapira, K., Poskanzer, D. C., and Miller, H., *Brain*, 1963, **86**, 315.
[8] Poskanzer, D. C., Schapira, K., and Miller, H., *Lancet*, 1963, **2**, 917.

Early Discharge of Maternity Patients

SIR,—The leading article and papers on the early discharge of maternity patients (26 August, pp. 508, 517, and 520) contained no reference to the importance of restoring the mother who has a young family to her home as soon as possible. The separation of a child for even a few days from its mother can be very traumatic indeed, especially when it coincides with the arrival of a sibling. It is made even more traumatic by the refusal of maternity hospitals to allow children to visit their mothers even when their hospital stay is prolonged. I feel sure that most family doctors would agree that no mother should be retained in hospital for more than 48 hours unless she is a primipara or requires medical and nursing care not available at home.—I am, etc.,

Hornchurch,
Essex.

S. E. BROWNE.

SIR,—The first intimation I usually receive that a patient has been discharged from hospital within two or three days of delivery (26 August, pp. 508 and 517) is an urgent demand for "pills to stop the milk." The patient has usually had an oestrogen for this purpose before leaving hospital, but has no idea of the dose or preparation, nor does the discharge letter give the information, even if it arrives as soon as the anxious friend or relative. It is difficult to assess what quantity of oestrogen to use under these circumstances, and I suggest it would be safer and more economical for each patient to be given the balance of her course of tablets with appropriate instructions on leaving hospital.

Very few patients breast-feed their babies in South Wales, and nearly all believe they must have pills "to stop the milk." A doctor I know gets very good results and no fear of side-effects by giving a placebo, but even this might lead to an oestrogen withdrawal haemorrhage.—I am, etc.,

Port Talbot,
Glamorgan.

R. S. SAXTON.

Chest Pain After Infarction

SIR,—I have read with interest your leader on "Chest Pain After Infarction" (5 August, p. 321), and the article by Professor R. R. H. Lovell and Dr. A. Verghese (same issue, p. 327).

In my opinion the mechanism which causes these pains without any controllable organic lesion is the same as I have described elsewhere.[1] There is anguished fixation of attention upon organs or functions which were the localization of a serious disease suffered by the same patient or by other people closely connected with him. Pain and other somatic complaints are not seldom signs of a libidinous concentration on certain organs. This raising to the first plane of consciousness is a defensive mechanism for an early detection of possible alterations, and, as in somatic medicine, is by itself the cause of symptoms. In Spanish colloquial language "alzaprimar" means to raise the value of something, so that nobody will pay this price and the seller will be hurt.—I am, etc.,

J. CALVO MELENDRO.

Hospital Provincial,
Soria, Spain.

REFERENCE

[1] Calvo Melendro, J., *Pren. méd. argent.*, 1966, 53, 243.

Changed Character of Osteomyelitis

SIR,—May I endorse and enlarge on Mr. D. R. Richard's comments from Nigeria (19 August, p. 497) on "Changed Character of Osteomyelitis" (29 July, p. 255). I would like to stress particularly that, although the pattern in Europe and North America may have changed, both acute and chronic osteomyelitis must still be very common conditions in over three-quarters of the world's population. The complications caused by sickle-cell osteomyelitis and malnutrition add further to the problem. In Uganda osteomyelitis is common, and we have made the following observations:

(1) Although the metaphysis is the usual site for *non*-sickle-cell osteomyelitis to start, secondary involvement of the epiphysis of the lower and upper ends of the femur is common in small children. Patients often come for treatment late, and we have a number of cases with complete disappearance of the head of the femur and partial destruction of the lower end of the femur.

(2) In sickle-cell anaemia, also, the whole diaphysis[1] may be involved in the first few days. All four limbs may also be affected at the same time[2] and multiple fractures are common. *X*-ray changes as early as three days have been seen[3] and gross fragmentation of the bone at one week has been described.[4]

(3) Complete resolution and healing of pathological fractures as early as one month after early conservative treatment in young children is usual, but not inevitable. Patients may sometimes be very ill when pus is under tension, and the toxicity in itself may necessitate urgent early operation and decompression in an ill anaemic child.

(4) Blood culture is helpful in acute cases and stool culture for salmonellae may be useful. A needle down to the site of a suspected abscess most commonly provides a culture of *Staphylococcus pyogenes* or a salmonella (not *typhi*). This procedure has the advantage that crystalline penicillin (or other antibiotic) can replace any pus aspirated.

(5) In the vast majority of patients treated *within three days* conservative treatment appears to have been successful and operation unnecessary, provided that antibiotic therapy has been adequate. Late osteomyelitis is common, and massive sequestra will of course necessitate operative intervention.

(6) In the acute case in which operation is indicated the periosteum is incised rather than stripped. Drilling is usually *not* necessary for the friable bone in sickle-cell osteomyelitis. A fine polyethylene tube and six-hourly instillations of penicillin and streptomycin, plus the appropriate systemic antibiotic, has proved of value in these cases, as it has in chronic osteomyelitis.

(7) A tourniquet should never be used in patients with sickle-cell osteomyelitis, as gangrene may result.[5]—I am, etc.,

R. L. HUCKSTEP.

Department of Orthopaedic
Surgery,
Makerere University College,
Kampala, Uganda.

REFERENCES

[1] Dunnagan, W. A., *N. C. med. J.*, 1960, **21**, 45.
[2] Huckstep, R. L., *Typhoid Fever and Other Salmonella Infections*, 1962, p. 260. Edinburgh.
[3] —— *J. roy. Coll. Surg. Edinb.*, 1966, **11**, 206.
[4] Konotey-Ahulu, F. I. D., and Kuma, E., *Brit. J. clin. Pract.*, 1965, **19**, 575.
[5] Henrickse, R. G., *Cent. Afr. J. Med.*, 1960, **6**, 45.

Ruptured Chordae Tendineae

SIR,—In reference to your leading article on ruptured chordae tendineae (12 August, p. 387) you state that "injection of contrast medium into the left ventricle . . . seldom shows the exact valvular lesion." While I would agree that it may be difficult to differentiate rupture of a papillary muscle from ruptured chorda, it is usually easy to distinguish the rigid valve of chronic rheumatic heart disease from the freely mobile flail valve seen when the subvalve apparatus parts company with the cusp. Two patients in whom ruptured chorda was correctly diagnosed preoperatively have been described.[1]

I would add that cineangiography as opposed to a slower filming technique is necessary to make this distinction.—I am, etc.,

London S.W.7.

R. S. O. REES.

REFERENCE

[1] Rees, R. S. O., Jefferson, K. E., and Harris, A. M., *Brit. Heart J.*, 1965, **27**, 498.

Drugs and Driving

SIR,—Do your contributors realize how frightening it is for a layman to read (24 June, p. 836, and 8 July, p. 109) that doctors can hold the opinion that informing patients that they should not drive while taking the drugs they prescribe would tend to vitiate the "rapport existing between the doctor and patient"?

Expecting trust or rapport to be possible in the face of such callous indifference to the safety of patients and others seems utterly incomprehensible.

Equally dangerous is the habit of some doctors of not offering information on whether small or large amounts of alcohol can alter the effectiveness of any drug and its safety.—I am, etc.,

London S.W.1. JOHN ALLAN.

Recognition of Heart Failure

SIR,—Having read the article "Recognition of Heart Failure" (22 July, p. 219), may I raise one point which is, I think, of some clinical importance? It is stated in the above article that the venous pulse is impalpable in congestive cardiac failure. From our experience, a venous pulse associated with congestive cardiac failure and tricuspid incompetence is often palpable, almost to the same degree as the arterial pulse.—I am, etc.,

Nicosia, Cyprus. S. H. NICOLAIDES.

Stress Incontinence Treated by Electrical Stimulation

SIR,—I am delighted that one who has done as much excellent work in elucidating the problems of urinary incontinence as Mr. S. A. Vincent should also have observed the curative effect of pelvic floor muscle stimulation in cases of stress incontinence. It is interesting that, although not mentioned in the paper published with Mr. P. F. Schofield (15 July, p. 150), the chance observation I first made that pelvic floor contraction improved incontinence was in a case of neurogenic bladder, which Mr. Vincent (19 August, p. 498) states he has also experienced. Occasionally since my original observation I have met with cases of neurogenic urinary incontinence, often following spinal injury in which there has been a large degree of recovery, in which the incontinence due to residual weakness of the pelvic floor muscles has been more in the nature of a true stress incontinence. In these treatment by maximum perineal electrical stimulation has sometimes cured the incontinence.

Mr. Vincent also mentions cases of urge incontinence. Whether the treatment does any good to these cases or not depends upon the aetiology. Where the urge is due to inflammatory changes in the urethra (female prostatitis) the treatment is not likely to do any good, but the patients may be better because of the urethral dilatation associated with a cystoscopy also carried out at the same time. The treatment is of no value in urge incontinence due to neurogenic lesions or in the true congenital enuretic, who I believe suffers from a congenital type of uninhibited neurogenic bladder due to delayed development of the function of the ascending and descending tracts in the spinal cord. It is possible that some cases of urge incontinence are due to weakness of the pelvic floor allowing the urethra to shorten. One may regard these patients as just about to develop stress incontinence. If other causes of the symptoms are excluded and the urethra is shown to be less than normal length in the standing position it is quite possible that this treatment might cause great improvement. I know of one urological colleague who treats such patients by the Lapides operation and in a short series so far has not failed to cure one.

Maximum perineal electrical stimulation is, however, much easier to give and less trouble for both patient and surgeon.—I am, etc.,

THOMAS MOORE.

Department of Urology,
Manchester Royal Infirmary,
Manchester.

Trephine Biopsy of the Lung

SIR,—In reply to Dr. A. L. Jocobs's letter published in your columns (29 July, p. 310), we should like to add that a further 46 biopsies have been performed since the first 100 reported in our article (1 July, p. 30) without any instance of air embolism. Our experience in this respect is supported by the results of other workers, among them Dahlgren and Nordenström, who did not encounter air embolism in a series of 843 biopsies performed with a non-rotating needle.[1] Although air might conceivably enter the lung along the trephine during the changeover from drill to syringe, this is done very rapidly and the gloved thumb can be used to prevent ingress of air.—We are, etc.,

S. J. STEEL.
D. P. WINSTANLEY.

London Chest Hospital,
London E.2.

REFERENCE

[1] Dahlgren, S. E., and Nordenström, B., *Transthoracic Needle Biopsy*, 1966. Stockholm.

Healing Processes in Wounds

SIR,—In your leading article "Healing Processes in Wounds" (2 September, p. 571) you report "dramatic acceleration of healing of open wounds in patients given zinc sulphate 2 mg. three times daily by mouth."

In fact Pories *et al.*[1] were using 220 mg. of zinc sulphate three times daily in their trial with no reported ill effects.—I am, etc.,

L. A. RAUSCHER.

St. Pancras Hospital,
London N.W.1.

REFERENCE

[1] Pories, W. J., Henzel, J. H., Rob, C. G., and Strain, W. H., *Lancet*, 1967, 1, 121.

Mandrax and Porphyria

SIR,—Correspondence in your columns on the subject of Mandrax (methaqualone, diphenhydramine hydrochloride) (10 December 1966, p. 1455; 31 December 1966, p. 1655; 4 February, p. 301; 8 April, p. 112) prompts me to record my own experience with this drug in relation to its use in porphyric subjects.

I suffer from inherited familial porphyria (protocoproporphyria, "South African" porphyria) and am a member of the original family investigated by Dr. Geoffrey Dean.[1] Many drugs, and particularly barbiturates, are known to precipitate acute attacks of porphyria, and the choice of hypnotics in such cases is limited. I have myself taken Mandrax in a dosage of half a tablet at night as a hypnotic on several occasions and this has not precipitated an acute attack and it has not aggravated my skin symptoms. Full investigation may show that this drug can be used as a hypnotic in other types of porphyria.—I am, etc.,

C. M. VAN ROOYEN.

Transvaal,
South Africa.

REFERENCE

[1] Dean, G., and Barnes, H. D., *Brit. med. J.*, 1955, 2, 89.

Side-effect of Antidepressant Drugs

SIR,—Paresis of visual accommodation often deprives depressed patients being treated with dibenzepin derivatives—that is, imipramine and related compounds—of the therapeutic pleasures of reading and sewing, and is perhaps the most troublesome side-effect of these drugs.

Recently, with the help of Surgeon Commander Humphrey Hahn, my ophthalmic colleague, I have kept a small stock of plus-one lenses in N.H.S. frames and have lent them to patients with this symptom.

This simple remedy has quickly proved a most effective and much appreciated adjunct to treatment for depression.—I am, etc.,

G. G. WALLIS.

Royal Naval Hospital,
Bighi, Malta, G.C.

Reprints: Who Should Pay?

SIR,—During the past year a few short items written by myself have been published in medical journals. Since their publication I have received several requests for reprints from doctors in other countries.

Although I am very pleased to receive these requests and to send the reprint requested, the cost of both the reprinting and postage is considerable, and should in my opinion be borne by those who request the reprints, possibly by paying into a central pool.—I am, etc.,

Shepperton, D. MURRAY-BRUCE.
Middx.

Smallpox Revaccination

SIR,—Dr. Elizabeth L. M. Perkins (9 September, p. 680) has misquoted my letter to her partner Dr. Frank. My letter (22 June) is given in full below:

> "I was very disappointed to read in your letter dated 20 June 1967 that you propose to omit the revaccination of children after the eighth birthday.
>
> "This revaccination is to all intents and purposes devoid of risk, and, by denying this service to your young patients, I think that you run the risk of exposing them to a much more serious hazard when they are vaccinated later in life.
>
> "The schedules of vaccination and immunization have been recommended by the highest national authorities, promulgated by the Ministry of Health, and agreed locally by the health authority and the local medical committee. I hope very much that you will reconsider what appears to be your decision in this matter, and that you will agree to continue the arrangements for revaccinating the junior school children."

—I am, etc.,

T. McL. GALLOWAY,
County Medical Officer of Health, West Sussex.

Chichester,
Sussex.

B.M.A. as a Negotiating Body

SIR,—Your correspondent Dr. John Sinson (5 August, p. 374) is under a misapprehension about the talks at present going on between the British Medical Association and the Junior Hospital Doctors' Association. Your readers should know that the B.M.A., to which a proportion of hospital junior doctors belong, is *not* negotiating with the Minister of Health or any official person or body on behalf of the J.H.D.A. Neither have we asked that they should.

The fact that the B.M.A. is having talks with the J.H.D.A. about hospital junior doctors' representation has received wide publicity. The 4,200-strong J.H.D.A., conscious of its long-term responsibility of ensuring a united profession for future negotiations with the Review Body and the Ministry, invited the B.M.A. to follow the lead of other European medical associations by establishing an independent third stream of representation for hospital junior doctors within one employee organization, with its own constitution, including rules and fixed dates for elections.

Latterly the B.M.A.'s Representative Body at its A.R.M. has supported the continuation of these important talks.—I am, etc.,

J. H. BRIGGS,
Chairman,
Junior Hospital Doctors' Association.
London W.C.2.

Sales Promotion

SIR,—I wonder if I am alone in noticing a considerable increase in the number of representatives who now visit our practices and the frequency with which these gentlemen call ? In the past I have regarded the visits of representatives of the drug firms as a not unwelcome break in the surgery and as a useful means of keeping oneself familiar with the products of their companies. Now, however, these frequent visits are becoming an embarrassment and a nuisance.

Many years ago I gave up trying to cope with mail from the drug houses, and ever since then have consigned all mail from them unopened to the wastepaper basket. If this pestering by commercial gentlemen continues there will be only one method of dealing with it, and that is to refuse to see any representatives, and the drug companies will have severed yet another line of communication with at least one member of the medical profession.

Can nothing be done to impress upon these companies the folly of their present policy of persistent badgering of an already fully occupied profession ?—I am, etc.,

Newick, Sussex. J. R. CALDWELL.

Junior Staff Representation

SIR,—The Junior Hospital Doctors' Association in their newspaper *On Call*[1] have printed the following statement:

"Hospital junior doctors are *not* able to choose their representatives on the new Regional Hospital Services Committees—consultants only have the vote."

As this will have been read by many junior doctors, I think it important that it is prominently stated that junior doctors will, of course, have the duty to elect their own representatives to these committees. In this region seven seats on the hospital services committee have been allocated for junior doctors. Our problem at the moment is not lack of representation but consideration of how we can most efficiently and fairly elect the seven members.

It is obvious that the consultants on the regional committee would neither wish nor be competent to undertake these elections for us.—I am, etc.,

J. H. WETHERILL,
Honorary Chairman,
Leeds Region Hospital Junior Staffs Group, B.M.A.
Leeds.

REFERENCE

[1] *On Call*, September 1967, **1**, No. 3.

Special Service for Doctors

SIR,—May I, through the courtesy of your correspondence columns, once again draw the attention of your readers to our special service for doctors which is to be held in All Souls Church, Langham Place, W.1, this year on Sunday, 8 October, at 11 a.m. ? We greatly value our link with the medical profession, and have been encouraged by the support which its members have given to these services during the last 15 years. Readers may be interested to know that this year the B.B.C. are recording the service for broadcast (in abbreviated form) on Sunday, 15 October, in the Home Service at 8 p.m. as well as in the World Service at 1715 hours and 0030 hours G.M.T. on 15 and 16 October respectively.

Lieutenant-General Sir Robert Drew, Director-General Army Medical Services, and Mr. D. F. Ellison Nash, consultant surgeon, St. Bartholomew's Hospital, and vice-president of the Christian Medical Fellowship, have kindly agreed to read the lessons.

A buffet lunch is again being arranged after the service at the Royal Society of Medicine, through the kind co-operation of the president and council of the society, at 15s. a head (adults) and 7s. 6d. a head (children aged 14 and under). A crèche will be open for children under 5 years in All Souls Church House during the service. We shall be happy to reserve seats in church for doctors and members of their families who apply for tickets in advance, and also to issue tickets for the lunch. Application (stating number of tickets required, and enclosing remittance for the luncheon) should be made to the Church Secretary, All Souls Vestry, 2 All Souls Place, London W.1, by Thursday, 5 October.

Special arrangements are available for doctors on call during the service, who may be contacted by telephone at All Souls Vestry, LAN. 3522.—I am, etc.,

JOHN R. W. STOTT,
Rector, All Souls Church.
London W.1.

Points from Letters

Mortality of the Ambulance Ride

Dr. E. M. HOARE (London N.W.3) writes: I have been interested to read the correspondence about the dangers of transporting very ill patients in ambulances (12 August, p. 438; 26 August, p. 560). . . . However, it is an aspect of the equipping of London ambulances which I wish to bring to your attention.

All ambulance crews are taught how to carry out external cardiac massage. Frequently gastric reflux occurs during this procedure—which is often provoked by the massage movements themselves. The patient is of necessity lying on his back, and in this position the risk of bronchial aspiration is considerable.

The crews are provided with no means of sucking out the mouth and pharynx if reflux occurs. Surely it would be a simple matter to install some sort of suction apparatus, perhaps of a type which operated off the vacuum of the vehicle's inlet manifold.

An even more obvious equipment lack is that of airways. Ambulances are not equipped with these despite their simplicity, cheapness, and efficiency in holding the tongue of the unconscious patient forward.

Twenty of the G.L.C. ambulances are equipped with tracheostomy tubes and a full set of surgical instruments (which are to be used only if a doctor is in attendance). Surely if this is justified the more elementary pieces of equipment suggested must be regarded as essential.

Casualty Department—or G.P. Service ?

Dr. A. J. BARSON (Toronto, Canada) writes: Casualty departments have most of the attributes of a good health centre. There is nursing and clerical help. Colleagues are always available for a second opinion and specialist services can easily be summoned. Pathological and radiological investigations essential to modern diagnostic work are readily obtained and the doctors who request them are more familiar with their interpretation than their older colleagues divorced from hospital medicine. Unfortunately, the hospital general-practitioner/casualty service falls short of the ideal in its lack of financial reward and consequent transience of its medical labour.

I was surprised that in Mr. B. J. Preston's survey (1 July, p. 46) no one said that they attended the casualty department because they received better treatment. Perhaps the public are a little more honest in the north of England where I did my casualty work. There the answer to the familiar question, "Why didn't you, see your own doctor about this ?" was all too often, "Oh, he would never examine me like they do here." When the general practitioner's surgery was open and across the road from the hospital I found the situation a little exasperating, but I could never bring myself to reprimand such a patient when he was obviously doing what his intelligence dictated.

Diet and Diverticulitis

Mr. HAROLD DODD (London W.1) writes: Referring to Mr. N. S. Painter's letter on diverticulitis (12 August, p. 434), may I say how much I agree with him ? In 1945, impressed by the contrast between the thin-walled normal colon, obviously designed to carry bulk, and the thickened small-lumened large bowel affected by diverticulitis, I advised not the conventional low residue diet but one leaving considerable bulk. Fresh and dried fruits, salads, vegetables, and a reasonable amount of protein supplanted the purées, minced, and sweet courses. An encouraging improvement followed. In a few a normal bowel action was regained, and in the majority the amount of aperient was reduced. . . . I am confident that the solution to the prevailing frequency of constipation, haemorrhoids, and diverticulitis lies in the return to natural unrefined foods, and that short-cuts in feeding with the abounding tinned and processed foods and sweets will not give the stable health that will stand the wear and tear of life without resort to medicines

Obituary Notices

J. A. HADFIELD, M.A., M.B., CH.B.

Dr. J. A. Hadfield, a former lecturer in psychopathology and mental hygiene at London University, and a well-known psychiatrist, died suddenly at his home at Whithurst Park, West Sussex, on 4 September. He was 84.

James Arthur Hadfield was born on 11 November 1882 in the Loyalty Isles, South Pacific, where his father, the Rev. James Hadfield, was a missionary. He was educated at Eltham College, Mansfield College, and Queen's College, Oxford, and at Edinburgh University. After graduation at Oxford Hadfield transferred to Edinburgh, where he graduated M.B., Ch.B. in 1916, and after house appointments at the Royal Infirmary he became a surgeon in the Royal Navy. Later he transferred to the R.A.M.C., and was neurologist at Ashhurst Neurological Hospital, Oxford. There his gifts as a teacher were quickly recognized by medical students. His next appointment was in 1920, as lecturer and university psychotherapist at Birmingham University. A year or two later he moved to London, and began his long career as a consultant in psychological medicine. Soon he joined the staff of the Tavistock Clinic, and also he lectured at Bethlem Royal Hospital on psychopathology. In 1931 he became lecturer in psychopathology and mental hygiene in London University, and held this appointment until 1958. At the university, and as director of studies at the Tavistock Clinic, Hadfield played a notable part in the training of medical men in psychiatry, to which he made many original contributions. In the 1930s he arranged lectures at the Tavistock Clinic for psychiatrists and general practitioners, and brought to London notable speakers from overseas, including C. G. Jung and William McDougall.

As a writer Hadfield's name became widely known through *Psychology and Morals* (1920), which ran into many editions. His colleagues pressed him to write more; but it was not until 1950 that *Psychology and Mental Health* appeared, followed four years later by *Dreams and Nightmares*. A further volume was to have been published this autumn.

Many doctors who later joined the staff of teaching hospitals went to Hadfield for a "training analysis," and for years a group of younger psychiatrists met regularly at his house for clinical discussions. Thus he exercised a wide influence on the development of dynamic psychotherapy.

Hadfield joined the R.A.M.C. in 1940, and attained the rank of lieutenant-colonel as officer in charge of a division at a war-time psychiatric hospital near Taunton. This hospital supplied many of the staff for the 41st Psychiatric Hospital in the Middle East. He was appointed a member of the Archbishop's Commission on Divine Healing in 1953.

Hadfield's wife qualified in medicine, as did two of his three sons. In his younger days Hadfield was keen on sailing and swimming, and at week-ends he kept open house for his friends at his country home in Sussex.—E. A. B.

B. T. SQUIRES, O.B.E., B.A., D.M.

Dr. B. T. Squires, a former director of medical services in Bechuanaland Protectorate, and a research worker at the National Institute of Medical Research in London, died suddenly in Bulawayo, Rhodesia, on 24 May, shortly after delivering a paper before the Scientific Conference on Nutrition, a subject very dear to him. He was 63.

Bernard Thomas Squires was born in Oxford on 12 June 1903, and began his academic life as a physiologist, taking a B.A. in animal physiology at University College, Oxford. His profound concern for mankind prompted him to enter the medical faculty at Guy's Hospital, and in 1929 he obtained the L.M.S.S.A. The following year he took the Conjoint diploma, and in 1931 he graduated B.M., B.Ch. The next five years were spent as a mission doctor working among the Bantu in South Africa, and during that time he submitted a thesis on medicine among the Basotho for which he was awarded the D.M. by Oxford University in 1936. In the same year Squires entered the medical service of Bechuanaland Protectorate, and while satisfying his missionary interests in caring for Bechuana he pursued his physiological researches into their state of nutrition, and developed techniques of study of tongue patterns and buccal smears. His contribution to the welfare of the Africans was recognized by the conferment of the O.B.E. in 1954, and by his appointment in 1956 as director of medical services.

When he retired in 1960 Dr. Squires continued his researches on nutrition, and he was the author of some forty papers on the subject. At the request of the National Institute for Medical Research in London he undertook in 1961 a nutritional survey in Basutoland for the Food and Agriculture Organization of the United Nations, and in 1964 he did a similar survey for the Aden Protectorate Government. In 1965 he returned to Africa, and continued working at Mpilo Hospital, Bulawayo. It is fitting that his last service to medicine and to mankind was a scientific paper on perhaps the world's greatest problem—nutrition.

It was a privilege to know and co-operate with Squires in Bechuanaland Protectorate, where he made such a magnificent contribution to the practice of medicine and to the understanding of our fellow men. His subtle humour and approachable manner endeared him to all—African and European alike. His colleagues held him in high esteem for his diagnostic ability and for his profound knowledge of basic medical principles. Above all, he was respected because he dealt justly, he loved mercy, and he walked humbly before his God. A missionary, a doctor, and a scientist has gone from our midst. To his widow, their three daughters, and a son—who is in practice as a barrister in Salisbury—we extend a deep and heartfelt sympathy.—J. M. S. M.

J. D. B. MACDOUGALL, M.D. F.R.C.S.ED.

Dr. J. D. B. MacDougall, senior lecturer in anatomy at the University of Dundee, died suddenly at his home in Dundee on 30 August. He was 49.

John David Bathgate MacDougall was born on 6 January 1918. Educated at Perth Academy and University College, Dundee, he graduated M.B., Ch.B. with commendation at the University of St. Andrews in 1942 and proceeded M.D. in 1946. Recurrent ill-health from the age of 17 years prevented him from joining the Services, though for a period he served as a civilian medical officer. Although he had a strong leaning to the practice of medicine, as is evident from his subsequent research interests, he decided to make anatomy his career, joining the staff of St. Salvator's College, St. Andrews, in 1943, and transferring to University College, Dundee, in 1946.

His interests in human anatomy and biology were wide; he had a long list of publications to his credit, and presented numerous communications to scientific societies. In the field of functional anatomy he made a particularly useful contribution in a special study of the masseter and temporalis muscles, correlating structure and function, and descriptions based on this work are now to be found in standard textbooks of anatomy.

Tissue culture was, however, his major research interest, and his early work in this field was concerned with the toxicity of materials in common clinical use, including various synthetic rubbers. The results obtained with silicone rubbers may have been partly responsible for its subsequent adoption in surgical practice and by the National Blood Transfusion Service. In 1956 he carried out research on tissue respiration at Columbia University, New York, and lectured at the Universities of Dalhousie, Toronto, and Western Ontario. In collaboration with the department of biochemistry he studied the effects of various sterols on the walls of arteries, and it is therefore particularly poignant that at the last he should be struck down by coronary heart disease.

Perhaps the most interesting developments in his research work since 1961 have been concerned with his initiation of the culture of adult organs under hyperbaric oxygen. In collaboration with a friend and colleague, this was subsequently extended to a wider study on the toxic effects of hyperbaric oxygen on cell structure and function. This work has revealed many hitherto unpublished changes in cell structure, and is currently being prepared for publication.

He was a most loyal and conscientious member of staff, and one who was both liked and respected by colleagues and students. Generations of medical and dental undergraduates will recall with gratitude his lucid lectures, interspersed as they were with the fruits of wide reading and a philosophic outlook, while junior staff preparing for the primary F.R.C.S. can have had no better guide. He was the kindliest of men, thoughtful, possessed of great integrity of character and an innate modesty. Students and staff alike will miss a genial member of the academic society, and our deepest sympathy goes to his widow, his young daughter, and his son, who is a medical student at St. Andrews.—D. R. D. and R. E. C.

J. B. DAVEY, M.B., D.T.M.

Dr. J. B. Davey, former principal medical officer and member of the executive council of Tanganyika Territory, died in Worthing on 29 June. He was 92.

John Bernard Davey, son of the Rev. John Davey, was born in Coatham, Yorkshire, on 31 March 1875, and was educated at Giggleswick School, Yorkshire, the Middlesex Hospital, and University College, London, qualifying with the Conjoint diploma in 1899 and graduating M.B. the following year. After early house appointments at the Middlesex Hospital he took part in the Boer War as civil surgeon to the South African Field Forces, and was awarded the South African War medal and clasp, before being appointed medical officer in the Nyasaland Protectorate from 1902 to 1919. During a period of leave he took the D.T.M. in 1907. He was seconded for a period of service with the scientific commission of the Royal Society, headed by Colonel Sir David Bruce, which went to Nyasaland in 1911 to investigate the relation of the African fauna to the existence and spread of the trypanosome diseases of man and domestic animals. In 1919 he was appointed principal medical officer in occupied German East Africa, later Tanganyika Territory, and the following year he became a member of the executive council. In 1923–4 he was president of the Tanganyika Branch of the British Medical Association, and in 1924 was a representative at the Annual Meeting. On his retirement from Tanganyika in 1924 he returned to London, and undertook a year's pathology at the Middlesex Hospital, after which he spent some eight years as a clinical pathologist in the Cheltenham area before retiring for a second time.

During the second world war, when there was an acute shortage of medical staff, he emerged from his second retirement and returned to Tanganyika for two years as provincial medical officer.

A colleague writes: When in 1902 Dr. Davey joined the Colonial Service in British Central Africa (Nyasaland) it is recorded that his was the only microscope there. After distinguished medical service in Africa he retired in 1924. Following a year's study of pathology at the Middlesex Hospital he was appointed clinical pathologist at Cheltenham, but was forced by double cataract to abandon microscopy in 1933. Never giving up medical work, during the second world war he again offered his services to the Colonial Office, and served for two years as a provincial medical officer in Tanganyika in the department of which he had been the first director. From 1948 he lived in South Africa, finally moving to Worthing in 1963. He married in 1913; and to his widow, Constance, who shared with him the hardships of those early days in Africa, and their two daughters we extend our sincere sympathy and mourn the passing of a distinguished colleague.

G. McL. writes: All of us who knew Dr. J. B. Davey in Tanganyika would agree that he made a success of an exceptionally difficult task when he directed the health services of that vast territory. It was then still suffering from the aftermath of war and the wartime influenza epidemic, and with its numerous parasitic diseases almost uncontrolled. There were, besides, several outbreaks of smallpox. In 1921 there was a new outbreak of plague, and in 1922 Rhodesian sleeping sickness, which had been smouldering for some time, was now appearing in epidemic form. With little more than a skeleton staff to begin with, and with barely enough funds to equip them properly, it was a disheartening situation. Dr. Davey persevered, however, building up a department with such slender means as he had at his disposal. When he left in 1924 the foundations were prepared for the extension of the medical services. Despite his many other duties, Dr. Davey was able to take a special interest in the sleeping sickness epidemic, and took an active part in the controversy—then renewed—of whether wild game acted as a reservoir of infection. He sided with those who incriminated game, but it was only after he had retired that it was shown experimentally that trypanosomes could infect man after passage through certain game animals.

Dr. Davey was a hard-working and conscientious public servant, and he upheld the best traditions of his profession.

K. A. W. LAW, M.B.E., M.B., B.S.

Dr. K. A. W. Law, a medical practitioner in Newcastle upon Tyne, died suddenly on 5 August after a short illness. He was 65.

Kenneth Arthur Waring Law, son of the Reverend W. L. M. Law of Hetton-le-Hole, Co. Durham, was born on 4 October 1901, and was educated at Durham School and University, graduating M.B., B.S. in 1926. He played Rugby for the school and university. After an appointment as house surgeon at the Royal Victoria Infirmary he was appointed a medical officer to the Blue Funnel Line in 1926–7, on the United Kingdom and Japan route. He was one of the founder members, with Professor Farquar Murray, of the Blue Funnel Club (medical) which meets annually in Newcastle, and was a most efficient secretary over the past 15 years. In 1927 he married, and after a short time in practice at Leigh-on-Sea he returned to Tyneside in 1932 to take a practice in Forest Hall, Newcastle upon Tyne, where he worked until his death. In 1938 he joined the Royal Auxiliary Air Force, and was called up for service with the Royal Air Force Medical Branch at the outbreak of the second world war. In 1944 the M.B.E. was conferred on him. Dr. Law was a keen committee man, and among his many activities he was chairman in 1951–2 of the Newcastle Division of the British Medical Association. He also served on the Branch council, and was a representative at the Annual Meeting in 1950 and 1952.

Kenneth was a real family practitioner, always willing to help his patients. He was a good sportsman, and in the later years enjoyed his "Tuesday foursome" at golf. Above all he was a great family man, dedicated to his wife and two daughters, and his four grandchildren. He was critical, but always helpful, to his junior colleagues, and I have never heard him speak badly of anyone. His family, his colleagues, and his friends have lost a good friend.—J. H. P.

G. JAMIESON, M.B., CH.B.

Dr. G. Jamieson, formerly in general practice at Chryston, in North Lanarkshire, died at his home on 25 August aged 70.

George Jamieson was born on 4 October 1896, and after serving his apprenticeship in the Royal Bank of Scotland, Airdrie, he decided that medicine was his vocation. He entered the University of Glasgow, but his studies were interrupted by the first world war, in which he served as surgeon sub-lieutenant in the R.N.V.R. After demobilization he completed his studies, graduating M.B., B.S. in 1920. He immediately entered general practice. Dr. Jamieson was chairman of the Lanarkshire Division of the B.M.A. in 1940–1, and was a member of the N.H.S. executive council for the County of Lanarkshire. He was a founder member of the College of General Practitioners, and served on the board of management of the north-eastern group of mental hospitals. He was past-president of the local nursing association and also past-chairman of the committee of management of the Lanarkshire Association of District Nurses. Other appointments he held were factory doctor and Treasury medical officer. In 1938 he was appointed a justice of the peace for the County of Lanarkshire, and thereafter served on various licensing boards.

Dr. Jamieson was the born general practitioner. He was tremendously interested in people, and looked on his patients as friends, being interested not only in their illnesses but in their everyday lives. He was always willing to help in any capacity, and was the "doctors' doctor," keeping himself continually up to date, always seeking postgraduate experience. He had boundless energy, and participated in all the activities which took place around the area of his practice. He was shrewd and disarming, and had he not been so devoted to his work there is no doubt that he would have been very successful in business.

He is survived by his wife, two daughters, and two sons. Both daughters and one of his sons are in the medical profession. The sympathy of all his friends and colleagues is extended to his widow and family.—J. J.

D. SKINNER, M.B., CH.B.

Dr. D. Skinner, a general practitioner in Burnley, died on 22 August, only three weeks after his retirement. He was 66.

David Skinner was born on 8 October 1900 in India, where his father was principal of the Madras Christian College. He was brought to Scotland as a child, and was educated first at St. Andrews and later at Aberdeen Grammar School and Aberdeen University, graduating M.B., Ch.B. in 1924. After house appointments in hospitals in Aberdeenshire he joined a partnership in a large general practice in Burnley in 1925, where his outstanding qualities as a doctor were soon recognized. As well as being a fine clinician he was a very skilled anaesthetist, and for over 30 years held appointments as an anaesthetist to the Burnley group of hospitals. As a member of the Volunteer Reserve of the Royal Air Force he was called up at the outbreak of the second world war, serving mostly in the Mediterranean area with the 8th Army, reaching the rank of wing commander and being mentioned in dispatches for his services. Invalided out of the R.A.F. in 1945, following a coronary thrombosis, he returned to general practice in Burnley.

A member of the panel committee in the N.H.I. days, he was a member of the local medical committee from 1948 to 1951, from 1951 to 1960 he was honorary secretary, and was chairman from 1960 to 1965. He was also a member of the Burnley Executive Council from 1952 to 1965, and for many years served on the hospitals medical advisory committee. A member of the Burnley Division of the British Medical Association, he was a representative at the Annual Meeting in 1952, and served as chairman of the Division for the year 1952–3. At the time of his death he was a member of the ethical committee of the Division.

David Skinner's great love, apart from the practice of medicine, was fishing, at which he excelled, and all his holidays were spent in pursuit of this hobby. Enjoying an ideal family life, his quiet competent manner, his dry sense of humour, his ability and integrity endeared him to his patients and friends, and our sympathy is extended to his widow, son, and daughter.—R. S. McG.

J. M. DAVIDSON, M.B., CH.B.

Dr. J. M. Davidson, formerly in general practice at Docking, Norfolk, died suddenly at his home in Kendal on 26 August. He was 64.

John Macrae Davidson, son of an Edinburgh practitioner, was born on 21 March 1903, and was educated at Loretto School and Edinburgh University, graduating M.B., Ch.B. in 1929. As an undergraduate he took an active part in the corporate life of the university, serving on the committee of the Union, and playing hockey for the university. After an appointment as house-surgeon at Chalmers Hospital, Edinburgh, he went into general practice in the Midlands for a short time before settling down in a rural practice at Docking, in Norfolk, where he remained until his retirement four years ago. Always interested in community life, he devoted much of his leisure to parish and church work, and for a time he was chairman of the parish council. In this community work he was ably supported by his wife, and many were the gestures of appreciation on his retirement. Even in retirement the habits of a lifetime were not broken, and he entered into community work in Kendal with his accustomed vigour, continuing to lead a full life for the benefit of others.

He is survived by his widow and three children, who in their hour of sorrow must be proud to remember his sense of duty and life of service.—G. G.

JANET WHYTE HEPBURN, M.B. CH.B., D.P.H.

Dr. J. W. Hepburn, a former senior assistant medical officer of health for maternity and child welfare, Grimsby County Borough, died on 9 August 1967. She was 72.

Janet Whyte Hepburn graduated M.B., B.S. from Glasgow University in 1918, and later studied at Cambridge for the diploma in Public Health. She worked in a Glasgow children's hospital and later moved to the West Norfolk Hospital. Her duties with the Grimsby Health Department began in 1922, and at once she exerted great influence on the development of Grimsby's maternal and child welfare clinics.

Grimsby then had three clinics. They were always crowded and often had between 80 and 100 mothers packed into the waiting-room at each of them. When she retired in September 1960, after 38 years' service, Dr. Hepburn was able to say that real want had gone, family allowances helped mothers in need, and those who attended clinics did so mainly for advice.

She always inspired great trust, and had an unbeatable record of service. She will be remembered chiefly for her excellent mother-and-child work.—R. G.

B. E. A. HARLEY, M.R.C.S., L.R.C.P. D.O.

Dr. B. E. A. Harley, honorary ophthalmic surgeon at the Wangaratta District Base Hospital, died suddenly at his home at Wangaratta, in Victoria, Australia, on 21 November 1966. He was 57.

Brian Erskine Alfred Harley, son of Dr. H. Harley, a general practitioner in Wealdstone, Middlesex, was born in Harrow on 1 July, 1909, and educated at Felstead, Essex, and at the Middlesex Hospital, qualifying with the Conjoint diploma in 1933. Within a month of his qualification his father died, and he returned home to take over the practice. He later moved to Lorley, Yorkshire, where he practised until the outbreak of the second world war, when he volunteered for service with the Royal Air Force. During his service he was stationed in England, Scotland, and Wales. While in Scotland he organized the Mountain Rescue Service, developing much of the equipment which is still in use to this day. After demobilization he returned to general practice in Lorley until 1948, when he moved to Didbrook, Gloucestershire, where he bought a mixed farm. He took the diploma in ophthalmology in 1954, and in the same year moved with his family to Australia, where he bought the Wangaratta portion of Dr. Rosen's ophthalmic practice. He became honorary ophthalmic surgeon at the Wangaratta District Base Hospital, and also consulted in Benalla. The Victorian police sought his assistance in forming a search and rescue squad, and some of the equipment was patterned on his mountain rescue equipment.

Brian took part in many activities in Wangaratta, and was a Rotarian and a member of the regional library committee. His friends will always remember him, his warmth, gaiety, and gentleness; and he was loved by his patients. To Isabel and their two daughters we extend our deepest sympathy. —D. M. W.

TERENCE EAST, M.A., D.M., F.R.C.P.

D. S. M. writes: I remember very clearly the first time I saw Terence East (obituary, 9 September, p. 684). He gave the introductory lecture to the course in medicine at King's. As he entered the lecture theatre I was aware immediately of the presence of a great man. His walk was distinctive: he inclined his head very slightly to one side and appeared to look into the far distance. He was tall and strongly built, with bronzed skin and iron-grey hair. He spoke with a deep voice that was melodious and difficult to hear until you got used to it. He explained simply and clearly, writing little on the blackboard. His ward rounds and clinics were fascinating. The round began with his reading the student notes carefully and making helpful comments on them. Then he would demonstrate the physical signs, waiting patiently until each student was confident of them. Afterwards he would explain the pathology by use of the museum specimens, many of which he had prepared himself. His clinics were conducted in the same way. What remains, above all, is his voice in my mind's ear as he taught and described. He would make a point by quotations from ancient and modern literature, and by observation of current events. His interests were varied. His mind ranged widely, and always constructively. "Only connect . . ." —and he could.

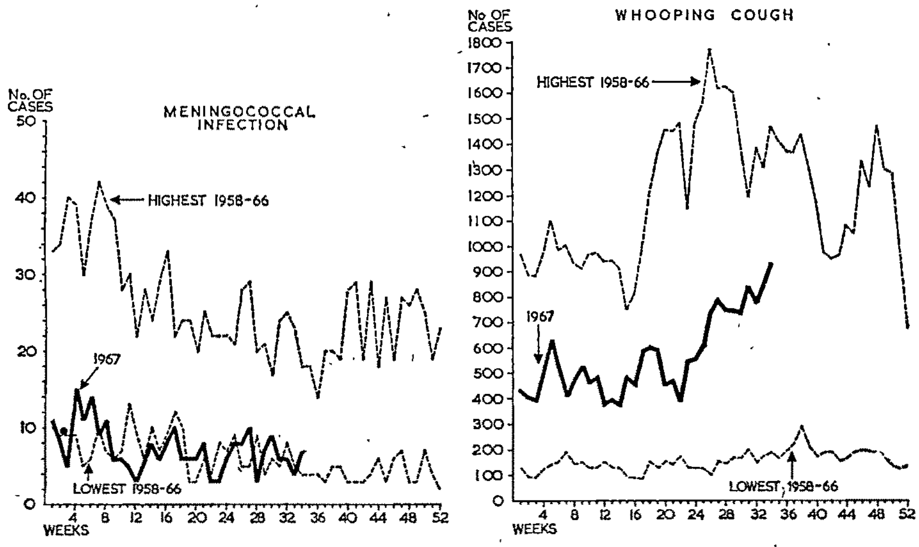
It is a tragedy that many misunderstood him, and because they could not hear (he did not like to repeat, conscious of his difficult enunciation) took no trouble and missed so much. The last time I met him, a few months before he died, we sat on a bench in his garden in Cornwall. He talked, as ever, with great interest. He had new plans and ideas. He could still illuminate. He was one of the great men I have been privileged to know and to learn from.

News and Notes

EPIDEMIOLOGY

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of meningococcal infection and whooping-cough in England and Wales. Figures for 1967 are compared with the highest and lowest figures for each week in the previous years shown.



Scotland in First Quarter

The birth rate for the first quarter of 1967 was 19.7 per 1,000 population. This was 0.9 above the rate for the first quarter of 1966 and 0.3 below the average of the five preceding first quarters. The infant mortality rate was 21 and the neonatal mortality rate was 13 per 1,000 live births. These were 4 and 3 respectively below the rates for the first quarter of 1966. Stillbirths formed 15 per 1,000 total births, giving a rate of 4 below the average. The general death rate was 12.4 per 1,000 population and was 2.8 below the rate for the corresponding quarter of 1966 and 2.1 below the average.

Sixty-two deaths were registered from respiratory tuberculosis and 6 from other forms of tuberculosis; these were 33 and 10 respectively fewer than in the first quarter of 1966. Deaths attributed to cancer of the respiratory system were 757 and were 32 fewer than in the corresponding quarter of 1966. Deaths due to motor-vehicle accidents numbered 172 and were 20 more than in the

INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **26 August** (No. 34) and corresponding week 1966.

Figures of *cases* are for the countries shown and for Greater London. Figures of *deaths* and *births* are for the whole of England and Wales (London included) Greater London, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	0	0		1	0	0	0	
Dysentery ..	198	40	65	5	8	231	35	64	5	2
Encephalitis, acute ..	1	0		0		3	0		0	
Enteric fever: Typhoid ..	3	0	0	0	3	6	3	0	0	0
Paratyphoid	6	0	0	0	0	2	0	0	0	1B
Food-poisoning	153	33	17	2		181	41	6	5	
Infective enteritis or diarrhoea under 2 years				23	45				22	64
Measles* ..	1,726	110	8	26	39	5,123	600	57	41	47
Meningococcal infection ..	7	0	0	0	1	10	0	1	0	
Ophthalmia neonatorum	15	1	0	0		18	1	1	0	
Pneumonia† ..	55	8	50	2		79	9	55	0	
Poliomyelitis, acute: Paralytic ..	1	0	0	0		0	0	0	0	
Non-paralytic	0	0	0			0	0	0		
Puerperal fever§	103	37	1	1		72	32	2	0	
Scarlet fever ..	133	21	11	6	4	155	18	7	1	6
Tuberculosis: Respiratory ..	191	38	24	9		205	57	41	4	
Non-respiratory ..	41	5	4	1		43	16	12	0	
Whooping-cough	929	128	63	11	32	458	75	38	10	11

DEATHS	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0		0	0	0	0		0		0
Dysentery ..	0	0		0		0	0			
Encephalitis, acute ..					0					0
Enteric fever ..	0	0	0	0		0	0	0		
Infective enteritis or diarrhoea under 2 years	6	0	1	0	2	1	1	1		0
Influenza ..	0	0	0	0	0	1	0	0		0
Measles ..	0		0	0	0	0		0		0
Meningococcal infection ..			0					0		
Pneumonia ..	565	101	19	19	5	468	89	25		2
Poliomyelitis, acute ..	0	0		0	0	1	1			0
Scarlet fever ..	0		0	0	0	0		0		0
Tuberculosis: Respiratory ..	34	8	2	0	0	50	7	4		2
Non-respiratory ..				1	0					0
Whooping-cough	0	0	0	0	0	0	0	0		0
Deaths 0-1 year	223	46	14	6	19	266	37	28		4
Deaths (excluding stillbirths)	9,133	1492	489	111	179	8,896	1431	545		124
LIVE BIRTHS	15,401	2475	929	259	352	16,703	2803	882		427
STILLBIRTHS	233	36	16			242	27	16		

* Measles not notifiable in Scotland, whence returns are approximate. † Includes primary and influenzal pneumonia. § Includes puerperal pyrexia.

first quarter of 1966. The 267 deaths due to accidents in the home were 87 fewer than in the corresponding quarter of 1966.

Infectious Diseases

Areas where numbers of notifications were high in the latest two weeks for which figures are available.

	Week Ending 25 Aug.	Week Ending 1 Sept.
Dysentery		
Greater London	40	**53**
Redbridge	16	**22**
Kent	1	**20**
Malling R.D.	0	**17**
Lancashire	40	**34**
Manchester C.B.	8	**11**
Yorkshire West Riding	35	**41**
Glasgow	25	**58**
Edinburgh	14	**11**
Food-poisoning		
Greater London	33	**36**
Lancashire	30	**25**
Liverpool C.B.	8	**14**
Warwickshire	2	**26**
Birmingham C.B.	1	**25**
Glasgow	7	**12**
Measles		
Devonshire	41	**118**
Ashburton U.D.	0	**81**

MEDICO-LEGAL

Soul and Conscience Reports

The Chairman of the B.M.A. Scottish Council, Dr. J. Riddell, has written to all doctors in Scotland commenting on " soul and conscience " reports. The letter refers to cases in which a family doctor has felt unable to sign a death certificate, either because he has not seen the patient in the weeks immediately preceding death or because of some other kind of uncertainty. It has been reported, says Dr. Riddell, that in such cases the procurator-fiscal asks a second doctor who had not previously seen the patient to give a " soul and conscience " report as to the cause of death. On receipt of the report permission to bury the body is given by the procurator-fiscal.

The Crown Office has stated that such action on the part of procurators-fiscal is in accordance with instructions laid down by the Lord Advocate. These instructions make it clear that the fact that the cause of death is, in the medical sense, unexplained is not a ground for ordering a post-mortem examination at the public expense if the extrinsic circumstances sufficiently explain the cause of death and do not raise a suspicion of criminality or negligence. Therefore, so long as there is no suspicion of criminality or negligence, the procurator-fiscal is not concerned with ascertaining the actual cause of death where this is not apparent from an external examination of the body. Nor is he interested in cases which might give rise to civil actions.

The Scottish Council has told the Crown Office that doctors are more likely to feel that in cases of doubt crime cannot be excluded until the cause of death has been definitely ascertained, usually by post-mortem examination. It was suggested by the Crown Office, however, that as the procurator-fiscal cannot go beyond the instructions of the Lord Advocate it is for the B.M.A. to advise its members that a death certificate, or a soul and conscience report, should not be issued by a doctor if he is in any doubt that death was not from natural causes.

The view of the Scottish Council is that a death certificate, or a soul and conscience report, should be given only when the certifying doctor is absolutely sure that criminal activity was not the direct or a contributory cause of death.

MEDICAL NEWS

Sergeant-Surgeon to the Queen

Sir RALPH MARNHAM, surgeon to the Queen since 1953 and before then surgeon to George VI, has been appointed sergeant-surgeon to the Queen. He succeeds Sir ARTHUR PORRITT, who has resigned. Sir Ralph, who is surgeon to St. George's Hospital, London, was educated at Gonville and Caius College, Cambridge, and at St. George's. He was president of the Association of Surgeons of Great Britain and Ireland in 1965.

£500,000 Gift for Cancer Research

Mr. MICHAEL SOBELL, of Bakeham House, Englefield Green, Surrey, has given £500,000 for the purpose of acquiring premises in London that will serve as a permanent head-quarters for the College of Pathologists and the British Empire Cancer Campaign for Research. The object is to facilitate and strengthen collaboration between these two bodies.

Fellowships in Medicine

The following appointments have been made by the Medical Research Council to Fellowships in Medicine for the academic year 1967–8.

Medical Research Council Travelling Fellowships : Dr. D. C. FLENLEY, Dr. A. V. HOFFBRAND, Dr. D. OGSTON, Dr. B. E. B. MOSELEY, Dr. J. A. SONNABEND, and Dr. P. C. WILKINSON. *Sir Henry Wellcome Travelling Fellowships :* Dr. M. FRIEDMAN, Dr. T. A. MCNEILL, Dr. D. P. ROSE, Dr. J. STEINER, and Mr. J. W. TURNER. *Clinical Research Fellowships :* Dr. S. P. ALLISON, Dr. J. A. BIRTCHNELL, Dr. T. J. PETERS, Dr. G. M. STERLING, and Dr. R. P. H. THOMPSON. *Dorothy Temple Cross Research Fellowship :* Dr. I. D. GREEN. *Alexander Pigott Wernher Memorial Trust Fellowships in Ophthalmology and Otology :* Mr. M. D. SANDERS and Dr. B. SHUKLA. *United States Public Health Service Fellowships :* Dr. J. BRADLEY, Dr. D. R. FERGUSON, Dr. H. FOX, Dr. J. A. MCBRIDE, Dr. R. O. WELLER, and Dr. M. R. WILLS. *Lilly International Fellowship :* Dr. F. J. GOODWIN.

Drug Industry Report

According to a leaflet issued by the Association of the British Pharmaceutical Industry only 2d. per person per day is spent on N.H.S. medicines, compared with 17d. on smoking and alcohol. In hospitals pharmaceutical supplies are said to account for only 2.4% of the total expenditure. The association points out that the number of patients in mental hospitals has fallen by 25,000 since the mid-1950s, when the tranquillizers and antidepressives were first marketed. It also notes that the introduction of the sulphonamides, penicillin, and other antibiotics has reduced the number of deaths from puerperal sepsis from 657 in 1935 to 5 in 1965. The industry in Britain spends about £12m. a year on research. In 1966 its return on capital averaged 20% to 25%, "a figure which is in line with that achieved by the successful and efficient sector of British industry."

Hospital Pharmacy Staffing

The London branch of the Guild of Public Pharmacists has found in its area an overall shortage of hospital pharmacists (35%). According to a survey less than half the established posts have been filled by the same pharmacist for more than two years. Of the pharmacists who resigned their posts during the 12 months preceding the survey less than a third took up other hospital appointments. About half the reported vacancies for the senior grades have remained unfilled for over two years. In the basic grade the deficiency of full-time pharmacists exceeded 80%. Besides indicating a serious shortage of staff in the area, the survey has suggested that the service is not considered by the possible young entrant to offer a worth-while career.

Royal Medical Benevolent Fund

At the annual general meeting, held on 5 September, the following officials were re-elected: *president,* Sir ZACHARY COPE ; *honorary secretary,* Dr. T. ANWYL-DAVIES ; *honorary treasurer,* Mr. G. H. BATEMAN. During 1966 a total of £55,482 was distributed in grants and annuities.

Royal Society of Tropical Medicine and Hygiene

Professor A. CORRADETTI, director of the department of parasitology and entomology, Istituo Superiore di Sanità, Rome, and Dr. CLAY G. HUFF, chief parasitologist at the Naval Research Institute in Washington, have been elected Honorary Fellows of the Royal Society of Tropical Medicine and Hygiene.

Designing for the Disabled

Special facilities for the disabled should be provided in public buildings. This is advocated in an article in the September issue of the *Journal of the Royal Institute of British Architects*. The writer, Mr. Selwyn Goldsmith, an architect and himself partly disabled, is the author of *Designing for the Disabled* (see *B.M.J.*, 1964, 18 January, p. 172). In planning buildings, he says, architects should think in terms of a normal population and of a parallel and distinct abnormal population as well. There is a moral obligation on the architect and his client to provide suitable arrangements for the physically handicapped. Usable lavatory facilities, he points out, are commonly of much greater concern to disabled people than the presence or absence of steps at the entrances to buildings.

Extension of Benefit

A scheme amending the Pneumoconiosis, Byssinosis and Miscellaneous Diseases Benefit Scheme, 1966, adds three diseases to those in respect of which benefit is payable. They are carcinoma of the mucous membrane of the nose or associated sinuses and primary carcinoma of a bronchus or of a lung; papilloma of the bladder; and diffuse mesothelioma. The scheme came into operation on 31 August.

T.U.C. Conference

Delegates at the T.U.C. conference last week approved a motion urging the Government to take steps to safeguard the health of all workers using asbestos, and to introduce licensing and inspection arrangements. A resolution was also carried calling for the institution of an occupational health service.

World Medical Association

The address of Mr. H. W. Paines, honorary secretary of the British Supporting Group of the World Medical Association, is now 1 Sandy Lodge Way, Northwood, Middlesex.

Medical Guide for Ships

A medical guide for ships has been designed for use by all countries. It consists of a medical guide proper, a ship's medicine chest, and a medical code of signals. Each section is co-ordinated with the others, so that the task of the ship's master and of the doctor radioing advice is made as simple as possible. The guide has been sponsored by the International Labour Office, the International Maritime Consultative Organization, and the World Health Organization and is the first attempt to overcome the limitations of national guides. (H.M.S.O., £2.)

Animal Welfare

A Farm Animal Welfare Committee has been set up by the Minister of Agriculture and the Secretary of State for Scotland to advise on matters relating to the welfare of animals kept under intensive husbandry systems. The chairman is Professor H. R. Hewer, professor of zoology at Imperial College. Other members include Dr. M. H. Draper, of the physiology department, Edinburgh University; Dr. J. A. B. Gray, second secretary, Medical Research Council; and Major W. N. Scott, scientific secretary, Universities Federation for Animal Welfare.

People in the News

▶ Sir Harry Crane has been appointed chairman of the Industrial Injuries Advisory Council in succession to Professor Sir Arnold Plant.

▶ Dr. R. I. S. Bayliss has been appointed the McLaughlin Gallie Travelling Professor of the Royal College of Physicians and Surgeons of Canada. He will be visiting Canada from 8 October to 4 November.

News in Brief

The Luton and Dunstable Hospital medical centre, which was opened in April (see *B.M.J.*, 8 July, p. 120), plans to issue a journal three times a year. Its first number tells the story of the centre. Regular features will include postgraduate news, B.M.A. notes, and reviews and annotations.

Recent Publications

Your Home and Your Rheumatism, an illustrated booklet, is intended to help people who are disabled to overcome difficulties in their everyday living. The aids referred to in the text are listed at the end with addresses of suppliers. Copies of the booklet can be obtained from the Arthritis and Rheumatism Council, 10 Charing Cross Road, London W.C.2, price 2s., including postage.

Reports of a series of conference and discussion sessions held last year at the Scottish Hospital Centre are available in a single publication (*Collected Conference Reports, 1966*, Scottish Hospital Centre, Crewe Road South, Edinburgh 4, 10s.).

Selected Annotated Bibliography: Home Care Services of the Chronically Ill and Aged, revised 1967, prepared by the Institute of Gerontology, University of Iowa, Iowa City, Iowa, U.S.A.

Coming Events

Royal College of General Practitioners (South Ireland Faculty).—Annual postgraduate course, 2–6 October, University College, Cork. Details from Dr. John Gowen, Strand House, Youghal, County Cork.

King Edward's Hospital Fund for London.—Showing of filmstrips on voluntary services in hospitals, 4 October, Hospital Centre. Fee 6s. or 10s., including buffet lunch. Exhibition on display, "The Patient within the Community."

British Association of Manipulative Medicine.—Lecture by Dr. A. W. Spence on "Obesity," Thursday, 5 October, 8 p.m., in London. Details from honorary secretary, 3 Arundel Terrace, Brighton 7, Sussex.

Institute of Diseases of the Chest.—Free clinical demonstrations for medical practitioners, Fridays, 5 p.m., 6 October to 8 December, Institute's lecture theatre (in grounds of Brompton Hospital), Fulham Road, London S.W.3.

Carworth Europe.—Second annual symposium, "The Interaction of the Laboratory Animal with its Microflora," 6 October, Large Lecture Theatre, Physiological Laboratory, Downing Street, Cambridge. Details from Carworth Europe, Alconbury, Huntingdon.

British Medical Association (Edinburgh and South-east Scotland Branch).—Conference, "Better Medical Care—Which Road?" 7 October, David Hume Tower, Edinburgh University. Applications, enclosing 5s. registration fee, to B.M.A. Scottish House, 7 Drumsheugh Gardens, Edinburgh 3. It is hoped there will be a large attendance of B.M.A. members and others interested.

British Diabetic Association.—Symposium for general practitioners, 8 October, 11 a.m., King's College Hospital (School of Nursing Lecture Theatre), London S.E.5. Details from Dr. D. M. Hill, Royal Sussex County Hospital, Brighton 7.

Royal Free Hospital School of Medicine.—Inaugural address by Professor Sir John McMichael, F.R.S., 11 October, 3 p.m., Senate House, London W.C.1.

The Industrial Society.—Conference on industrial health, 12 October, Café Royal, London W.1. Details from Mr. Angus Stewart, Robert Hyde House, 48 Bryanston Square, London W.1.

Fever Hospital Medical Services Group and Association of Infectious Diseases Physicians.—Joint meeting, 13–14 October, St. Ann's General Hospital, Tottenham, London N.15. Details from Dr. S. R. Jamieson, Castle Hill Hospital, Castle Road, Cottingham, Yorkshire.

Institute of Urology.—Week-end Course on "Urology for Higher Examinations," 20–22 October. For details see advertisement on p. xxxvii.

Biochemical Society.—Meeting, 20–21 October, National Institute for Medical Research, Mill Hill, London N.W.7. Programme will include colloquium on "Functions of Nucleic Acids in the Cytoplasm." Details from Executive Secretary, Biochemical Society, 7 Warwick Court, London W.C.1.

British Council.—Course in anaesthesia in collaboration with the faculty of anaesthetists of the Royal College of Surgeons of England, 4–17 February 1968. Applications by 31 October. Details from Director, Courses Department, British Council, 97/99 Park Street, London W.1.

Societies and Lectures

For attending lectures marked ● a fee is charged or a ticket is required. Applications should be made first to the institution concerned.

Monday, 18 September

Chelmsford Medical Education and Research Trust.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 5.30 p.m., clinical meeting.

Kingston-upon-Thames Medical Centre.—5.15 p.m., Dr. M. E. A. Powell: Slide Seminar—Kidney.●

Medical Research Council.—At National Institute for Medical Research Laboratories, Hampstead, London N.W., 4.30 p.m., Dr. D. H. Lewis: Family at Sea—a Study of Crowded Isolation.

Tuesday, 19 September

B.B.C. 1 Television.—11.20 p.m. (approximately) medicine today: Fits. (Sponsored by A.S.M.E.)

Institute of Obstetrics and Gynaecology.—At Hammersmith Hospital, (1) 2 p.m., Mr. D. J. Neal Smith: Scope and Value of Cervical Cytology Clinics; (2) 4.30 p.m., Professor V. Dobrovici (Rumania): Obstetrical Attendance in Rumania—a New Interpretation of the Trial Labour. (Admission by ticket only, obtainable from Secretary, Institute of Obstetrics and Gynaecology, Chelsea Hospital for Women, London S.W.)●

Leukaemia Research Fund.—At Institute of Child Health, London W.C., 5.30 p.m., Professor H. S. Kaplan (Stanford University, U.S.A.): On the Natural History of the Murine Leukaemias.●

WHIPPS CROSS HOSPITAL MEDICAL EDUCATION CENTRE.—1 p.m., clinical meeting.

Wednesday, 20 September

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 12 noon, surgical meeting.

STOKE MANDEVILLE HOSPITAL.—6 p.m., Dr. D. C. Watt: Psychiatric Examinations and Diagnosis.

Friday, 22 September

KINGSTON-UPON-THAMES MEDICAL CENTRE.—2.30 p.m., Dr. A. A. Cunningham: Neonatal Resuscitation.

NORTHAMPTON MEDICAL SOCIETY.—8 for 8.30 p.m., presidential address by Dr. D. G. H. MacQuaide.

SUSSEX POSTGRADUATE MEDICAL CENTRE. — At Brighton General Hospital, 8.30 p.m., Professor G. M. Carstairs: Over-population and Behaviour Pathology—Observations in Animals and Man.

Appointments

ARMY.—E. G. Muir, M.B., M.S., F.R.C.S. (honorary consultant in surgery to the Army).

NATIONAL HOSPITALS FOR NERVOUS DISEASES.—H. Ludman, M.B., F.R.C.S. (consultant surgeon in neuro-otology at the National Hospital, Queen Square, London W C.).

NORTH-EAST METROPOLITAN REGIONAL HOSPITAL BOARD.—R. H. Robinson, M.B., F.F.A. R.C.S. (consultant anaesthetist to Harlow Group of Hospitals).

SOUTH-EAST METROPOLITAN REGIONAL HOSPITAL BOARD.—Dorothy J. Whitney, M.B., F.R.C.S., M.R.C.O.G. (consultant in obstetrics and gynaecology, Mid-Sussex group) ; E. B. Lewis, M.B., B.Chir., F.F.A. R.C.S. (consultant in anaesthetics, South-east Kent group) ; J. L. Dawson, M.B., M.S., F.R.C.S. (consultant in general surgery, Bromley group) ; B. A. Latham, M.B., M.R.C.P., M.R.A.C.P., D.Phys.Med. (consultant in physical medicine, Brighton and Lewes group) ; A. K. McKinlay, B.M., F.F.R., D.M.R.D. (consultant in radiology, Woolwich group) ; T. A. Casey, M.B., M.Ch., F.R.C.S., D.O. (consultant in ophthalmology, Tunbridge Wells, Central Kent, and Brighton and Lewes groups) ; P. J. Jennings, M.B., F.R.C.S. (consultant in general surgery, Medway and Gravesend group) ; J. Rhodes, M.B., F.F.R., D.M.R.D. (consultant in radiology, Eastbourne and Hailsham groups) ; J. T. Snow, M.B., F.R.C.S., D.O. (consultant in ophthalmology, South-east Kent and Canterbury groups).

New Issues of Specialist Journals

Obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London W.C.1.

JOURNAL OF NEUROLOGY, NEUROSURGERY AND PSYCHIATRY

Contents of the August issue are as follows :

Effects of Neonatal Hypoglycaemia on the Nervous System : a Pathological Study. John M. Anderson, R. D. G. Milner, and Sabina J. Strich.

Peripheral Neuropathy of Metachromatic Leucodystrophy : Observations on Segmental Demyelination and Remyelination and the Intracellular Distribution of Sulphatide. A. D. Dayan.

Independence of the Galvanic Skin Reflex from the Vasoconstrictor Reflex in Man. B. J. Prout.

Excitability of Spinal Motor Neurones in Normal Subjects and Patients with Spasticity, Parkinsonian Rigidity, and Cerebellar Hypotonia. P. Zander Olsen and E. Diamantopoulos.

An Improved Technique for Radial Nerve Conduction Studies. Allan W. Downie and Thomas R. Scott.

Laterality Differences in the Perception of Pressure. Eileen Fennell, Paul Satz, and Robert Wise.

Granulomatous Meningitis and Diffuse Parenchymatous Degeneration of the Nervous System Due to an Intracranial Epidermoid Cyst. B. E. Tomlinson and John N. Walton.

Subacute Necrotizing Encephalopathy in an Acidotic Child. Peter G. Procopis, Brian Turner, and George Selby.

Does Pregnancy Increase the Risk of Multiple Sclerosis ? Uri Leibowitz, Aaron Antonovsky, Rachel Kats, and Milton Alter.

Choreoathetosis in Porto-systemic Encephalopathy. P. J. Toghill, A. W. Johnston, and J. F. Smith.

Long-term Effects of Anterior Temporal Lobectomy on Certain Cognitive Functions. C. B. Blakemore and Murray A. Falconer.

Depressive Symptoms in Parkinson Patients Referred for Thalamotomy. J. W. Warburton.

Metabolic Balances of Copper in Patients with Hepatolenticular Degeneration Submitted to Vegetable and Mixed Diets. Horacio M. Canelas, Francisco Bastos de Jorge, and Waldir A. Tognola.

Plasma and Erythrocyte Magnesium in Huntingdon's Chorea. Laura W. Fleming, Montagu G. Barker, and William K. Stewart.

Book Reviews.

Volume 30, No. 4. Yearly subscription (6 numbers) £4 4s., abroad £4 15s.

BRITISH JOURNAL OF VENEREAL DISEASES

Contents of the September issue are as follows :

Editorial.

Gonococcal Bartholinitis. E. Rees.

Demethylchlortetracycline in the Treatment of Gonorrhoea. R. R. Willcox.

Therapeutic Trial of Trimethoprim as a Potentiator of Sulphonamides in Gonorrhoea. G. W. Csonka and G. J. Knight.

Gonorrhoeal Urethritis in Males Treated with One Oral Dose of Oxytetracycline. D. G. McLone, J. D. Kiley, and J. F. Hackney.

Immunofluorescent Antibody Technique in the Diagnosis of Gonorrhoea by Direct Smears from the Female. J. M. D. Gallwey, C. S. Nicol, and M. Ridley.

Treatment of Relapses and Re-infections in Non-specific Urethritis. A. I Morrison.

Osteolytic Lesions in Early Syphilis. M. F. Bauer and C. M. Caravati, Jr.

General Paralysis of the Insane with Gumma of Skull. S. B. Mahapatra.

Haemagglutination Test utilizing Pathogenic *Treponema pallidum* for the Sero-diagnosis of Syphilis. T. Rathlev.

Fluorescent Treponemal Antibody Inhibition Test. A. E. Wilkinson.

Treponemal Immobilization Tests in Leprosy. H. G. S. Ruge.

Metronidazole in Human Infections with Syphilis. A. H. Davies.

A Note on the Effect of Metronidazole on the Nichols Strain of *Treponema pallidum in vitro* and *in vivo*. A. E. Wilkinson, P. Rodin, J. A. McFadzean, and S. Squires.

Improved Methods of Contact Tracing. B. Muspratt and L. I. Ponting.

Comparison of Amphotericin B and Nystatin Pessaries in *Candida* Infection of the Vagina. G. W. Csonka.

Herpes Genitalis : Clinical and Virological Studies. J. D. J. Parker and J. E. Banatvala.

Book Review. Notes. Abstracts.

Volume 43, No. 3. Yearly subscription (4 numbers) £3 3s., abroad £3 10s.

THORAX

Contents of the September issue are as follows :

Heterograft Aortic Valve Replacement : Initial Follow-up Studies. M. F. O'Brien, J. K. Clarebrough, I. G. McDonald, G. S. Hale, H. S. Bray, and J. F. Cade.

Some Histological Features of Canine Cardiac Transplants. Jacqueline Leandri.

Aspiration Biopsy of Thoracic Lesions. Anthony F. Lalli, Bernard Naylor, and Walter M. Whitehouse.

Cystic Thymomas and Thymic Cysts : A Review. N. H. Dyer.

Functional Disturbance in Hiatal Hernia in Infants and Children. A. R. Chrispin and G. W. Friedland.

Mixed Glandular and Squamous-cell Carcinoma of the Bronchus. D. J. B. Ashley and H. Duncan Davies.

Acute Wegener's Granulomatosis. David Leak and G. P. Clein.

Tridimensional Photographic Reconstruction in a Study of the Pathogenesis of Honeycomb Lung. J. Cortez Pimentel.

Regional and Overall Inequality of Ventilation and Blood Flow in Patients with Chronic Airflow Obstruction. M. C. F. Pain, J. B. Glazier, H. Simon, and J. B. West.

Survey of Spontaneous Pneumothoraces in the Royal Air Force. I. R. Cran and C. A. Rumball.

Congenital Oesophageal Achalasia in the Dog. Richard J. Earlam, Paul E. Zollman, and F. Henry Ellis, jun.

Communication Between the Left Ventricle and Right Atrium. R. S. Barclay, J. M. Reid, E. N. Coleman, J. G. Stevenson, T. M. Welsh, and N. McSwan.

Proceedings of the Thoracic Society.

Volume 22, No. 5. Yearly subscription (6 numbers) £4 4s., abroad £4 15s.

Universities and Colleges

LONDON

Dr. Felix Beck, senior lecturer at University College, Cardiff, has been appointed to the readership in anatomy tenable at the London Hospital Medical College.

The title of reader in oncology has been conferred on Dr. J. G. Azzopardi, in respect of his post at the Royal Postgraduate Medical School.

PH.D.—*In the Faculty of Medicine :* M. J. Creek.

BIRMINGHAM

Appointments.—Dr. P. J. K. Maskery (temporary lecturer, Department of Obstetrics and Gynaecology) ; Dr. S. R. Meadow (senior research fellow, Institute of Child Health) ; Mr. G. D. Oates (part-time lecturer in general surgery for dental students, Department of Surgery).

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW

On 4 September the following were admitted Fellows *qua* Surgeon: O. Z. A. El Mannan, K. N. Ramaswamy, M. K. Rana, J. M. Urasa ; Members *qua* Physician: A. P. Agarwal, M. K. Attia, W. R. Chapman, A. W. Dickie, J. F. Mackay, V. Mahadev, J. D. H. Mahony, M. Nuruzzaman, B. K. Pal, A. K. Rastogi, A. Razzaq, S. C. Shah, V. Singh, P. N. Srivastava, C. B. C. Wariyar.

SOCIETY OF APOTHECARIES OF LONDON

L.M.S.S.A.—K. P. Adamson, M. A. M. Ali, I. E. A. Alloub, N. F. Angley, P. B. Arteen, A. R. Crawford, M. A. El Batata, M. I. El Gamal, N. R. H. El-Maraghi, A. R. Erlam, M. A. Gad, E. Gordon, I. Greenhalgh, K. A. S. A. B. Hamadah, C. W. H. Harrison, S. R. Hirsch, I. T. Houghton, S. M. A. Khalik, T. C. Ko, A. Kumar, B. Magnusson, A. K. Mangat, B. S. Mangat, J. F. McCurdy, S. R. Osmani, A. J. Polyzoides, A. F. M. Radwan, K. Ratib, G. F. Salib, E. Savides, B. Sen, R. K. Sharma, R. S. Shenouda, A. K. Shinnawi, Y. M. Sobhy, C. M. Squire, S. G. Tadros Attalla, J. D. Timothy, K. R. Visvanathan, N. R. Youssef, G. C. D. Zaphiropoulos.

DIPLOMA IN INDUSTRIAL HEALTH.—D. Ashcroft, E. Bougas, W. E. Brooke, C. P. Cooper, G. Dalton, D. Dean, P. Drummond, S. Ellison, E. M. Ensor, E. U. Essien, S. H. M. Logan, D. E. Oakley, J. W. Porter, D. G. L. K. Russell, D. B. Sugden, W. G. Thomson.

DIPLOMA IN MEDICAL JURISPRUDENCE (CLINICAL). D. P. Brown, M. E. Glanvill, J. K. Murphy, A. N. Pearson.

DIPLOMA IN MEDICAL JURISPRUDENCE (PATHOLOGY). —R. S. Forrester, P. Pullar.

Deaths

Clyde.—On 20 August 1967, at his home, Neil Provan Rutherford Clyde, M.B., Ch.B., Squadron Leader, R.A.F.M.S. (retired), aged 57.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON W.C.1. TELEPHONE: 01-387 4499. TELEGRAMS: *Aitiology, London W.C.1.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.

Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs.

ADVERTISEMENT AND SUBSCRIPTION ORDERS should be addressed to The Manager at B.M.A. House, London, or at 415 Bourke Street, Melbourne, Victoria, Australia.

MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the British Medical Association, B.M.A. House, London, or to the Scottish Secretary, B.M.A. Scottish Office, Drumsheugh Gardens, Edinburgh.

BRITISH MEDICAL JOURNAL

LONDON SATURDAY 23 SEPTEMBER 1967

Pointers

Leukaemia: Survey in Greater London (p. 755) gives "weak support" for clustering of leukaemia in children. Survey in Lewisham (p. 759) finds no evidence of clustering of the disease in both adults and children. Leader at p. 750.

Colonic Diverticulosis: Transit times of food residues studied radiographically were substantially shorter than normal in patients with diverticula or irritable colon syndrome (p. 760). Study of prevalence of diverticulosis in healthy volunteers in the Oxford area shows incidence of one in three in the over 60's with a female preponderance (p. 762). Letter at p. 800. Leader at p. 751.

Burned Hands: Small children grasping electric-fire elements sustain severe injury requiring prolonged treatment, and the importance of prevention of such accidents is emphasized (p. 764).

Common Cold: Half the volunteers inoculated with "new" respiratory virus developed colds, and half of these subjects showed rising titres of antibody against the virus (p. 767). Leader at p. 752.

Polyarthritis in Leprosy: Syndrome simulating acute rheumatoid arthritis in two patients with erythema nodosum leprosum may have been due to an autoimmune mechanism (p. 770).

Epidemiology of Infectious Hepatitis: Seasonal trend and association between incidence of disease and poor living conditions was noted in a three-year study in Leicester, but no criteria of transmission were elucidated which could assist in preventive measures (p. 773).

Refsum's Syndrome: Three generations of a family investigated but no evidence of biochemical abnormality found in any one except the two patients who were siblings (p. 777).

Case Reports: Peritonitis causing respiratory failure (p. 779); Procainamide incriminated in lupus-like syndrome (p. 780); Hypoparathyroidism and malabsorption syndrome (p. 781); Schizophrenia in a male pseudohermaphrodite (p. 783); Spontaneous haemorrhage from tongue (p. 784).

Today's Drugs: Tolnaftate (p. 785)

Warming Blood: Description of appliance capable of raising blood temperature from 4° to 37° C. in five minutes (p. 787).

Alcohol and Traffic Safety: Proceedings of international conference reviewed (p. 788).

Rehabilitation of Congenital Handicap: Orthopaedic contribution to the management of children successfully operated for myelomeningocele (p. 791).

Twenty-first World Medical Assembly: Report of Madrid conference (p. 795). Leader on this page.

Vocational Training for General Practice: G.M.S. Committee debate (*Supplement*, p. 131). Leader at p. 754.

World Medical Assembly

Last week in Madrid the World Medical Association held its twenty-first General Assembly. Delegations from 32 national member associations attending it included those of the United States, Britain, Australia, Canada, India, Pakistan, most of the countries of Continental Europe, and of countries so far apart as the Philippines, Ecuador, and the Republic of China. After a three-day business meeting there were scientific sessions on the population explosion and birth control and "Medicine and Society." These were appropriate themes for an Assembly in Spain, said Dr. Alfonso de la Fuente in his presidential address, for the Spanish medical profession desired above all to uphold the dignity of the individual and to stress the dangers of weakening family life and of losing sight of the traditional doctor–patient relationship in university medical education. An account of the proceedings appears at page 795.

The W.M.A. is once again showing an interest in some of the more urgent problems of modern medicine. For this much credit must go to the Secretary General, Dr. Alberto Romualdez. Medical ethics has always been a field to which the W.M.A. has contributed fruitfully. Today the relevance of its Declaration of Helsinki,[1] which sets out guiding principles for the clinical research worker, is greater than ever. The public endorsement of these principles by responsible medical bodies in different countries, such as recently in Britain by the Royal College of Physicians of London,[2] is gradually extending their influence. Early in its existence the W.M.A. adopted an International Code of Medical Ethics, and its Declaration of Geneva related the Hippocratic Oath to twentieth-century medicine. Too often the emphasis on the scientific and technical aspects in medical education leaves too little time for students to get a true understanding of the ethical obligations of a doctor. It was therefore welcome that this year the General Assembly, at the instance of the B.M.A., underlined the importance of adequate undergraduate instruction in medical ethics, and recommended that on graduation doctors should be given copies of the Declarations of Geneva (or the Hippocratic Oath) and of Helsinki. This is something that every medical school should be ready to do.

Search for an international definition of the precise moment of death concerns more than just the decision when an organ for transplantation may be removed, important though that is. The problem is sharpened by a physician's ability artificially to maintain circulation and respiration more or less indefinitely. When is it right to switch off the machines? The W.M.A. decided to go on studying this question, helped by evidence collected in a special number of the *World Medical Journal*[3] and the findings of last month's Congress on International Medical Law in Ghent. Already there is legislation in some countries regulating organ transplantation, so the urgency of finding an acceptable definition is plain.

The Assembly showed its awareness of the situation created by world overpopulation and endorsed family planning, though it emphasized that

© *British Medical Journal*, 1967. All reproduction rights reserved.

the final responsibility must be personal. It invited each national organization to study the problem. Those who might consider this a mild achievement, or who regret the absence of any mention of the dangers of excessive child-bearing on the health of the mother or her ability to bring up her family healthily, should remember that the W.M.A.'s resolution had to prove acceptable to doctors from all over the world and of all creeds.

Medical education is another of the W.M.A.'s chosen fields. The Assembly approved plans to hold a fourth World Conference, on the theme "Medical Education: A Collective Responsibility." Under this it is hoped to include the education of paramedical workers. Certainly their increasingly important place in the medical team justifies this. The conference will be held in Europe in 1972, and national medical associations are to be asked to suggest subjects and speakers and to set about raising funds for it. With Britain's entry into the Common Market on the cards, this conference could provide a useful clearing house for information about medical education in Europe, and for this reason alone should evoke the interest of the profession in Britain.

The W.M.A. is a federation of national medical associations from 59 countries, together representing some 700,000 doctors.[4] Through its regional offices and its committee on medico-social affairs, which deals with the payment of doctors and social legislation affecting medical practice, it keeps member associations in touch with developments in other parts of the world. As communications shorten and the world contracts an increasing number of medical questions need debate or action on an international rather than a national or regional level. Some are most appropriately dealt with by the World Health Organization, an intergovernmental body; others by the W.M.A. What the W.M.A. is able to achieve depends on how much its members are prepared to put into it. Medicine is not one of the fields in which Britain has declined as a world force, and the British Medical Association should not be grudging in its support for the W.M.A.

[1] See *Brit. med. J.*, 1964, **2**, 177.
[2] Ibid., 1967, **3**, 429.
[3] *Wld med. J.*, 1967, **14**, No. 5 (September–October, 1967).
[4] Romualdez, A. Z., *Medecina de España*, 1967, **3**, No. 14, p. 19.

Epidemiological Studies of Leukaemia

The specific aetiology of human leukaemia is unknown. But the leukaemias of some animals (mice and cats) can undoubtedly be transmitted by specific agents with viral characteristics.[1 2] It is therefore tempting to seek evidence for leukaemogenic viruses or infective agents in man.

Such evidence can be obtained in two ways—firstly, by a direct search for identifiable virus particles in leukaemic cells, and secondly by an epidemiological approach aimed at detecting associations of cases of leukaemia in time and place. Though the experimental quest for specific infective agents in human leukaemia has so far been inconclusive,[3] investigators in different countries have reported "clustering"—that is, the close occurrence in place and time of cases of leukaemia. Among the earliest reports are those of C. Aubertin and P. G. Bosviel[4] and C. E. Kellett.[5] More recently G. Knox[6] has presented statistical evidence for clustering in north-east England. These and other observations[7 8] support the possibility that an infective agent might contribute in some way to the causation of human leukaemia. But epidemiological opinion is not unanimous, because some investigators[9–12] have failed to find evidence of clustering.

The detection of significant clustering requires reliable diagnostic and statistical techniques, and in this issue of the *B.M.J.* we publish two more papers reporting careful analyses of cases in the London area. Dr. S. P. Lock and Mrs. Maxine Merrington (page 759) have analysed 115 cases of all types of leukaemia in both adults and children diagnosed between January 1957 and December 1963. The area covered was the former London borough of Lewisham. In the other paper Drs. Morwenna M. Till, R. M. Hardisty, M. C. Pike, and Richard Doll (page 755) report their studies of a larger series restricted to children who developed leukaemia under 10 years of age while resident in Greater London during the period 1952–61. Lock and Merrington confined their analysis to the date and place of residence of the patient at the onset of the disease, while Till and her colleagues extended their study to include information about the patients' date and place of birth. The latter workers point out that factors of aetiological importance are likely to exert their effect a considerable time before the disease becomes clinically apparent, and indeed the experimental work on the animal leukaemias has shown that the disease was most successfully transmitted when the animals were inoculated at or about the time of birth. Thus, if a virus is a cause of the disease, space-time clustering of births rather than time of onset might be more likely.

Both groups of workers used similar statistical techniques but reach somewhat different conclusions. Lock and Merrington could not find evidence of clustering of leukaemia, though their data do not provide evidence against clustering of one or other subtypes of leukaemia. They point out that the same statistical technique has shown clustering of cases of Burkitt's lymphoma in Africa, and furthermore that other statistical methods, while showing clustering of infectious diseases such as poliomyelitis and infectious hepatitis, have failed to show clustering in leukaemia. However, Till and colleagues give some support, though weak, for the general hypothesis that cases of leukaemia tend to occur in clusters more often than would be expected by chance alone, the evidence for clustering being stronger at birth than at onset of the disease. They thus provide some evidence for the possibility of the existence of a contagious agent in human leukaemia.

The difference between the conclusions reached in the two papers are probably the result of differences in the data analysed. The negative findings of Lock and Merrington,

[1] Gross, L., *Proc. Soc. exp. Biol. (N.Y.)*, 1951, **76**, 27.
[2] Jarrett, W. F. H., *Proc. roy. Soc. Med.*, 1966, **59**, 661.
[3] Negroni, G., ibid., 1966, **59**, 662.
[4] Aubertin, C., and Bosviel, P. G., *Arch. Mal. Cœur*, 1923, **16**, 696.
[5] Kellett, C. E., *Arch. Dis. Childh.*, 1937, **12**, 239.
[6] Knox, G., *Brit. J. prev. soc. Med.*, 1964, 18, 17.
[7] Heath, C. W., Manning, M. D., and Zelkowitz, L., *Lancet*, 1964, **2**, 136.
[8] Mainwaring, D., *Brit. J. prev. soc. Med.*, 1966, **20**, 189.
[9] Ederer, F., Myers, M. H., and Mantel, N., *Biometrics*, 1964, 20, 626.
[10] Barton, D. E., David, F. N., and Merrington, M., *Ann. hum. Genet.*, 1965, **29**, 97.
[11] Ager, E. A., Schuman, L. M., Wallace, H. M., Rosenfield, A. B., and Gullen, W. H., *J. chron. Dis.*, 1965, **18**, 113.
[12] Lundin, F. E., Fraumeni, J. F., Lloyd, J. W., and Smith, E. M., *J. nat. Cancer Inst.*, 1966, **37**, 123.

while statistically valid, would not necessarily exclude the existence of an infectious agent in human leukaemia. If, on the other hand, leukaemia is a truly infectious disease, it would be more useful to look for an association between the date and place of residence of one child during the period of infectivity and that of another child during the period of susceptibility to the disease. This suggestion might be extended to a study of the parents of affected children, since they will have had the closest and longest contact with the child. But this illustrates the complexity of the epidemiological problem, since nothing is known of these presumed periods of infectivity and susceptibility, and if the proposition is valid the collection of such information will depend on the development of more refined analytical methods.

The hypothesis that human leukaemia is a contagious disease is appealing, and the evidence from the animal leukaemias provides in itself sufficient reason for the experimental approach in studying the human disease. Isolation of a causative organism offers the hope of rational and effective treatment, both immunological and chemotherapeutic, which in the final analysis can be achieved only in the experimental laboratory. But apart from providing evidence for infective agents the epidemiological approach might point to environmental factors which could be controlled. If leukaemia is an infectious disease it must be one of a very special kind, and perhaps the epidemiologist will discover some of these peculiarities. Moreover, in view of its potentially useful epidemiological value the history of all cases of leukaemia should be as detailed as possible and should include information on exposure to other human infections or prolonged contact with animals, insects, and chemical agents.

Diverticular Disease of the Colon

Maxwell Telling and O. C. Gruner,[1] of Leeds, gave an exhaustive account in 1917 of the natural history of diverticulosis of the colon. But not until recently was much attention paid to the aetiology of this common and increasingly important condition.

The diverticula may occur anywhere in the colon but congregate especially in the sigmoid. They lie in two columns alongside the lateral taeniae coli, where they are often overlapped by the appendices epiploicae. Unlike diverticula of the small bowel, which project into the mesentery, the colonic diverticula never protrude primarily into the mesocolon. The distribution of colonic diverticula corresponds precisely to the points of penetration of the blood vessels into the bowel wall, as H. Drummond[2] first showed, and they doubtless produce areas of weakness in the colonic musculature.

Basil Morson[3] made an important contribution to our knowledge of the aetiology of this disease by taking attention away from the saccules themselves and concentrating more on the colonic wall. He reported his investigations of 173 specimens of colon removed for diverticulitis at St. Mark's Hospital, London. Of these, 112 (64%) showed evidence of diverticulitis, which was extensive in 67 and focal in 45 cases. In 61 specimens there was no inflammation at all, and 5 of these indeed did not even show diverticula, yet in all cases operation had been performed because diverticulitis had been diagnosed on both clinical and radiological evidence. However, all the specimens showed striking abnormalities in the muscle wall. The taeniae coli were thickened and almost cartilaginous; the circular muscle was also thickened and arranged in concertina-like folds, with the orifices of the diverticula opening between their corrugations. This thickening of the plain muscle appeared to be a shortening rather than a true hypertrophy, and it accounted for the characteristic redundancy of the mucosa, which was itself thrown into folds and appeared to contribute to the obstruction so common in this condition.

N. S. Painter and S. C. Truelove[4] [5] have shown by cineradiography and other methods that the resting pattern of pressures in the normal sigmoid colon and in the colon affected by diverticulosis is the same, but very high pressures develop in the diseased segments in response to morphine and prostigmine. In these cases cineradiography showed that the colon was divided by contraction rings into a series of segments whose outflow was obstructed, and the consequent localized high pressures were seen on occasions to distend the related diverticula considerably. There is thus in diverticular disease good evidence of abnormal segmentation and the generation of high pressures after certain drugs, together with histological proof of an abnormal circular muscle. Investigation of other causes of excessive segmentation—diet, drugs, and purgatives, for example—may lead to important information on the pathogenesis of diverticulosis. Dietary factors may well be of importance. Diverticulosis is a common condition in so-called civilized communities which enjoy a refined diet and is extremely rare in less sophisticated populations living on a bulky vegetable diet.[6]

Not only are we still ignorant about the exact aetiology of diverticulosis, but also there is a surprising lack of accurate information on its frequency in the population as a whole. The incidence has been calculated from barium-enema studies on hospital patients and from post-mortem examinations, both highly selected population groups. However, the investigations have certainly given some useful information. Thus T. P. Dearlove,[7] in his extensive necropsy study of nearly 7,000 cases at the Royal Adelaide Hospital, found that diverticulosis was almost unknown under the age of 40 years. In the 40s the incidence rose to approximately 1%, in the 50s to 1.7%, in the 60s to 3.5%, and in patients over the age of 70 years to 7%. Large series of patients examined by barium enema have shown diverticula in 5 to 10% of the cases.

In this issue of the *B.M.J.* Dr. Truelove together with Drs. O. N. Manousos and K. Lumsden present an important study of a barium follow-through examination on 109 persons without gastrointestinal symptoms (page 762). Twenty were found to have diverticula. Above the age of 60 15 out of 43 people had them (about one in three), and below that age 5 out of 66. None of the 14 people under the age of 40 had any diverticula. The condition was more common in women than in men. Though the numbers are comparatively small, the study is of particular value in that it deals with a population either healthy or at least completely free of gastrointestinal symptoms. It therefore gives a good indication of the incidence of colonic diverticula in the general population in Britain.

As to the aetiology of colonic diverticula, it is interesting that these workers, in a separate study reported at page 760, have found the colonic transport time to be considerably shorter in patients with diverticula than in normal persons, and the same fast transit time was noted in patients with the irritable colon syndrome. They conclude that their evidence supports the hypothesis that incoordinated colonic activity is the basic abnormality in diverticular disease of the large bowel.

---

[1] Telling, W. H. M., and Gruner, O. C., *Brit. J. Surg.*, 1917, 4, 468.
[2] Drummond, H., ibid., 1917, 4, 407.
[3] Morson, B. C., *Proc. roy. Soc. Med.*, 1963, 56, 798.
[4] Painter, N. S., and Truelove, S. C., *Brit. med. J.*, 1963, 2, 33.
[5] —— *Ann. roy. Coll. Surg. Engl.*, 1964, 34, 98.
[6] Campbell, G. D., *Brit. med. J.*, 1967, 3, 243.
[7] Dearlove, T. P., *Med. J. Aust.*, 1954, 1, 470.

New Respiratory Virus

The complex aetiology of acute respiratory disease has been gradually revealed during the past fifteen years with the discovery of one after another "new" virus. Each one in turn has been studied for its pathogenesis in man and eventually allotted a place in one of the various virus families on the basis of its physical, chemical, and morphological properties.

The myxovirus family, besides having the true influenza viruses A, B, and C, has had added to it five different parainfluenza viruses and probably also the respiratory syncytial virus. The adenovirus family contains 31 different serotypes, and the picornavirus family, the home of poliomyelitis, E.C.H.O., and Coxsackie viruses, now shelters about 80 rhinoviruses, all isolated from patients with common colds.

The veils of mystery surrounding respiratory illness are gradually being lifted. With the right technique one of these many organisms can increasingly be found to be the cause of disease. However, there still remains a fair proportion of cases in which nothing can be found to account for the patient's symptoms and the hunt is by no means over.

A new technique developed by B. Hoorn and D. A. J. Tyrrell[1] involved the use of fragments of trachea and nasal epithelium from the human embryo to provide an "organ culture" for the viruses. This procedure was found to increase the frequency of virus isolation from patients with colds to a considerable extent. The viruses grown in this way were sometimes familiar ones which could be grown in tissue culture, but it was quickly recognized that there were others which were clearly multiplying in the organ cultures and producing colds in volunteers, but refusing to behave like other viruses in ordinary tissue cultures.

D. Hamre and J. J. Procknow[2] had earlier isolated from students with colds some other fastidious viruses, which, though they grew in tissue culture, did so only with special techniques. J. D. Almeida and Tyrrell[3] then put these fastidious viruses and those grown on organ culture under the electronmicroscope and discovered not only that the two groups were morphologically similar but that they differed from the usual human respiratory viruses. Though the new viruses contain R.N.A. and are destroyed by ether, and have therefore some characters of the myxoviruses, in their structure they can be readily distinguished. In place of the fine frill surrounding the myxovirus particle well-spaced wedge-shaped projections can be seen in these viruses round the circumference of the particle. It was also noted that these human viruses were apparently identical in structure with a virus known to cause infectious bronchitis in fowls and with one causing hepatitis in mice.

So far as is known neither of these last two viruses is pathogenic for man, but antibody to mouse hepatitis virus has been detected in human sera, and J. W. Hartley and colleagues,[4] investigating respiratory illness among military recruits, detected during three successive winters a wave of serological changes suggesting that the recruits had experienced an epidemic of infection with mouse hepatitis virus or with a virus of a similar antigenic composition.

A further six strains of this virus with the new look were isolated by K. McIntosh and colleagues,[5] who extended their studies of respiratory disease to include organ culture. Since they had not included symptomless controls in their series, they were unable to be certain that the viruses were in fact responsible for the disease. The evidence was certainly suggestive, as was that obtained by Hamre and Procknow,[2] whose isolates were in every case but one from patients with illness. But it was clear that a strain would have to be tested in human volunteers under controlled conditions if this point was to be decided for certain.

In this issue of the *B.M.J.* Mr. A. F. Bradburne, Dr. M. L. Bynoe, and Dr. Tyrrell produce evidence that this virus has a pathogenic role (page 767). Twenty volunteers given saline remained healthy, whereas half of those given virus developed a fairly typical common cold with a profuse nasal discharge, mild fever, and a significant rise in serum antibody to the virus.

The connexion of what must now be recognized as a human respiratory pathogen with the morphologically identical fowl and mouse viruses has still to be determined. Preliminary results suggest they are serologically distinct, and it appears that we have a whole new virus family with possibly multiple serotypes. Another veil is down; our ignorance is less; but every additional virus must dampen our hopes for a vaccine to control acute respiratory illness.

---

[1] Hoorn, B., and Tyrrell, D. A. J., *Brit. J. exp. Path.*, 1965, **46**, 109.

[2] Hamre, D., and Procknow, J. J., *Proc. Soc. exp. Biol. (N.Y.)*, 1966, **121**, 190.

[3] Almeida, J. D., and Tyrrell, D. A. J., *J. gen. Virol.*, 1967, **1**, 175.

[4] Hartley, J. W., Rowe, W. P., Bloom, H. H., and Turner, H. C., *Proc. Soc. exp. Biol. (N.Y.)*, 1964, **115**, 414.

[5] McIntosh, K., Dees, J. H., Becker, W. B., Kapikian, A. Z., and Chanock, R. M., *Proc. nat. Acad. Sci. (Wash.)* 1967, **57**, 933.

Overwhelming Infection after Splenectomy

A late complication of splenectomy is fulminating generalized infection. This hazard was first reported in 1952 by H. King and H. B. Shumacker in five infants who had undergone splenectomy for hereditary spherocytosis.[1] Though the relationship between splenectomy and overwhelming infection has been doubted,[2 3] most people agree that there is a significant connexion between the two. Children are more vulnerable than adults, and most cases of infection occur within the first few years of splenectomy.[4 5]

A. J. Eraklis and his colleagues[6] have recently reviewed 467 cases of splenectomy followed up for at least three years, and in many instances up to ten years. They found that about 5% of patients died of overwhelming infection, and that the incidence of this disaster depended on the antecedent condition. No patient whose spleen was removed because of traumatic rupture, idiopathic thrombocytopenic purpura, extrahepatic portal-vein thrombosis and portal hypertension, or localized tumour died of infection. The incidence was very low in those with hereditary spherocytosis and aplastic anaemia, but it was higher in cases of thalassaemia major, cirrhosis of the liver, histiocytosis (Letterer–Siwe disease), and lipidosis (Niemann–Pick disease and Gaucher's disease). Four patients with the Wiscott–Aldrich syndrome all died of infection after splenectomy. The condition is characterized by thrombocytopenic purpura, recurrent infections, and eczema, and there is often an associated dysgammaglobulinaemia.[7] It is important to distinguish this condition from idiopathic thrombocytopenic purpura, for the former does not respond to splenectomy.

---

[1] King, H., and Shumacker, H. B., *Ann. Surg.*, 1952, **136**, 239.

[2] Gofstein, R., and Gellis, S. S., *Amer. J. Dis. Child.*, 1956, **91**, 566.

[3] Laski, B., and MacMillan, A., *Pediatrics*, 1959, **24**, 523.

[4] Smith, C. H., Erlandson, M., Schulman, I., and Stern, G., *Amer. J. Med.*, 1957, **22**, 390.

[5] Horan, M., and Colebatch, J. H., *Arch. Dis. Childh.*, 1962, **37**, 398.

[6] Eraklis, A. J., Kevy, S. V., Diamond, L. K., and Gross, R. E., *New Engl. J. Med.*, 1967, **276**, 1225.

[7] Aldrich, R. A., Steinberg, A. G., and Campbell, D. C., *Pediatrics*, 1954, **13**, 133.

A. J. Eraklis and his colleagues found that the incidence of infection was greatest in children below the age of 4 years, but it was not especially high in infancy. Most of the deaths occurred within four years of splenectomy, but in one case the interval was nine years. The infection was usually overwhelming meningitis with septicaemia or else a fulminating bout of pneumonia, and the infecting organisms were most often the pneumococcus, meningococcus, and *Haemophilus influenzae*.

The role of the spleen in preventing bacterial infection is unknown. Perhaps by virtue of its high content of reticuloendothelial cells it acts as a filter for circulating bacteria. It is in patients with underlying diseases affecting the reticuloendothelial system—for example, the lipidoses and histiocytosis—that splenectomy is most often followed by infection. But, whatever the mechanism, it is advisable to treat any pyrexial condition in a patient who has undergone splenectomy with particular concern.

Obstetric Forceps or Vacuum Extractor?

Foetal distress in labour is the inviolable indication for immediate delivery, and in this situation the sooner the baby is born the better. However, the obstetrician must not only exercise his skill to deliver the baby from its obstetric dilemma but he must also protect the baby from any damage or delay caused by the operation itself. In modern obstetric practice a choice must be made between forceps and the vacuum extractor—each instrument can be a life-saver, but each has its own operative complications.

Advice on the choice of instrument has often been confusing in the past. Now, J. G. Schenken and D. M. Serr,[1] who are practising obstetricians, have recorded their experience of the definitive indications for the use of each instrument, and, indeed, they found that these indications rarely overlapped.

It is not merely tradition that makes the obstetric forceps the preferred instrument for the management either of delay in the advance of the foetal head or of foetal distress in the second stage of labour. Firstly, the delivery will be quicker, because the trained obstetrician is able to introduce the forceps deftly and apply them safely round the foetal head within a matter of minutes, whereas the preparations for the use of the vacuum extractor take at least a quarter of an hour—setting it up, applying the cup, and building up the pressure. Secondly, delivery is safer because a doctor cannot hope to apply the forceps correctly and effectively until he has checked the position of the occiput. The danger with the cup is that it can be applied to the foetal scalp irrespective of the position of the occiput—and if it is applied to the skull in the occipito-posterior position the unwary obstetrician can lead himself into either a failed or a difficult vacuum extraction, and so expose the child to risk of cerebral haemorrhage. Properly applied obstetric forceps should not damage the brain, and certainly they should not lacerate the scalp, whereas damage to the scalp by necrosis at the site of the application of the vacuum cup is not uncommon, particularly if it is applied for any length of time. Furthermore, if the cup is suddenly and unexpectedly released from its attachment during traction petechial haemorrhage on the surface of the baby's brain can easily result.

The place of the vacuum extractor is pre-eminent in facilitating delivery where foetal distress has occurred or there has been delay in progress of the first stage of labour. The cup may be slipped through a cervix which is half-dilated or more, then with firm, steady traction the head may be pulled down within the pelvic cavity, so facilitating cervical dilatation. The application of forceps is completely contraindicated under these circumstances, and such a procedure would invite failure and disaster. Vacuum extraction with an undilated cervix should be undertaken only by a skilled obstetrician and always in an obstetric hospital, where if foetal distress occurs a caesarean section may be performed with the least delay.

Neither instrumental technique has any place if the foetal head is not engaged in the pelvis, or indeed if there is any cause to suspect disproportion which might necessitate caesarean section. The vacuum extractor has no place on the district or in a general practitioner maternity unit. But the use of the obstetric forceps for assisting a delivery in the second stage will always remain one of the most valued skills of the general practitioner obstetrician.

---

[1] Schenken, J. G., and Serr, D. M., *Amer. J. Obstet. Gynec.*, 1967, **98**, 32.

Menace of Smoking

On 18 July the Minister of Health invited the leaders of the tobacco industry to consider whether they could agree on proposals for limiting the sales promotion of cigarettes. Last week they informed the Minister that they had been unable to reach agreement on a scheme of limitation. Consequently, as the Ministry of Health has announced, the Minister "thanked them for the earnest efforts that had been made by all concerned" and said that the Government would consider the position.

In 1965 there were over 26,000 deaths from cancer of the lung in England and Wales, and the figures for Scotland and Northern Ireland bring the total up to about 30,000 for the United Kingdom. The evidence can no longer be doubted that the great majority of these deaths were due to cigarette smoking. Since E. L. Wynder and E. A. Graham[1] and A. Bradford Hill and R. Doll[2] first clearly showed the association between smoking and cancer numerous independent studies have confirmed and amplified their conclusions. In addition, the relationship of smoking to chronic bronchitis and emphysema is well proved.

Now a report coming from the U.S. Public Health Service[3] brings up to date the one it issued three years ago.[4]

---

[1] Wynder, E. L., and Graham, E. A., *J. Amer. med. Ass.*, 1950, **143**, 329.

[2] Doll, R., and Hill, A. B., *Brit. med. J.*, 1950, 2, 739.

[3] *The Health Consequences of Smoking*, U.S. Department of Health, Education, and Welfare, Public Health Service Publication No. 1696, 1967. Washington.

[4] *Smoking and Health*, U.S. Department of Health, Education, and Welfare, 1964.

[5] *Brit. med. J.*, 1967, 2, 460.

The recent studies increasingly suggest that smoking, in addition to its undoubted connexion with lung cancer, plays some part in the development of cancer of the mouth, larynx, oesophagus, and possibly pancreas. But no association with cancer of the stomach has been found despite investigations into the question. Epidemiological, clinical, and experimental data also point to a relationship between smoking and cancer of the bladder, though whether it is causal remains so far uncertain. Evidence continues to accumulate showing that cigarette smokers, both men and women, are much more liable to coronary artery disease than are non-smokers. Moreover, a reduction in the risk follows cessation of smoking. According to the report, too, additional evidence strengthens the association between cigarette smoking and cerebrovascular disease.

The smoking of tobacco, and especially of cigarettes, is surely the greatest menace to the public health of our time, causing death and disability on a scale reminiscent of the epidemic diseases of earlier centuries. But a dilemma faces any Government that attempts to diminish the scourge of smoking, for it is not, like the epidemics, a communicable disease—except by example—so that the general public might not be as willing to accept compulsory measures of restriction as they were in the case of infectious diseases. Moreover, special difficulty in educating the public comes from the long interval between a man's beginning to smoke and his death from lung cancer—usually some decades. If the chances of a smoker contracting cancer were the same as now but the interval before death was only some months it is scarcely conceivable that cigarettes would be marketed at all, or, if they were, that legislation would be long delayed to prohibit them altogether. Since the Government is unlikely to adopt that course at present, it must consider others. The measure most often canvassed is a complete ban on the advertising of cigarettes. If this and other restrictions are imposed they will need to be supplemented by much more thorough educational campaigns than have been carried out so far, directed especially to young people[5] and with a skill that will communicate firm conviction rather than mere knowledge of the harm that follows smoking.

Good General Practice

As reported in the *Supplement*, the General Medical Services Committee has in the main approved its advisory committee's report on vocational training for general practice. Any criticism was mostly of details and not of principles. The report has been sent with the G.M.S. Committee's blessing to the Royal Commission on Medical Education and to the Central Committee on Postgraduate Medical Education, set up in June, under the chairmanship of Sir Robert Aitken, by the universities with medical schools and the medical colleges of England and Wales and Scotland.[1] This Committee, which has now incorporated " (Great Britain) " in its title[2] in recognition of its concern with Scotland as well as with England and Wales, has already discussed the organization of medical training in the first three years after registration. Also published early this month were the Royal College of General Practitioners' views[3] on how its earlier proposals for vocational training should be implemented.

There is no longer any real dispute about the need for vocational training for general practice in the same way as it is needed for other specialized branches of medical practice. The only remaining questions are on how it should be done and when it should begin. Vocational training must be seen as part of the whole of medical education, and it cannot be considered separately from postgraduate education. Further events must await the report of the Royal Commission on Medical Education, expected early next year. It may be supposed that the Commission has had the benefit of the views of the Central Committee on Postgraduate Medical Education in addition to those of the General Medical Council, the colleges, the B.M.A., and the other bodies that have given evidence to it. Those who are anxious for progress will therefore be looking to the Royal Commission's recommendations to provide the impetus that is needed.

Not surprisingly, the views of the Royal College of General Practitioners and of the G.M.S. Committee's Advisory Committee on Vocational Training and Continuing Education for General Practice were very similar. They shared many members in common, and also vocational training for general practice is now so old a concept that ideas on it have had plenty of time to crystallize out. If the trainee practitioner scheme has not been the success that was hoped for it has certainly provided a source of valuable experience on which to build. So also have some other schemes, notably the Wessex experiment in training for general practice. Against this background of general agreement some cautionary notes sounded in the G.M.S. Committee's debate should be heeded. The demands on, in some cases, seriously overworked doctors to provide medical care for patients are certain to conflict with what those who have to administer the Health Service are bound to consider as the less pressing needs of medical education. The essence of traineeship is to be a learner first and a doer—a pair of hands—second. The urgent need of the Health Service is for more and more pairs of hands. For this reason the responsibility for vocational and for all postgraduate training must surely be with educational committees. An organization with the Central Committee on Postgraduate Medical Education (Great Britain) at its head seems ideal for the purpose. Likewise, it would be better to regard vocational training as a university responsibility and not a Health Service one. This implies that the money for it should come mostly from the University Grants Committee and not from the Ministry of Health. This is something the medical profession should lay stress on.

Short of making vocational training compulsory—and the wisdom of taking so big a step to begin with is questionable—participation in any scheme must depend on the incentives which prospective general practitioners are offered. They will not enter a scheme if they suffer disadvantage from their keenness. They must be paid properly while they train, and afterwards their added skills must be rewarded. The current vocational training payments in general practice are derisory. In this, as in other respects, the country must be prepared to pay for a good medical service or to have a poorer one. But there will be no inducement to young doctors to add three to four years to their training if they cannot use their skills when they go into practice. Vocational training is important, but it would be putting the cart before the horse to train first-class doctors for third-class working conditions. Emigration would increase, not decrease. If general practice is to attract recruits it must offer them the facilities for practising good medicine.

---

[1] *Brit. med. J.*, 1967, **2**, 833.

[2] Ibid., 1967, **3**, 687.

[3] *Implementation of Vocational Training*, Reports from General Practice No. VI, Royal College of General Practitioners, 1967.

Papers and Originals

Childhood Leukaemia in Greater London: a Search for Evidence of Clustering

MORWENNA M. TILL,* B.A., M.B., D.C.H.; R. M. HARDISTY,* M.D., M.R.C.P.; M. C. PIKE,† PH.D.
RICHARD DOLL,† M.D., D.SC., F.R.C.P., F.R.S.

Brit. med. J., 1967, 3, 755–758

The suggestion that viruses might play a part in the causation of leukaemia has reawakened interest in the epidemiology of the disease, and has led many investigators to search for evidence of its occurrence in clusters. Little attention was paid to Kellett's (1937) original report of an epidemic in the area around Newcastle upon Tyne; but at least 19 similar reports have been made in the past eight years. Heath, Manning, and Zelkowitz (1964) noted 13 besides their own, and other reports have been made by Knox (1964), Meighan and Knox (1965), Mustacchi (1965), Dowsett (1966), and Mainwaring (1966). It was not until 1963, however, that the importance of distinguishing between clustering in space, in time, and in space and time considered together was fully appreciated (Knox, 1963), and not until the following year that a serious attempt was made to assess the probability that an observed cluster in both space and time could occur owing to chance alone (Knox, 1964).

Knox (1964) noted the addresses and dates of onset of all cases of childhood leukaemia in Northumberland, Durham, and part of Yorkshire over the ten-year period 1951–60 and found that there was a statistically significant excess of pairs of affected children in whom the onset of symptoms began before their sixth birthday, who lived within one kilometre of each other, and in whom the dates of onset were within 60 days. The implications of this finding, however, are limited by the fact that the clustering was found only for one clinical subgroup of the cases and for limited space and time intervals, and that those characteristics which defined the positive cluster were thrown up by the investigation itself and not by a preceding hypothesis. Thus Knox's findings should be regarded as constituting a sound basis for formulating a hypothesis to be tested against further observations and not as proof of the existence of real clustering. We have therefore sought to test the hypothesis by examining the distribution of childhood leukaemia (defined for this study as leukaemia with onset of symptoms before 10 years of age) in another area.

From the point of view of theoretical oncology the concept that the *onset* of leukaemia should occur in clusters is not particularly attractive, as factors of aetiological importance are likely to exert their effect a considerable time before the disease becomes clinically apparent. Clustering in space and time of the births of the leukaemic children would seem to be a much more likely event if a virus played any part in the production of the disease. We have therefore also looked into this possibility.

Material

Copies of the death entries were examined of all the children who died of leukaemia under 15 years of age during the ten years 1952–61 and who were resident in Greater London at the time of their death. Only children in whom the primary cause of death was certified as leukaemia were included and no attempt was made to find children who, though born or developing the disease in Greater London, were resident elsewhere when they died. Altogether 618 children were studied. For each of these the hospital case records were sought and the clinical and haematological details reviewed. In addition Dr. Alice Stewart allowed us access to all the data she had collected on these children during the Oxford Survey of Childhood Malignancies.

As a result of this review 135 children were excluded: (*a*) 105 because they were more than 10 years old when symptoms first occurred; (*b*) 11 because they were born and living outside Greater London at the time of onset of symptoms; and (*c*) 19 because the diagnosis of leukaemia was not confirmed—in eight the hospital records suggested that death was due to some other cause, in two the diagnosis rested solely on the post mortem findings, which in our opinion were inconclusive, and in nine the medical records had been destroyed or could not be traced.

Birth certificates were sought for the remaining 483 children and were obtained for all but 18—6 who were known to have been adopted, 9 who were known to have been born abroad, and 3 others.

The following data were used for the analysis:

(1) *Date of onset,* taken as the date of the first symptoms referable to leukaemia in the medical records. This was always recorded as a specific day even though the exact choice of date was known to be to some extent arbitrary. For example, "one month ago" was taken to mean exactly one calendar month before the date on which the history was recorded; symptoms dating from a specified month were recorded as starting on the 15th of the month, and symptoms said to have been present for "several weeks" or "several months" were dated from three weeks or three months previously. The onset in one infant in whom leukaemia was present at birth was taken as three months antenatally.

Table I shows the frequency distribution of the lengths of history recorded according to these conventions. In each case the length of history was taken to be the time between the onset and the date of the first relevant medical record, even though a firm diagnosis of leukaemia was not always made until some time later. In 235 cases the history was of four weeks or less or was referable to an exact date, and in these the date of onset was probably accurate to within a week. In a further 126 cases the duration recorded was "one month," was referable to a month by name, or was not more than two months with symptoms of abrupt onset, and in these the date of onset was probably accurate to within two weeks. Thus three-quarters of the dates of onset are likely to have been accurate to within two weeks; the remainder were probably accurate to within two months and usually to within much less.

* The Hospital for Sick Children, Great Ormond Street, London W.C.1.
† Medical Research Council's Statistical Research Unit, University College Hospital Medical School, London W.C.1.

(2) *Address at time of onset of symptoms,* taken from the medical records. In the absence of specific evidence to the contrary this was taken to be the same as the address at the time of the nearest subsequent medical attendance. Two children were living outside Greater London at the time of onset and are therefore excluded from analyses of clustering at this stage in the course of the disease. For 252 of the remaining children (52%) the address at onset was the same as the place of residence at birth.

TABLE I.—*Number of Children With Different Lengths of History at Presentation (Onset Under* 10 *Years of Age)*

Length of History (in weeks)	No. of Children	Cumulative Percentage of Total
2 or less	122	25
-4	84	43
-6	113	66
-8	68	80
-13	42	89
-26	39	97
More than 26	15	100
All durations	483	100

(3) *Date of birth,* taken from the birth certificate when available.

(4) *Place of birth and home address at birth,* taken from the birth certificate. Of the 465 children whose birth certificates were traced, 42 were born outside Greater London and 28 had home addresses outside Greater London. The numbers of children for whom it was possible to examine evidence of space-time clustering in relation to date and place of birth and date of birth and home address at birth were therefore reduced to 423 and 437 respectively. The map references of all addresses were found correct to within 100 metres. When the child was born in hospital the middle of the hospital was taken to give the map reference.

(5) *Cytological and clinical type of leukaemia,* determined after a review of the reports of peripheral blood counts, marrow examinations, and clinical and post mortem findings. Three hundred and seventy-four cases were classified as acute lymphoblastic leukaemia; 52 as acute myeloblastic leukaemia; 16 as acute monocytic leukaemia; and 3, in which abnormal erythroblasts were the predominating cell type, were classified as acute erythroleukaemia. Four children aged 5 to 9 years showed blood, marrow, and clinical findings typical of the adult form of chronic granulocytic leukaemia, and the series also included two children previously described as having the juvenile form of the disease (Cases 1 and 2 in the series described by Hardisty, Speed, and Till, 1964) and eight other children aged 2 months to 2 years, so closely resembling these in their haematological and clinical features that it seemed justifiable to classify them in the same group—making a total of 14 cases of chronic granulocytic leukaemia. In 15 cases it was not possible to ascertain the cytological type, though there was no doubt about the diagnosis of acute leukaemia, and these were classified as acute unspecified leukaemia. Finally, nine cases in which the evidence of leukaemia was suggestive but incomplete were unclassified.

The distribution of cases by type, sex, and age at onset is shown in Table II.

Results

Clustering in Space

The distribution of cases throughout the Greater London conurbation is shown in Table III. The population at risk has been taken to be the mean of the population under 10 years of age at the censuses of 1951 and 1961. At these dates the Greater London area was divided into 95 London boroughs and municipal boroughs in the home counties, and the populations of most of these areas were too small for individual examination. The areas have therefore been combined to provide units that correspond as nearly as possible to the boroughs of the new Greater London Council. The highest incidence is recorded in Sutton, Epsom, and Ewell (7.7 per 100,000 children per year) and the lowest in Hounslow (1.7 per 100,000 children per year).

TABLE III.—*Incidence of Leukaemia in Different Parts of Greater London (Children With Onset Under* 10 *Years of Age)*

Borough	Incidence per 100,000 Children per Year	No. of Cases	
		Observed	Expected at Rate for Whole Area
*City of Westminster	3·9	11	11·8
Camden	3·8	11	12·1
Islington	4·9	19	16·5
Hackney	4·2	16	16·2
Tower Hamlets	4·8	16	14·2
*Greenwich	5·2	18	14·7
Lewisham	3·2	14	18·4
Southwark	3·2	16	21·0
*Lambeth	4·2	14	14·2
*Wandsworth	4·8	29	25·6
Hammersmith	3·3	10	12·8
Kensington and Chelsea	3·9	9	9·8
*Waltham Forest	6·0	22	15·5
*Redbridge	3·3	16	20·1
*Barking	4·9	14	12·1
*Newham	2·8	12	17·8
*Bexley	4·9	19	16·3
*Bromley	5·0	18	15·2
Croydon	5·4	25	19·6
*Sutton	7·7	28	15·5
Merton	4·7	12	10·8
*Kingston-on-Thames	4·0	11	11·7
Richmond-on-Thames	3·9	9	9·8
*Hounslow	1·7	6	15·0
Hillingdon	3·8	13	14·6
Ealing	5·0	20	17·0
Brent	4·2	17	17·0
*Harrow	5·0	16	13·4
*Barnes	3·9	19	20·7
Haringey	3·1	11	15·1
Enfield	2·7	10	15·9

* Boundaries do not correspond exactly with the borough of this name in the new Greater London.

Inspection of the map of London shows that there is no tendency for high and low areas to lie close to one another, and statistical analysis reveals that the amount of variation between the boroughs is no more than can easily be attributed to chance ($\chi^2=33.4$, $n=30$, $P=0.3$).

Clustering in Time

Table IV shows the distribution of cases by year of onset, separately for the two principal cytological types, and for cases with ages of onset under and over 6 years. As the data are derived from information about deaths in the years 1952–61 a relatively small number of cases is to be expected in 1960–1. Between 1952 and 1959 the annual number shows little variation.

Table V shows the distribution of cases by month of onset. No seasonal peaks are evident, neither for all cases taken together, nor for lymphoblastic cases alone, nor for children with onset under 6 years of age; in all groups the numbers arising in summer and winter—defined by Knox (1964) as May to October and November to April—are practically identical.

TABLE II.—*Number of Children with Different Types of Leukaemia by Sex and by Age at Onset (Onset under* 10 *Years of age)*

Type	Age (in years) at Onset										Sex		Total
	0	1	2	3	4	5	6	7	8	9	M	F	
Acute lymphoblastic	21	33	64	71	53	31	29	24	25	23	213	161	374
Acute myeloblastic	8	7	2	4	5	7	8	6	3	2	31	21	52
Acute monocytic	0	0	2	1	1	0	3	0	5	4	11	5	16
Other acute and unclassified	7	1	3	5	2	2	2	4	1	0	18	9	27
Chronic granulocytic	3	5	2	0	0	1	0	1	0	2	7	7	14
Total	39	46	73	81	61	41	42	35	34	31	280	203	483

TABLE IV.—*Number of Children Developing Leukaemia in Different Years, by Cytological Type and by Age at Onset (Onset Under* 10 *Years of Age in Greater London)*

Category	Year											All Years
	Before 1952	52	53	54	55	56	57	58	59	60	61	
Acute lymphoblastic	12	35	34	39	46	41	41	46	37	27	14	372
Acute myeloblastic	3	4	9	7	8	4	4	2	5	5	1	52
Others	3	7	9	3	5	3	7	5	3	8	4	57
Onset before 6th birthday	13	35	34	31	40	33	31	41	34	36	11	339
Onset after 6th birthday	5	11	18	18	19	15	21	12	11	4	8	142
All categories	18	46	52	49	59	48	52	53	45	40	19	481

TABLE V.—*Number of Children Developing Leukaemia in Different Months, by Cytological Type and by Age at Onset (Onset under* 10 *Years of Age in Greater London)*

Category	Month												All Months
	Jan.	Feb.	Mar.	Apr.	May	June	July	Aug.	Sept.	Oct.	Nov.	Dec.	
Acute lymphoblastic	25	26	31	36	27	36	31	29	22	40	31	38	372
Acute myeloblastic	5	5	4	2	4	7	6	3	3	3	6	4	52
Others	8	6	6	1	8	4	7	4	3	2	3	5	57
Onset before 6th birthday	29	26	31	31	25	36	32	28	19	29	21	32	339
Onset after 6th birthday	9	11	10	8	14	11	12	8	9	16	19	15	142
All categories	38	37	41	39	39	47	44	36	28	45	40	47	481

Clustering in Space and Time

The data were examined for evidence of clustering in both space and time together by Knox's (1964) method—that is, by seeing whether pairs of cases that occurred close together in space also occurred close together in time. All cases were examined as one set, and separately in various subsets consisting of lymphoblastic cases only, cases with onset under 6 years of age, and cases with deaths under 6 years of age. Clustering was looked for in regard to place and date of onset, place and date of birth, and place of mother's residence at the child's birth and the child's date of birth. Subsets of data relating to date of birth were also examined for children born in 1952–5, to ensure that all members of a cohort who died under 6 years of age were included.

Since the data were derived from information about deaths in 1952–61 the number of cases known to have had their *onset* in years before 1952 and in 1961 (the last year of the period studied) must be deficient; examination of the interaction between date and place of onset was therefore limited to the period 1952–60.

The various sets of data used and the types of interaction examined are shown in Table VI. In each case evidence of clustering was looked for over all combinations of 12 critical times apart (15, 30, 45, 60, 75, 90, 105, 120, 135, 150, 165, and 180 days) and 12 critical distances apart (0.25, 0.5, 0.75, 1, 1.25, 1.5, 1.75, 2, 2.5, 3, 3.5, and 4 kilometres). In only three instances was any evidence of positive clustering found —that is, significantly more pairs of cases within the critical times and distances of one another than would be expected from the whole subset of data under examination. No statistically significant clustering was found in the subset originally specified by Knox—that is, clustering of onsets among children in whom the disease began before their sixth birthday—nor was any significant clustering found when the examination of this subset of children was limited to those with lymphoblastic leukaemia.

Details of the amount and character of the clustering in the three instances in which statistically significant results were obtained are shown in Table VII. Each subset includes lymphoblastic cases only. In two instances there is weak evidence of clustering of times and places of onset; the excess numbers of pairs are small (3 to 5), but it is notable that the distances and times within which the cases occurred (¾ km. and 60–75 days) are similar to those recorded by Knox (1964). In the third subset the clustering relates to the date of birth and the mother's place of residence when the child was born. The probability of as many or more clusters occurring due to chance alone is lower and the excess numbers of pairs are somewhat greater (9 to 24), but the clusters are less striking in that the distances in both time and space separating individual members of each pair are much greater.

Four sets of data were also examined for clustering at the onset of the disease by an alternative method suggested by David and Barton (1966). Each set consisted of cases with onset in the period 1952–60, the groups being composed of (*a*) all children, (*b*) children with lymphoblastic leukaemia, (*c*) all children with onset before their sixth birthday, and (*d*) children with lymphoblastic leukaemia with onset before their sixth birthday. In none of the groups was any evidence of clustering obtained. Comparison of the results obtained by these two methods showed that David and Barton's (1966) method was less sensitive to the presence of small clustering in this type of material and the method was not used to examine the other sets.

Discussion

Our data have failed to provide clear evidence in support of Knox's hypothesis that leukaemia in children under 6 years

TABLE VI.—*Examination Made for Evidence of Space–Time Clustering*

Subset of Leukaemic Children	Type of Interaction	No. of Children
All with onset 1952–60	Date and place of onset	444
All with onset 1952–60 before 6th birthday	Date and place of onset	315
All with onset 1952–60 and death before 6th birthday	Date and place of birth	282
All with onset 1952–60 and death before 6th birthday	Date of birth, place of residence at birth	292
All with birth 1952–55 and death before 6th birthday	Date and place of birth	116
All with birth 1952–55 and death before 6th birthday	Date of birth, place of residence at birth	118
*Lymphoblastic with onset 1952–60	Date and place of onset	346
Lymphoblastic with onset 1952–60 before 6th birthday	Date and place of onset	252
*Lymphoblastic with onset 1952–60 and death before 6th birthday	Date and place of onset	230
Lymphoblastic with onset 1952–60 and death before 6th birthday	Date and place of birth	224
*Lymphoblastic with onset 1952–60 and death before 6th birthday	Date of birth, place of residence at birth	232
Lymphoblastic birth 1952–55 and death before 6th birthday	Date and place of birth	89
Lymphoblastic birth 1952–55 and death before 6th birthday	Date of birth, place of residence at birth	91

* Evidence of statistically significant clustering, see Table VII.

TABLE VII.—*Categories of Leukaemia with Significant Evidence of Clustering in Space and Time*

Subset of Patients	Interaction	No. of Children	Critical Time (Days)	Critical Distance (Kilometres)	No. of Pairs	Expected No. of Pairs	Standard Deviation	Probability*
Lymphoblastic leukaemia onset 1952–60	Date and place of onset	346	60	0·75	8	4·60	1·96	0·051
			75	0·75	10	5·06	2·20	0·034
Lymphoblastic leukaemia onset 1952–60, death before 6th birthday	Date and place of onset	230	75	0·75	6	2·67	1·60	0·054
Lymphoblastic leukaemia onset 1952–60, death before 6th birthday	Date of birth, place of parents' residence at child's birth	232	120	2·00	31	21·56	4·52	0·033
			135	2·00	35	24·53	4·81	0·025
			165	1·75	32	22·81	4·61	0·040
			165	2·00	41	30·01	5·30	0·028
			165	3·50	102	83·68	8·84	0·023
			180	3·00	88	69·23	8·02	0·014
			180	3·50	116	91·83	9·24	0·007
			180	4·00	139	115·70	10·36	0·017

* Probability of an equal or greater excess number of pairs being observed by chance from the Poisson distribution.

of age tends to occur in clusters, children who live within one kilometre of each other tending to develop symptoms of the disease within 60 days of each other. It should be noted, however, that 9 of the 10 children who formed the clusters in Knox's original data had lymphoblastic leukaemia and all developed their disease under 4 years of age; and our data provide some some weak evidence of clustering at the onset of the disease within similar critical limits (¾ km. and 75 days) in children who *died* of lymphoblastic leukaemia under 6 years of age (in fact the ages of the children at onset were under 4 years in 10 out of 12 cases). In view of the fact that Knox was studying an area with a population scattered over large and small towns and villages, whereas we were studying a single conurbation, this degree of similarity between the results is notable and provides some weak support for the general hypothesis that cases of leukaemia do tend to occur in clusters more often than would be expected by chance alone.

In our data the strongest evidence of clustering occurs with date and residence at birth, and a leukaemogenic agent is presumably more likely to be effective at or around this period than at any other in the child's life. The dimensions of the cluster are, however, too large to suggest a single focus of infection (4 km. and 180 days), and, as with Knox's (1964) original data, the statistical tests employed do not have the significance normally attached to them. A large number of possible critical times and distances were examined, and, logically, the analysis does no more than allow us to pick out a new hypothesis, which can be tested only on further data.

With the methods now available we have been able to look for clustering only in relation to a few specified periods in the natural history of the disease, and these would not necessarily be the most relevant if the disease was truly contagious. Under these conditions it would be more appropriate to look for interaction between, say, the date and place of residence of one child during his period of infectivity and the place of residence of another child during a period of susceptibility—which might be several years before the disease was clinically apparent. Without knowledge of the periods when infectivity and susceptibility occur, this is a problem of some complexity. A general method of searching for interaction between different hypothetical periods of infectivity and susceptibility has been developed by one of us (Pike, 1967), but it will be some time before it can be tested adequately.

Summary

The hypothesis that cases of childhood leukaemia occur grouped together in space and in time has been tested by examining the distribution of the disease in Greater London.

Altogether 618 children were certified as having died of leukaemia under 15 years of age in Greater London during the period 1952–61. For each of these children the hospital records were sought and the clinical and haematological details reviewed. Four hundred and eighty-three children were accepted as having developed leukaemia under 10 years of age while resident in Greater London, and for these children information was obtained about the date and place of birth, the parents' place of residence at the child's birth, and the date and place of residence of the child at the onset of the disease.

The incidence of leukaemia varied between the 31 boroughs of the new Greater London Council, but the amount of variation (from 1.7 to 7.7 per 100,000 children per year) could easily be accounted for by chance variation of small numbers.

No evidence was found to suggest that the disease had been unusually common in any one year, or to suggest that it occurred more commonly at any one season, nor was there any evidence of temporal variation in the incidence of any of the principal subgroups of the disease (lymphoblastic and myeloblastic leukaemia and leukaemia occurring before or after the sixth birthday).

Evidence of clustering in space and time taken together was sought by examining whether pairs of cases that occurred close together in space also occurred close together in time. Thirteen subsets of the data were examined, and weak evidence of clustering was found for all cases of lymphoblastic leukaemia in regard to date and place of onset, and for cases of lymphoblastic leukaemia leading to death under 6 years of age in regard both to date and place of onset, and to date of birth and the place of the parents' residence at the child's birth.

The results obtained in relation to the onset of the disease are similar to but not identical with those reported previously by others, and provide some weak support for the general hypothesis under examination.

We are grateful to the Leukaemia Research Fund and the Medical Research Council for grants to one of us (R. M. H.) for the purpose of this study; to Mrs. Ranjana Ash and Mrs. Jean Bridger for locating the map references of the addresses and tracing the case records; to Mrs. Anna Frackiewicz (M.R.C. Clinical Effects of Radiation Research Unit) for extracting copies of the death entries of children in Greater London who died of leukaemia; to Mrs. Serina Bell for assistance in the computer programming; to Dr. Alice Stewart for allowing us access to her records; and to our colleagues in many London hospitals for their willing co-operation in making their case records available.

REFERENCES

David, F. N., and Barton, D. E. (1966). *Brit. J. prev. soc. Med.*, **20**, 44.
Dowsett, E. G. (1966). *Brit. J. Cancer*, **20**, 16.
Hardisty, R. M., Speed, D. E., and Till, M. (1964). *Brit. J. Haemat.*, **10**, 551.
Heath, C. W., jun., Manning, M. D., and Zelkowitz, L. (1964). *Lancet*, **2**, 136.
Kellett, C. E. (1937). *Arch. Dis. Childh.*, **12**, 239.
Knox, G. (1963). *Brit. J. prev. soc. Med.*, **17**, 121.
—— (1964). Ibid., **18**, 17.
Mainwaring, D. (1966). Ibid., **20**, 189.
Meighan, S. S., and Knox, G. (1965). *Cancer*, **18**, 811.
Mustacchi, P. (1965). Ibid., **18**, 362.
Pike, M. C. (1967). *Biometrics* (in press).

Leukaemia in Lewisham (1957-63)

S. P. LOCK,* M.A., M.B., M.R.C.P.; MAXINE MERRINGTON,† B.SC.

Brit. med. J., 1967, 3, 759–760

Several workers have reported that cases of leukaemia occur in clusters in place and time—for example, Kellett (1937), Heath and Hasterlick (1963), Knox (1964), Meighan and Knox (1965), and Mainwaring (1966). Conversely, it has also been reported that the disease does not occur in clusters (Clemmesen *et al.*, 1952; Ederer *et al.*, 1964; Barton *et al.*, 1965; Ager *et al.*, 1965; Lundin *et al.*, 1966). Until recently there have been no adequate statistical tests for detecting clustering; furthermore, the records of victims of leukaemia have not usually been available for the application of such statistical tests.

We here report our analysis of the incidence of leukaemia in a particular area—the former London borough of Lewisham—with special reference to the question of clustering. We have confidence that these records are largely complete and would expect to be able with these data to detect clustering if it occurred.

Materials and Methods

The patients studied had been diagnosed between 1 January 1957 and 30 December 1963 as having any type of leukaemia. At the time of diagnosis they were living in the London borough of Lewisham. Their names were obtained in a variety of ways: from case notes, with necropsy records from all the local hospitals, including Lewisham General Hospital, which provides a district haematological service for the area; from records of the South Metropolitan Cancer Registry, which are derived from the notifications from individual hospitals; and from the death certificates of all patients in the borough dying from leukaemia, kindly made available by Dr. W. M. Court Brown, of the Medical Research Council Clinical Effects of Radiation Research Unit in Edinburgh. The case notes of all the patients were obtained from the hospitals concerned.

In all, 115 patients were diagnosed as suffering from leukaemia; their ages ranged from 2 to 89 years. The clinical types were distributed as follows: 37 acute myeloid, 18 acute lymphatic, 4 myelomonoblastic, 21 chronic myeloid, 32 chronic lymphatic, and 3 erythroleukaemia. In almost every instance the diagnosis had been made from conventional haematological examinations, but one case of chronic lymphatic leukaemia had been diagnosed only at necropsy. The date of the first symptom, the date of diagnosis, and the date of death were all recorded. The addresses of the patients when they developed leukaemia were obtained. The location of each individual address was accurately determined by visiting it.

Statistical Analysis

Several statistical techniques are now available for determining whether a group of patients who develop a particular disease at about the same time also live near each other.

Two methods have been applied to the 115 cases of leukaemia in Lewisham. The first (David and Barton, 1966) is worked out on the basis of testing whether the spatial pattern is random within a group of cases in time. Initially all the cases are written down chronologically. They are then divided into groups in time according to a rule, which must be decided on before the statistical analysis is calculated. Unless there is some particular reason for choosing a special interval it is usual to choose the groups with several different time intervals between them and to repeat the same statistical analysis for each interval. The next step is to find the distances between all cases. This may be done by taking the map readings of each patient's address from the National grid; with these as co-ordinates the distances are calculated. The David and Barton statistical test is the ratio of the variation within time groups to the variation of all the possible distances between the cases. If the cases are randomly distributed this ratio will be unity; the closer they are to each other within a time group the smaller the ratio will be. As a yardstick for deciding whether clustering exists we may subtract unity from this ratio and divide by the standard deviation. This is the David and Barton test criterion. If this measure is less than -2 it can be concluded that there is some clustering effect. The method of calculating the ratio and its standard deviation has been published (Barton *et al.*, 1965; David and Barton, 1966).

This test was calculated for each group of patients suffering from the different clinical types of leukaemia; it was also calculated for all 115 cases combined together. It was applied by using various time intervals between groups of patients. Finally, the patients were divided into adults and children (under 15 years old), and again the test was calculated. In none of these tests was the difference between the ratio and unity even as much as one and a half standard deviations. Therefore it must be concluded that among the cases of leukaemia in Lewisham during 1957 to 1963 there was no evidence of any clustering effect.

The second method used for detecting clustering is that devised by Knox (1964). All the cases are considered in pairs; their distance apart is calculated and their time apart is noted. If the number of cases with a short distance and a short time apart is larger than would be expected if they were randomly distributed then clustering must occur. Whatever specific distances and times were chosen for the test, there were no excessive numbers of pairs of cases close to each other in place and time. Thus this statistical test also provided no evidence of clustering.

Discussion

The difficulty with all statistical tests for space–time clustering is that the definition of what is "close" in time and what is "close" in distance will vary enormously. The results given by Knox (1964) for childhood leukaemia in Northumberland and Durham show that pairs of cases occurring within 60 days and within 1 km. of each other were unduly frequent. The conclusions reached by Meighan and Knox (1965) for childhood leukaemia in Portland, Oregon, showed that an excessive number of pairs of cases were closer than 250 days apart and closer than 4 km. apart. The results for acute leukaemia in childhood in the Liverpool area given by Mainwaring (1966) show an excessive number of pairs with short distances and short times apart, the highest levels of significance being for

---

* Lately Senior Registrar, Department of Pathology, Lewisham Hospital, London S.E.13.
† Department of Statistics, University College, London W.C.1.

pairs of cases with intervals less than 300 days and 4 km. Other investigators have drawn conclusions based on personal observations rather than on the results of any statistical tests. For example, Heath and Hasterlick (1963) reported eight cases of leukaemia among children living in Niles, Illinois, between 1957 and 1960. This was at a time when the population was expanding sharply (in 1950 the population was about 3,500 and in 1960 about 20,000). Wood (1960), describing leukaemia in Cornwall over a 12-year period, stated that there was a tendency to find tiny foci of victims living in close proximity but there was no significant predominance in any particular district. Dowsett (1966) reported similarly of cases in Kingston, Surrey. Heath and Manning (1964) described 14 cases in four communities in the United States.

The statistical test put forward by David and Barton (1966) has the advantage that it picks out non-randomness without the need for defining a " close " distance. The criterion is based on the overall average of all possible distances between all cases. A definition of shortness in time must be made. This test was carried out (Barton *et al.*, 1965) on cases of acute leukaemia in Northumberland and Durham, Liverpool, Birmingham, Bristol, Sheffield, and Cornwall. The results gave no evidence for the presence of clustering. Both this test and Knox's test were used by Pike *et al.* (1967) in analysing the incidence of Burkitt's tumour in the West Nile district of Uganda; both tests demonstrated significant space–time clustering.

In an investigation in Connecticut, Ederer *et al.* (1964, 1965), using a different statistical technique, analysed over 300 cases of leukaemia in children between 1945 and 1959 and found no evidence of " calendar-year clustering within towns," though, using their statistical technique, they did find evidence for clustering of poliomyelitis and hepatitis.

The 115 cases studied in Lewisham included several different clinical types of leukaemia (cytological and clinical), and the numbers of any one type were small. The data indicate that there is no evidence of clustering of leukaemia taken as a whole, nor do they provide evidence of clustering of one or other specific subtypes of leukaemia. It would appear that if cases of leukaemia are clustered at all the degrees of clustering must be very slight, and quite unlike that found in poliomyelitis and infectious hepatitis.

Summary

Two statistical criteria for testing the association of cases of leukaemia in place and time were calculated for 115 patients in the London borough of Lewisham between 1957 and 1963. The analysis gives no evidence for any clustering of these cases.

We wish to acknowledge with thanks the help given by many doctors and medical records officers in hospitals in South-east London and elsewhere. Mr. P. M. Payne, Director of the South Metropolitan Cancer Registry, kindly gave us details of his registered cases of leukaemia in the district.

The calculations were carried out on the I.C.T. Atlas Computer at the University of London Institute of Computer Science. We wish to acknowledge gratefully the expert assistance given us by Mrs. Pat Hills, Miss Norma Pateman, and Miss Pat Williamott, of University College, London, in processing these data. Dr. Malcolm Pike, of the M.R.C. Statistical Research Unit at University College Hospital Medical School, London, kindly helped us concerning the calculations with the Knox test.

References

Ager, E. A., Schuman, L. M., Wallace, H. M., Rosenfield, A. B., and Gullen, W. H. (1965). *J. chron. Dis.*, **18**, 113.
Barton, D. E., David, F. N., and Merrington, M. (1965). *Ann. hum. Genet.*, **29**, 97.
Clemmesen, J., Busk, T., and Nielsen, A. (1952). *Acta radiol. Diagn.*, **37**, 223.
David. F. N., and Barton, D. E. (1966). *Brit. J. prev. soc. Med.*, **20**, 44.
Dowsett, E. G. (1966). *Brit. J. Cancer*, **20**, 16.
Ederer, F., Myers, M. H., Eisenberg, H., and Campbell, P. C. (1965). *J. nat. Cancer Inst.*, **35**, 625.
—— —— and Mantel, N. (1964). *Biometrics*, **20**, 626.
Heath C. W., and Hasterlick, R. J. (1963). *Amer. J. Med.*, **34**, 796.
—— and Manning, M. D. (1964). *Lancet*, **1**, 1394.
Kellett, C. E. (1937). *Arch. Dis. Childh.*, **12**, 239.
Knox, E. G. (1964). *Brit. J. prev. soc. Med.*, **18**, 17.
Lundin, F. E., Fraumeni, J. F., Lloyd, J. W., and Smith, E. M. (1966). *J. nat. Cancer Inst.*, **37**, 123.
Mainwaring, D. (1966). *Brit. J. prev. soc. Med.*, **20**, 189.
Meighan, S. S., and Knox, E. G. (1965). *Cancer (Philad.)*, **18**, 811.
Pike, M. C., Williams, E. H. and Wright B. (1967). *Brit. med. J.*, **2**, 395.
Wood, E. E. (1960). Ibid., **1**, 1760.

Transit Times of Food in Patients with Diverticulosis or Irritable Colon Syndrome and Normal Subjects

O. N. MANOUSOS,* M.B., D.PHIL.; S. C. TRUELOVE,* M.D., F.R.C.P.; K. LUMSDEN,† M.B., B.CHIR., D.M.R.E.

Brit. med. J., 1967, **3**, 760–762

The rate of passage of food residue through the alimentary canal of normal human subjects has been studied extensively, but there are no relevant data with regard to patients with diverticula of the colon.

Hurst (Hertz) (1907) administered bismuth carbonate mixed with food to normal subjects and followed the progress of the food residue by means of radiographs; he found that a proportion of the radio-opaque material was still in the large bowel three days after its administration. Alvarez and Freedlander (1924) studied the transit times by means of small glass beads taken with food and found that only 70% of the beads had been passed by the third day. Similar results were obtained by Burnett (1923), who used millet seeds as the tracer substance. Todd (1930) and Lönnerblad (1951) studied the transit time of the small intestine by using barium sulphate mixed with water, but, as Cole (1914) suggested, unless the tracer substance is mixed with an ordinary meal the results are not representative of the actual progress of food residues through the gastrointestinal canal.

The figures of transit times given by Hurst (1919) for the normal are generally accepted (Barclay, 1933; Feldman, 1948). The food reaches the caecum in three to four hours, the hepatic flexure in six hours, the splenic flexure in 10 hours; between 18 and 24 hours the sigmoid is filled and some of the contents have been expelled; but, as was pointed out by Hurst himself, there is a wide variation in the normal transit. Indigestible material (roughage) increases the speed of food residue through the digestive tract, as has been shown by the comparative studies of McCance *et al.* (1953). They studied radiologically the transit time of white and brown bread administered with a small amount of barium sulphate to normal subjects. It was found that the residue from the brown bread left the colon 24 hours sooner than that from the white bread.

---

* Nuffield Department of Clinical Medicine, the Radcliffe Infirmary, Oxford.
† Consultant Radiologist, United Oxford Hospitals, Oxford.

Present Study

The transit time of food through the digestive tract was studied in 43 patients with diverticulosis (20 males and 23 females ; mean age 68 years), 75 patients with the irritable colon syndrome (40 males and 35 females ; mean age 42 years), and 88 normal subjects (42 males and 46 females ; mean age 59 years).

A minority of the patients with diverticulosis and some of the patients with the irritable colon syndrome were on treatment with anticholinergic drugs because of chronic intermittent symptoms ; the medication in these patients was stopped at least two days before the period of observation started.

Methods.—The subjects studied were instructed to drink 30 ml. of a preparation of barium sulphate (Fotogel or Micropaque) with each of their four main meals in one day. The next morning a radiograph of the abdomen was taken, and this was repeated on each successive morning (up to a maximum of six) until the radio-opaque material had virtually disappeared. (This procedure has also been used in order to obtain information regarding the incidence of diverticulosis in the general population (Manousos *et al.*, 1967b).) Two factors were examined: (1) the head of the barium column indicating the progress of food eaten 24 hours previously, and (2) the number of days that the barium—that is, the food—took to disappear from the gastrointestinal tract.

Results

As shown in Table I, the head of the barium column 24 hours after administration of barium with food was above the sigmoid colon in more than 27% of the normal subjects, whereas the proportions of patients with diverticulosis and the irritable colon syndrome were 9.3% and 5.3% respectively. Table II shows that the difference in transit of food residue between normals and patients with diverticulosis is statistically significant.

When the number of days required for the radio-opaque material to leave the colon is taken as a measure of the progress of food residue through the alimentary canal it is found that five or more days are required by 33% of the normal subjects, 23.3% of the patients with diverticulosis, and 18.1% of the patients with the irritable colon syndrome (Table III). Again the difference between normals and patients with diverticulosis is statistically significant (Table IV).

TABLE I.—*Progress of Food 24 Hours After Ingestion*

	Rectum		Sigmoid		Descending		Splenic Flexure or Above		Total not Reached Sigmoid	
	No.	%	No.	%	No.	%	No.	%	No.	%
Normal controls	54	61·4	10	11·4	7	8·0	17	19·3	24	27·3
Patients with diverticulosis	36	83·7	3	7·0	3	7·0	1	2·3	4	9·3
Patients with irritable colon syndrome	68	90·7	3	4·0	2	2·7	2	2·6	4	5·3

TABLE II

	Rectum or Sigmoid	Above Sigmoid	Total
Normal controls	64	24	88
Patients with diverticulosis	39	4	43
Total ..	103	28	131

$\chi^2 = 5{\cdot}5$. n = 1. $P < 0{\cdot}02$.

TABLE III.—*Number of Days Before the Food Left the Gastrointestinal Tract*

	2		3		4		5 or More	
	No.	%	No.	%	No.	%	No.	%
Normal controls ..	3	3·4	29	33·0	27	30·7	29	33·0
Diverticulosis ..	7	16·3	17	39·5	9	20·9	10	23·3
Irritable colon ..	13	18·1	33	45·8	13	18·1	13	18·1

TABLE IV

	3 Days or Less	4 Days or More	Total
Normal controls	32	56	88
Patients with diverticulosis ..	24	19	43
Total	56	75	131

$\chi^2 = 4{\cdot}5$. n = 1. $P < 0{\cdot}05$.

Discussion

Constipation has been thought to be a factor of aetiological significance in the development of diverticula by many investigators (Fischer, 1900 ; Beer, 1904 ; Turell, 1959 ; De La Vega *et al.*, 1964), and according to Jordan (1926) diverticulosis is a special manifestation of chronic intestinal stasis. The term "constipation" often has a vague meaning (Johnson, 1943), but when constipation is defined as "undue delay of passage of stool and, therefore, the difficult expulsion of hard dry matter," then the incidence of constipation in diverticular disease is only 14% (Horner, 1958).

Barclay (1933) pointed out that the statements of patients about constipation are often proved to be unreliable when they are examined radiologically.

The present study of the transit times shows that intestinal stasis is not present in patients with diverticulosis. On the contrary the progress of food through the gastrointestinal canal is significantly faster in patients with diverticulosis than in normal controls.

The similarity of the pattern of transit times between patients with diverticulosis and those with the irritable colon syndrome is of interest. The chronic intermittent symptoms of the two conditions are identical, and Bockus (1964), who made repeated radiological examinations in patients with the irritable colon syndrome, found that a proportion of them develop diverticula some years after the diagnosis of irritable colon, and pointed out that colonic irritability may be a predisposing factor in the development of diverticula.

Pathological studies (Keith, 1910 ; Edwards, 1939 ; Morson, 1963 ; Williams, 1963) suggest that diverticulosis may be the result of incoordinated activity of the colonic musculature. The function of the colon in patients with diverticulosis has not been studied extensively. Painter and Truelove (1964) found that injection of morphine produced high pressures inside segments of the colon bearing diverticula. They suggested that in diverticulosis the colon may show exaggerated responses to normal stimuli—for example, food or drink. The effect of eating a meal on the motility of the sigmoid colon of patients with diverticulosis has been studied (Manousos *et al.*, 1967a). The results indicate that the effect is greater than that observed in normal subjects, and, again, a similarity was observed between the response of the colon in patients with diverticula and patients with the irritable colon.

As shown by the study of the transit times and the review of the literature, there are many points in common between colonic diverticulosis and the disorders of colonic motor activity covered by the term "irritable colon syndrome." It appears likely that in both conditions the underlying mechanism is a functional disorder of the colonic musculature. The fact that many cases of colonic diverticulosis are quite symptomless seems to contradict this idea, unless we accept the view put forward by Williams (1963) that incoordinated muscular activity of the colon may be present without causing any symptoms.

Summary

The transit times of food residues through the gastrointestinal tract have been studied by administering food mixed with a small amount of barium sulphate. Observations were made on 88 normal subjects, 75 patients with the irritable colon syndrome, and 43 patients with diverticulosis. The transit times were found to be substantially shorter in the patients with diverticula than in normal subjects and to follow closely the transit shown by patients with the irritable colon syndrome. This finding is put forward as evidence supporting the hypothesis that incoordinated colonic activity is the basic abnormality in diverticulosis.

We wish to express our gratitude to all the patients and normal subjects who volunteered to take part in this study, the radiographers of the United Oxford Hospitals for their help, and the Medical Research Council for financial support.

REFERENCES

Alvarez, W. C., and Freedlander, B. L. (1924). *J. Amer. med. Ass.*, **83**, 576.
Barclay, A. E. (1933). *The Digestive Tract*, p. 279. London.
Beer, E. (1904). *Amer. J. med. Sci.*, **128**, 135.
Burnett, F. L. (1923). *Amer. J. Roentgenol.*, **10**, 599.
Cole, L. G. (1914). *Amer. J. med. Sci.*, **148**, 92.
Edwards, H. C. (1939). *Diverticula and Diverticulitis of the Intestine*, p. 195. Bristol.
Feldman, M. (1948). *Clinical Roentgenology of the Digestive Tract*, 3rd ed., p. 473. London.
Fischer, M. H. (1900). *J. exp. Med.*, **5**, 333.
Horner, J. L. (1958). *Amer. J. dig. Dis.*, **3**, 343.
Hurst (Hertz), A. F. (1907). *Guy's Hosp. Rep.*, **61**, 389.
Hurst, A. F. (1919). *Constipation and Allied Intestinal Disorders*, 2nd ed. London.
Johnson, T. A. (1943). In H. L. Bockus's *Gastroenterology*, vol. 2, p. 683. Philadelphia.
Jordan, A. C. (1926). *Chronic Intestinal Stasis*, 2nd ed. London.
Keith, A. (1910). *Brit. med. J.*, **1**, 376.
Lönnerblad, L. (1951). *Acta radiol. (Stockh.)*, Suppl. No. 88.
McCance R. A., Prior, K. M., and Widdowson, E. M. (1953). *Brit. J. Nutr.*, **7**, 98.
Manousos, O. N., Ritchie, J., and Truelove, S. C. (1967a). To be published.
—— Truelove, S. C., and Lumsden, K. (1967b). *Brit. med. J.*, **3**, 762.
Morson, B. C. (1963). *Brit. J. Radiol.*, **36**, 385.
Painter, N. S., and Truelove, S. C. (1964). *Gut*, **5**, 201.
Todd, T. W. (1930). *The Beaumont Foundation Lectures*, series No. 9, p. 79. Baltimore.
Turell, R. (1959). *Diseases of the Colon and Anorectum*, vol. 2, p. 633. London.
Vega, de la, J. M., Gonzalez, J. N., and Ponce de Leon, A. (1964). In H. L. Bockus's *Gastroenterology*, 2nd ed., vol. 2, p. 933. Philadelphia.
Williams, I. (1963). *Brit. J. Radiol.*, **36**, 393.

Prevalence of Colonic Diverticulosis in General Population of Oxford Area

O. N. MANOUSOS,* M.B., D.PHIL.; S. C. TRUELOVE,* M.D., F.R.C.P.; K. LUMSDEN,† M.B., B.CHIR., D.M.R.E.

Brit. med. J., 1967, **3**, 762–763

It has been generally accepted that diverticulosis of the colon is a common condition in Western countries, especially in the older age groups (Barborka, 1958; Reichman and Watkins, 1962). However, up to the present time the frequency of diverticulosis has been calculated from radiological studies carried out on patients or from post-mortem examinations in hospital, and consequently the results apply only to selected sections of the population. Spriggs and Marxer (1925) examined 1,000 consecutive barium enemas and found diverticula in 10%. Rankin and Brown (1930) studied 24,620 barium enemas and found diverticula in 5.7%. They reported a similar prevalence of diverticulosis (5.2%) in 1,925 necropsies. All except one of the necropsies were carried out on subjects older than 40 years.

Pemberton *et al.* (1947) reviewed a large number of radiographs of the colon and found diverticula in 8.5%. Welch *et al.* (1953) examined 2,000 barium enemas and found diverticula in 20% of the patients over the age of 60.

Until some years ago diverticula were more common in men than in women (Spriggs and Marxer, 1925; Ochsner and Bargen, 1935); recently, however, it appears that a change in sex ratio is taking place and a female preponderance is now commonly observed (Ford, 1953; Brown and Toomey, 1960). Table I shows the sex ratio in diverticulosis and diverticulitis reported by various authors. In a recent study on the prognosis of diverticulosis and diverticulitis (Manousos and Truelove, 1967) it was found that whereas below the age of 60 diverticula were equally common in men and women, above that age the condition was much more common in women. It was also shown that the number of patients admitted to hospital with diverticulosis, diverticulitis, and the complications of diverticular disease is increasing, and this probably indicates a true increase in the prevalence of the disease as a whole.

In view of the lack of accurate information on the frequency of diverticulosis in the population at large the present study was made.

TABLE I.—*Illustrating a Change in Sex Ratio in Diverticulosis and Diverticulitis. A Female Preponderance in Recent Years is Shown*

Authors	Male:Female ratio
Telling and Gruner (1917)*	2:1.0
Spriggs and Marxer (1925)†	2·7:1·0
Mayo (1930)†	1·7:1·0
Rankin and Brown (1930)†	2·3:1·0
Ochsner and Bargen (1935)†	1·25:1·0
Brown and Marcley (1937)†	1·6:1·0
Laufman (1941)*	1·7:1·0
Smithwick (1942)*	1·6:1·0
Ford (1953)†	1·0:1·5
Ford (1953)*	1·0:1·2
Friesen and Schmidt (1955)*	1·0:1·3
Greene (1957)†	1·0:1·4
Greene (1957)*	1·0:1·5
Boles and Jordan (1958)†	1·0:1·2
Brown and Toomey (1960)†	1·0:1·5
Brown and Toomey (1960)*	1·0:1·3
Botsford and Curtis (1961)*	1·0:1·3
Bevan (1961)*	1·0:2·0
Reichman and Watkins (1962)*	1·0:1·7
Manousos and Truelove (1967)†	1·0:1·8
Manousos and Truelove (1967)*	1·0:1·4

* Diverticulitis and its complications. † Diverticulosis.

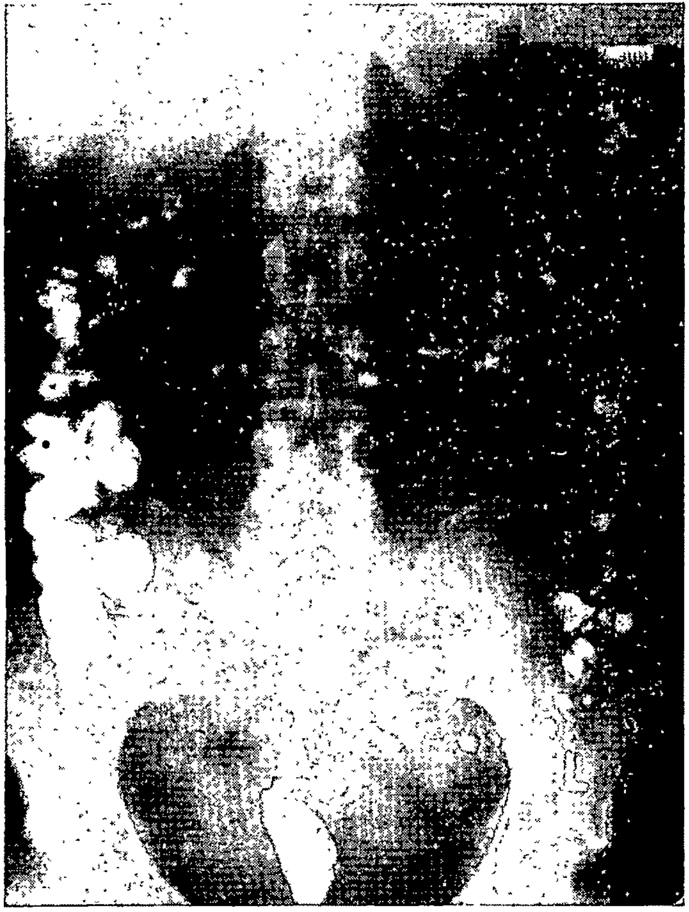
Methods and Subjects

The radiological appearances of the colon of 109 subjects without gastrointestinal symptoms were studied. The majority of the subjects were healthy volunteers who were either members of the staff of the Radcliffe Infirmary or visitors to inpatients. A minority of the subjects were patients in a geriatric unit (Cowley Road Hospital, Oxford) who were volunteers and who were completely free from gastrointestinal symptoms.

---

* Nuffield Department of Clinical Medicine, the Radcliffe Infirmary, Oxford.
† Consultant Radiologist, United Oxford Hospitals, Oxford.

The subjects studied were instructed to drink a small quantity of radio-opaque material (30 ml. of Micropaque or Fotogel) with each of their four main meals on one day. The next morning a radiograph of the abdomen was taken, and this was repeated on successive mornings (up to a maximum of six) until the radio-opaque material had virtually disappeared. The degree of accuracy of the method in demonstrating colonic diverticula (see Fig.) was tested on 20 known cases of diverticulosis in which the diverticula had been shown by barium enema. The follow-through method revealed the diverticula in every case.



Radiograph showing extensive diverticulosis of colon revealed by barium follow-through technique described in text.

It is interesting that in the first recorded case of colonic diverticula in which the diagnosis was made radiologically (Abbé, 1914) the diverticula were shown by follow-through examination whereas the radio-opaque enema had failed to demonstrate them.

By the follow-through method employed in the present study it was possible to obtain an estimate of the prevalence of diverticulosis. The method was also used as a measure of the transit times of food (Manousos, Truelove, and Lumsden, 1967).

Results

The radiographs were examined carefully, and only when the appearances were unequivocal were the diverticula accepted. The results (Table II) indicate that diverticulosis of the colon is slightly commoner in women than in men in the population studied. No cases of diverticulosis were found below the age of 40, but the prevalence of the condition increases steadily with age and reaches a peak above the age of 80 years. Above the age of 60 the condition was present in 15 out of 43 subjects (34.9%); below the age of 60 it was present in 5 out of 66 subjects (7.6%).

TABLE II.—*Prevalence of Diverticulosis in the Various Age Groups*

Age	Men			Women			Both Sexes		
	No. of Subjects	With Diverticula		No. of Subjects	With Diverticula		No. of Subjects	With Diverticula	
		No.	%		No.	%		No.	%
< 40	14	0	0·0	25	0	0·0	39	0	0·0
40–59	14	2	14·3	13	3	23·1	27	5	18·5
60–79	10	3	30·0	14	4	28·6	24	7	29·2
80+	10	3	30·0	9	5	55·5	19	8	42·1

Discussion

One of the best studies of the frequency of diverticulosis of of the colon is that of Debray *et al.* (1961), which was carried out in France. They studied the radiographs of 500 barium enemas taken at random from a much bigger number carried out in hospital or by their colleagues. They found a low frequency of diverticulosis in patients under the age of 40, but thereafter the frequency rose with each successive age group until it reached 40% over the age of 70 years. The weakness of their study is that many of the patients had gastrointestinal symptoms and therefore they cannot be regarded as an unbiased sample of the general population. The present study, though dealing with comparatively small numbers, has been concerned with subjects completely free from gastrointestinal symptoms, and therefore its results may be a closer reflection of the prevalence of diverticulosis of the colon in the general population.

Summary

An estimate of the prevalence of diverticulosis of the colon in the Oxford area has been obtained by studying healthy volunteers. A follow-through radiological method was used. Diverticulosis was found to be present in one in every three persons above the age of 60 years. Below that age the condition was present in 7.6% of the population studied. Diverticula were more common in women than in men. A review of the literature shows that a female preponderance in diverticulosis has been constantly observed during recent years.

We are grateful to the volunteers who took part in this study. We also wish to thank Dr. L. Z. Cosin and his staff for allowing us to study patients under their care, the radiographers of the United Oxford Hospitals for taking the radiographs, and the Medical Research Council for financial support.

REFERENCES

Abbé, R. (1914). *Med. Rec. (N.Y.)*, **86**, 190.
Barborka, C. J. (1958). *Gastroenterology*, **34**, 278.
Bevan, P. G. (1961). *Brit. med. J.*, **1**, 400.
Boles, R. S., and Jordan, S. M. (1958). *Gastroenterology*, **35**, 579.
Botsford, T. W., and Curtis, L. E. (1961). *New Engl. J. Med.*, **265**, 618.
Brown, D. B., and Toomey, W. F. (1960). *Brit J. Surg.*, **47**, 485.
Brown, P. W., and Marcley, D. M. (1937). *J. Amer. med. Ass.*, **109**, 1328.
Debray, C., Hardouin, J. P., Besançon, F., and Raimbault, J. (1961). *Sem. Hôp. Paris*, **37**, 1743.
Ford, H. S. (1953). *Canad. med. Ass. J.*, **69**, 506.
Friesen, L., and Schmidt, E. R. (1955). *Surg. clin. N. Amer.*, **35**, 1385.
Greene, W. W. (1957). *Amer. J. Surg.*, **94**, 282.
Laufman, H. (1941). *Int. Abstr. Surg.*, **73**, 222.
Manousos, O. N., and Truelove, S. C. (1967). Awaiting publication.
—— —— and Lumsden, K. (1967). *Brit. med. J.*, **3**, 760.
Mayo, W. J. (1930). *Trans. Amer. surg. Ass.*, 48, 301.
Ochsner, H. C., and Bargen, J. A. (1935). *Ann. intern. Med.*, **9**, 282.
Pemberton, J. de J., Black, B. M., and Maino, C. R. (1947). *Surg. Gynec. Obstet.*, **85**, 523.
Rankin, F. W., and Brown, P. W. (1930). Ibid., **50**, 836.
Reichman, H. R., and Watkins, J. B. (1962). *J. Amer. med. Ass.*, **182**, 1023.
Smithwick, R. H. (1942). *Ann. Surg.*, **115**, 969.
Spriggs, E. I., and Marxer, O. A. (1925). *Quart. J. Med.*, **19**, 1.
Telling, W. H. M., and Gruner, O. C. (1917). *Brit. J. Surg.*, **4**, 468.
Welch, C. E., Allen. A. W., and Donaldson, G. A. (1953). *Ann. Surg.*, **138**, 332.

Electric Fire Burn

ANDREW GUNN,* M.A., M.B., B.CHIR., F.R.C.S.

Brit. med. J., 1967, 3, 764–766

Electric fires are of three types: silica-sheathed, fireclay-mounted, and exposed rod. Children who grasp the heating element of electric fires of the exposed-rod type sustain severe burns of the hand. Wynn Williams (1955) reviewed 100 cases of children with burnt hands and noted that 36% were due to electric fires. Muir (1958) described and illustrated the electric bar fire burn of the hand, separating it from electric current burns and defining it as a thermal injury. Clarkson and Pelly (1962) also described it as a severe and specific injury of the hand in children. Evans (1962) recorded the impression that the injury was happening more often. This paper reviews the incidence and results of this burn and discusses prevention.

Incidence

From 8 February 1953 until 31 December 1966 the Children's Burns Unit at Guy's Hospital admitted 735 children for burns of all kinds. Of these, 19 were admitted with an electric bar fire burn of the hand. Since 1962 four additional children have been treated for flexion contracture due to the same cause after the burn had healed elsewhere.

The annual incidence of fresh burns is given in Table I; there appear to have been slightly more cases in recent years. The burns occur chiefly in winter, as do other burns (Clarkson, 1965); but children have been admitted in every month of the year.

TABLE I.—*Electric Fire Burn of Hand. Admissions to Children's Burns Unit: Annual Incidence*

	1953	54	55	56	57	58	59	60	61	62	63	64	65	66
No.	0	3	0	0	1	2	2	0	1	1	2	3	2	2

According to Clarkson (1965) 60% of the children were admitted for burns of all types from addresses in S.E. London and 20% from S.W. London postal districts. Twelve out of 19 children with an electric bar fire burn were admitted from S.E. or S.W. London.

The age and sex incidence of this injury is shown in Table II. A few more boys than girls are seen to be involved, but the predominance of male toddlers is noted. All these 19 children who were admitted up to 31 December 1966 were white; no immigrants have been admitted with this burn.

TABLE II.—*Electric Fire Burn of Hand. Age and Sex Incidence*

Sex	Age in Years												Total
	0–1	1	2	3	4	5	6	7	8	9	10	11	
M	0	2	8	0	0	0	0	0	1	0	0	0	11
F	0	1	1	1	1	1	1	0	0	1	0	1	8

Mode of Accident

The hospital notes are not always complete and the description of injury is not always full. However, it has been possible to trace some more recent patients, and their mothers have answered a questionary. From their answers and the case notes the following facts emerge.

(1) The accident may happen very quickly, even if adults are present in the room. Usually children are in the room alone or with other children.

(2) A small child can easily slip his hand through the guard or over or under it. The British Standard Specification (British Standard 1945) is not designed to prevent this happening, and a note of this is made in the text. The guard is designed to prevent severe clothing burns, and indeed the incidence of clothing burns in Birmingham has fallen since its adoption (Bull, Jackson, and Walton, 1964).

(3) A severe burn may be sustained even if the fire is grasped after being switched off or while the fire is warming up. When the fire first glows dull red the surface temperature of the nickel-chrome wire element is 550° C. At normal working temperatures the element glows a bright orange-yellow, and then the surface temperature is 800–850° C. (Belling, 1966).

(4) After grasping the element a small child may easily sustain a burn of the whole of the volar surface of one or both hands (Fig. 1). Only one infant had all the finger-tips of one hand burnt. If there are two or more elements in one fire then a child may burn the dorsum of the finger or hand on the second element (Fig. 2).

(5) It may be difficult to release a child who has grasped the fire. The burnt flesh of the hand may stick to the element. The closed hand may be trapped between the bars of the guard. An electrical effect causing muscle spasm may make it more difficult to release the child.

Treatment

None of the children admitted to the Guy's Children's Burns Unit after an electric fire burn have died, and burns have been confined to the part of the hand in contact with the heating element. The results are given in Table III and compared with the results of other burns. Though it is not the purpose of this paper to deal with treatment the results cannot be assessed without reference to it.

TABLE III.—*Results in 116 Children with Burns of the Hand*

Type	No. of Cases	No. whose Hand Grafted	Amputation	Late Surgery
Electric-fire burn ..	19	17	2	7
Electric-current burn:				
Low-voltage:				
Flash	5	0	0	0
Contact	10	8	0	0
High-voltage:				
T.V. set	2	2	1 finger	0
Conductor rail ..	2	2	2 major upper limb	0
Non-electric causes ..	78	9	1 finger	0

The following local measures are employed in electric fire burns after sedation (Gunn, 1967).

Toilet.—The whole upper limb is thoroughly cleaned with Savlon.

Extension Splintage.—In previous papers Wynn Williams (1955) and Clarkson and Pelly (1962) have stressed the importance of extension splintage. There are many advantages in treating superficial burns of the hand by exposure. Potentially deep burns of the palm or the volar surface of the fingers in children should be treated by extension splintage in order to prevent flexion contracture of the fingers. Flexion contracture can be prevented by splintage, but may develop within days without splintage. An established contracture may require prolonged treatment. In these children joint stiffness has not been seen even after prolonged extension splintage of the wrist and fingers.

---

* Children's Burns Unit, Guy's Hospital, London S.E.1.

Skin-grafting.—Deep burns require skin-grafting. In practice, burns which are unhealed after 14 days are regarded as deep. It is an advantage to delay grafting until the third week after burning for the following reasons. The diagnosis of depth is easier and unnecessary excision is avoided. The slough is more readily separated and haemorrhage is less, so that excision and grafting can be completed in one operation. Where the graft bed persistently bleeds grafting may be delayed for two to five days while the hand is dressed with polyurethane foam sponge. Discharges are readily absorbed and a clean granulating surface is left, which is ideal for grafting. As a rule thick split-skin grafts cut from the thigh give a reliable take and satisfactory permanent cover. If tendons, bones, or joints are exposed then flap cover is indicated.

In only two patients were the burns superficial, and these did not undergo skin-grafting. The remaining 17 required skin-grafting to heal. Of these 17, six developed flexion contractures of the fingers (Fig. 3) or adduction contracture of the thumb (Fig. 4) and required further surgical treatment. One patient underwent primary amputation of the ring finger (Fig. 5); another not only required primary amputation of the little finger but also developed a flexion contracture later.

On average these children were in hospital for 34.7 days. This figure does not take into account the fact that not all children were admitted on the day of burning. Nor does it allow for the fact that a few children had their hospital stay interrupted for some reason or other. The five-week average stay suggested that the time required for primary healing is likely to be five or six weeks. This agrees with the 6.5 weeks' hospitalization given by Wynn Williams (1955) for deep burns treated surgically.

Treatment of established contractures is apt to be protracted. Several operations may be required to correct all deformities

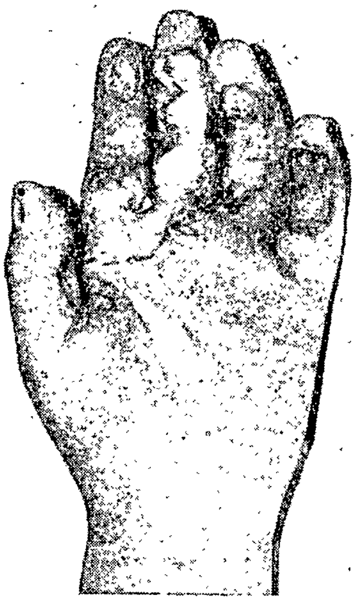


FIG. 1

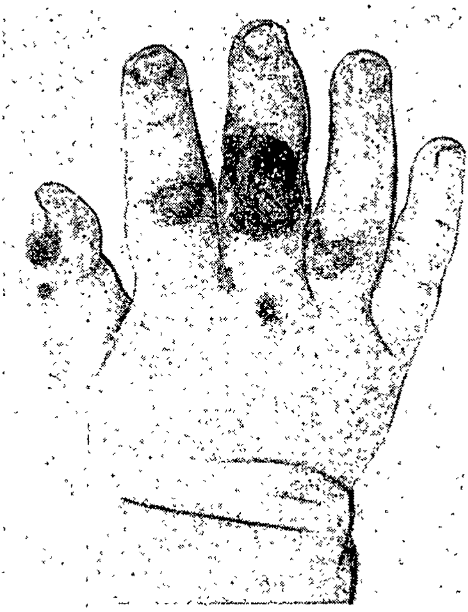


FIG. 2

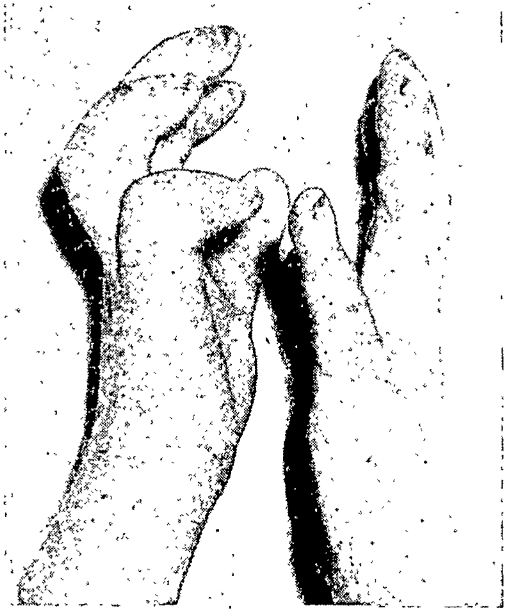


FIG. 3

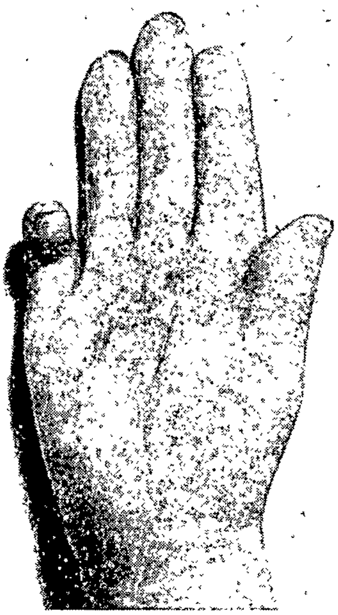


FIG. 4

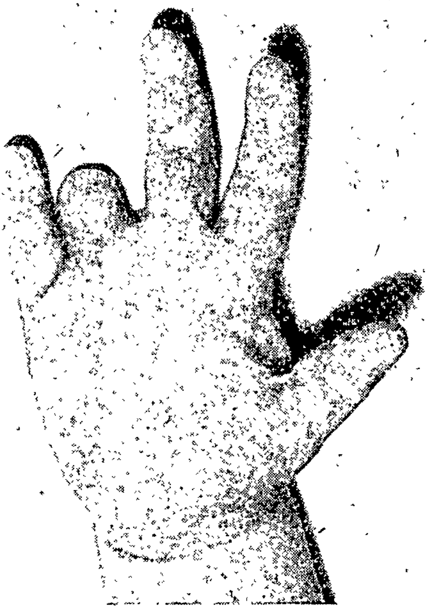


FIG. 5

FIG. 1.—Recent burn of the fingers. Lesions may be more extensive than this.

FIG. 2.—Dorsum of the middle finger shows a full-thickness burn requiring flap cover.

FIG. 3.—Severe flexion contractures of right little and ring fingers after healing; left ring finger and right middle finger are affected to a lesser degree.

FIG. 4.—This burn healed with adduction contracture of the thumb and severe flexion contracture of the little finger.

FIG. 5.—The right ring finger was so badly damaged that amputation was unavoidable.

when many fingers are scarred. Recurrence after correction is also a serious problem.

Results

The results show that the electric fire burn is potentially very serious because the element is very hot and a large area is burnt in a small hand. Comparison with other types of burn will also show that this is the most important burn of the hand in children. Most electric current contact burns of children occur at the normal domestic voltages and produce small burns which usually heal without complications after grafting. Low-voltage flash burns have all been superficial. High-voltage burns may be disastrous, but they seldom occur. Patients with a wide variety of non-electric burns have been admitted; the majority of them had extensive or potentially deep burns elsewhere and only a small number required skin-grafting to the hand.

It is therefore made clear that if a child grasps the heating element of an electric fire of the exposed rod type he will sustain a severe and potentially crippling injury. The incidence throughout the country remains uncertain. It may be that more or fewer cases than average are admitted to the Children's Burns Unit at Guy's Hospital. But it has been estimated that the Guy's Children's Burns Unit serves a population of 2,500,000 (Clarkson, 1965), and in recent years two to three new cases of electric fire burns have been admitted annually. The Guy's figures may not be representative; but if they are then 40 to 60 new cases may occur each year.

There are good reasons for believing that the risk is increasing. Figures supplied by the Electricity Council show that domestic consumption has increased. Estimates show that more people own electric space heaters and that more electricity is used by these heaters (Table IV).

TABLE IV.—*Electricity Statistics—England and Wales*

	1954–5	1965–6
Domestic consumption (million kWh) ..	17,017	50,829
Ownership of domestic consumers of electric space heater:		
% consumer owning	60·5	79·7
No. of consumers	7,275,000	12,156,000
Loading (MW)	17,000	41,875
Use of electricity space heating (million kWh)	4,000	12,500

Prevention

For the above reasons it is desirable to review measures which might prevent these accidents. (1) Doctors should know about these accidents and how serious they may be. In turn, they could warn the public and ensure that the victims got prompt and adequate treatment. (2) If these accidents were all notified the necessity for further prophylactic measures could be assessed. (3) The safety of electric space heaters and the design of their guards might be reviewed. It would be relatively easy to set a new British Standard for fireguards. It does not seem likely that cost would be prohibitive, but a new guard might greatly reduce the effectiveness of the space heater. (4) It is desirable for all electric space heaters to be in a clear space and protected by a guard, just as open fires and paraffin stoves should be. (5) If a suitable guard cannot be designed for electric space heaters of the exposed rod type, then it might be better to abandon them in favour of fireclay-mounted or silica-sheathed electric space heaters. Silica-sheathed electric space heaters are regarded as safest by the Consumers' Association (*Which?*, 1965).

Summary

The elements of electric fires of the exposed rod type are sometimes grasped by young children. The child sustains a thermal injury of the palm of the hand which is almost always deep and is potentially crippling: 89% require grafting, 10% lose a finger, and 37% need surgery for late complications. Late complications may require protracted treatment.

The electric fire burn is the most important burn of the hand in children. It is estimated that 40 to 60 may occur in Great Britain annually. As the use of electric fires increases so may the risk of this accident.

To reduce the incidence the following measures are suggested: the risk must be publicized; cases should be made notifiable; the design of the guards on these fires should be reviewed; electric fires must be enclosed by a guard; and electric fires of the exposed rod type may have to be discarded in favour of safer models.

I wish to thank Mr. P. W. Clarkson for kindly allowing me to study his patients, and for his constant encouragement in the preparation of this paper. The Electricity Council kindly supplied me with figures relating to the domestic consumption of electricity and the domestic use of electric space heaters, and allowed me to publish them. I am grateful to Mr. J. Rytina, of the Department of Medical Illustration, Guy's Hospital, for photographs illustrating this paper.

REFERENCES

Belling Electric Company (1966). Technical Inquiry.

Bull, J. P., Jackson, D. M., and Walton, C. (1964). *Brit. med. J.*, **2**, 1421.

Clarkson, P. W. (1965). *Ann. roy. Coll. Surg. Engl.*, **37**, 207.

—— and Pelly, A. (1962). *The General and Plastic Surgery of the Hand.* Oxford.

Evans, J. (1962). Personal communication to P. W. Clarkson.

Gunn, A. L. (1967). *Guy's Hosp. Rep.*, **116**, 15.

Muir, I. F. K. (1958). *Brit. J. plast. Surg.*, **10**, 292.

Which? 1965, **8**, 27.

Wynn Williams, D. (1955). *Brit. J. plast. Surg.*, **7**, 313.

Effects of a "New" Human Respiratory Virus in Volunteers

A. F. BRADBURNE,* B.SC.; M. L. BYNOE,* M.B., D.T.M.&H., D.OBST.R.C.O.G.
D. A. J. TYRRELL,* M.D., F.R.C.P., M.C.PATH.

Brit. med. J., 1967, 3, 767–769

We recently reported the cultivation in organ cultures of a virus, B814, which caused colds in volunteers but could not be detected or propagated in tissue cultures (Tyrrell and Bynoe, 1965). Hamre and Procknow (1966) have discovered a "new" virus in the respiratory tract of six students suffering from colds. There was a slight viral cytopathic effect in tissue cultures of human embryo kidney cells, but the virus was subsequently adapted to the WI-38 strain of human embryo fibroblasts. Both of these viruses were ether-labile but apparently unrelated serologically to any known myxoviruses. It now appears that they are morphologically identical and indistinguishable from the viruses of avian infectious bronchitis (Almeida and Tyrrell, 1967), and mouse hepatitis (Tyrrell and Almeida, 1967). The particles are 80–120 mμ in diameter, pleomorphic, and surrounded by a fringe of club-shaped projections about 20 mμ in length. Recently, further viruses of this morphological type have been isolated in organ cultures by McIntosh *et al.* (1967).

We have now given the prototype strain, 229-E, of Hamre and Procknow to volunteers in order to determine whether it causes colds and to study serum neutralizing antibody during infections with viruses of this type.

Materials and Methods

Virus.—The 229-E virus was received from Dr. Hamre as tissue culture fluid. It was then passed in human embryonic lung fibroblasts and in organ cultures of human embryo trachea. This material was not apparently contaminated with bacteria or other viruses and was inoculated into volunteers, in whom it was passed further. For the inoculation of volunteers organ culture fluids or nasal washings were diluted 1 in 10 in saline and 0.5 ml. was dropped into each nostril.

Tissue Cultures.—Locally propagated strains of human embryo lung fibroblasts were used. They were cultivated by the methods of Hayflick and Moorhead (1961) and maintained in a roller drum at 33° C. in a medium containing 2% ox serum and 98% Eagle's medium (Gibco: G13) with penicillin, streptomycin, and achromycin.

Organ Cultures.—These were maintained by a modification (Tyrrell and Blamire, 1967) of the original method of Hoorn (1966) with 1.25 ml. of Eagle's medium containing 0.2% bovine plasma albumin in an atmosphere of 5% CO_2 in air, at 33° C.

Virus Isolation.—Nasal washings were collected with about 10 ml. of sterile saline, mixed with an equal volume of nutrient broth, and stored at $-70°$ C. Two or three cultures of fibroblasts were inoculated with 0.2 ml. of nasal washings and changed six hours later. A widespread cytopathic effect appeared within four days of inoculation in the case of positive isolation. All isolated viruses were identified by neutralization with a specific antiserum produced in guinea-pigs and provided by Dr. Hamre.

Neutralization Tests.—Serial dilutions of inactivated serum were mixed with equal volumes of virus, held at room temperature for two hours, and 0.2 ml. of the mixture was inoculated into each of two or three cultures. The test was read about six days later. Complete neutralization of the virus was taken as the end-point. It was found essential to use small doses of virus in order to detect antibody, and in tests reported here between 25 and 100 TCD$_{50}$ were employed. In the serological survey all sera were tested at a dilution of 1 in 10. A number of preparations of 229-E virus fixed complement with volunteers' sera. However, no rising titres were detected in the sera from infected volunteers; it is therefore not certain that the fixation was specific, and consequently the results are not reported here.

Volunteers.—These were of both sexes, aged 18 to 50 years, and were cared for in isolation as described elsewhere (Andrewes, 1948; Tyrrell, 1965).

Sera were collected before inoculation and two to three weeks later, and nasal washings were collected daily for five days after inoculation.

Results

As a preliminary to volunteer inoculation we wished to know whether specific antibodies against the virus 229-E were present in the sera of inhabitants of Britain. Accordingly sera collected over the past 10 years from subjects living in various areas were tested at a dilution of 1 in 10 in the neutralization test. As can be seen from Table I, about 30% of sera neutralized the virus.

TABLE I.—*Presence of Neutralizing Antibody in Human Sera*

Age Group (years)	No. of Sera		Percentage Positive
	Tested	Positive	
0–5	32	8	25
6–10	23	5	23
11–15	39	10	26
16–20	40	8	20
21–50	81	32	41
Total	215	63	29

The adult sera were collected from volunteers arriving at the Unit over the past 10 years. The minors' sera were taken from hospital patients in Liverpool and Sheffield.

About 40% of adults possessed antibody, and though the incidence was lower in children it seemed that they also were being infected by this or an antigenically related virus even within the first five years of life.

Passage of Virus in Volunteers

The passage history of the virus is summarized in Fig. 1. This shows that after a total of seven passages in tissue cultures in the U.S.A. and here it multiplied freely in human tracheal epithelium. However, the cilia continued to beat for eight days and sections of the cultures showed little abnormality. Organ culture fluid apparently produced a cold in four out of six volunteers. Nasal washings were collected from a volunteer who developed a cold and excreted virus, and these were passed to more volunteers. At each of a total of four serial passages in volunteers, colds were produced. Virus was recovered in tissue culture, and the dose of virus in the diluted nasal secretion used for each passage is shown on the left of the diagram.

---

* From the Common Cold Research Unit, Salisbury, Wilts.

Twenty volunteers were given saline in parallel with these experiments and none developed colds. There is therefore no doubt that the virus did multiply in the human respiratory tract and apparently caused colds.

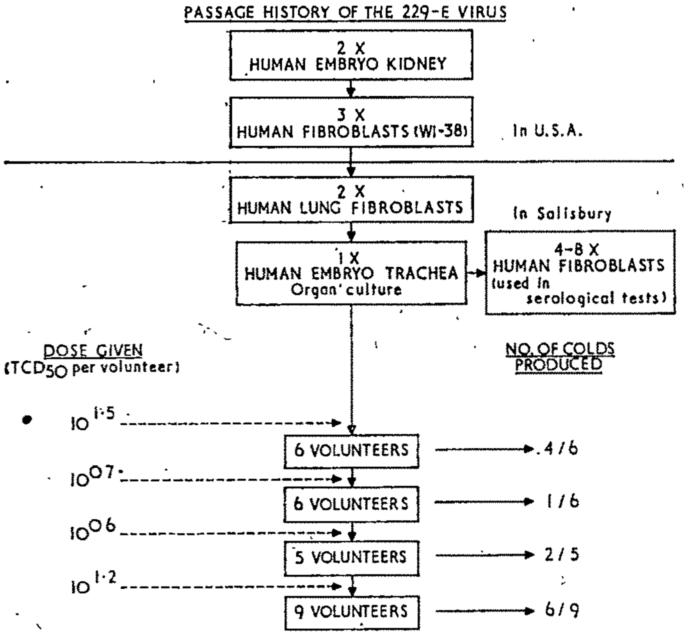

PASSAGE HISTORY OF THE 229-E VIRUS
2 X HUMAN EMBRYO KIDNEY
3 X HUMAN FIBROBLASTS (WI-38)
In U.S.A.
2 X HUMAN LUNG FIBROBLASTS
In Salisbury
1 X HUMAN EMBRYO TRACHEA Organ culture
4-8 X HUMAN FIBROBLASTS (used in serological tests)
DOSE GIVEN (TCD50 per volunteer)
NO. OF COLDS PRODUCED
$10^{1.5}$
6 VOLUNTEERS
4/6
$10^{0.7}$
6 VOLUNTEERS
1/6
$10^{0.6}$
5 VOLUNTEERS
2/5
$10^{1.2}$
9 VOLUNTEERS
6/9

FIG. 1.—Passage history of the 229-E virus.

Table II shows that half the inoculated volunteers developed colds; virus was recovered from all of these subjects but from only about one-third of those who remained well, and this difference is highly significant statistically. Nevertheless, the frequency of virus excretion varied a great deal from individual to individual, even when small doses of virus derived from man were given; this can be seen from Table III, the amount and period of virus excretion not apparently being related to the occurrence of colds. Only one volunteer excreted virus on the day after inoculation, and the frequency of virus excretion was at its peak at about the same time as the peak of clinical symptoms, as can be seen from Fig. 2. The titre of virus in 10 positive nasal washings ranged from $10^{0.5}$ to $10^{2.5}$ with a geometric mean of $10^{1.5}$.

TABLE II.—*Relation Between Virus Isolation and the Occurrence of Colds*

Type of Volunteer	Results of Virus Isolation Tests		
	Positive	Negative	Total
Inoculated { Colds	13	0	13
Inoculated { No colds	5	8	13
Uninoculated: No colds ..	0	6	6
Total	18	14	32

For the upper two rows of this table 0·01 > P > 0·001

TABLE III.—*Pattern of Virus Excretion in 14 Infected Volunteers in the Second to Fourth Passage Experiments*

	Duration of Virus Excretion (days)			
	1	2	3	4
No. of volunteers who excreted virus for indicated number of days ..	3	1	4	4
No. of above volunteers who developed colds	2	1	2	3

Serological Response to Infection

Neutralization tests were performed on the sera from all the inoculated volunteers and from four volunteers who were given saline (Table IV).

The only significant titre rises—that is, of fourfold or greater—were found in 7 of the 13 volunteers who developed colds. Colds occurred in both those with and without antibody at the time of inoculation, but antibody rises were found mainly among those with a titre of 5 or less.

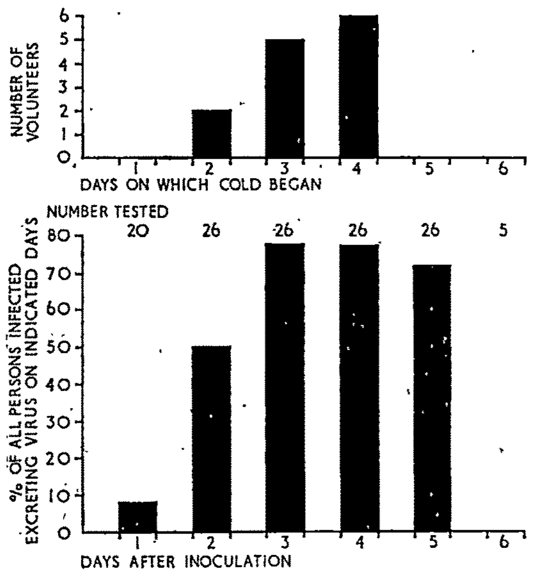


FIG. 2.—Time course of the onset of colds and the shedding of virus.

TABLE IV.—*Relation Between Antibody Titre and the Response to Inoculation*

Titre of Neutralizing Antibody in Serum Before Inoculation	No. of Volunteers in Indicated Category Who			Total
	Excreted Virus	Developed Colds	Developed Rising Antibody Titres	
≤5	7	6	4	8
5–	4	3	2	6
10–	6	3	1	8
40–160	1	1	0	4

Clinical Pattern of Colds Produced

The illnesses observed were all within the range of typical common colds. One was graded as severe (see Tyrrell, 1965), two as moderate, and the rest as mild. The main symptoms and signs are shown in Table V, alongside similar figures for volunteers infected with the B814 virus and with rhinoviruses. It can be seen that the pattern of illness was, in general, similar to that produced by the B814 virus. The proportion of colds produced by these viruses was not significantly greater than that produced by rhinoviruses, but the mean incubation period was significantly longer. The duration of illness was shorter, significantly so when B814 colds were compared with DC colds. On the other hand, there were no significant differences between the two strains of avian-infectious-bronchitis-like viruses or between the two types of rhinoviruses in these measurements.

The means of the peak numbers of handkerchiefs used were higher in colds due to avian-infectious-bronchitis-like viruses than in those due to rhinoviruses. Though the differences were not formally significant, the median values also were higher in avian-infectious-bronchitis colds than in rhinovirus colds. This was mainly due to the fact that very few people with colds due to avian-infectious-bronchitis-like viruses (1 out of 47) used fewer than eight handkerchiefs, while over a quarter (43 out of 155) did so among those infected with rhinoviruses. This difference is highly significant statistically. However, two volunteers, one infected with 229-E and one with B814, developed "streaming" colds, using over 100 paper handkerchiefs in one day. This was not seen after rhinovirus infections. Mucopurulent discharge was not seen at all after infection with 229-E, and, though this is unlikely to result solely by chance ($P=0.002$), the real significance is obscure. Malaise was more common than in rhinovirus colds and cough was less common, but these and other symptoms and signs were not significantly different in any of the groups. Over one-fifth of volunteers infected with 229-E had pyrexia, with an oral temperature between 99.2 and 100.4° F. (37.3 and 38° C.).

TABLE V.—*Clinical Features of Colds Produced by Inoculating Four Viruses*

	Avian-Infectious-Bronchitis-like		Rhinoviruses	
	229-E	B814*	Type 2 (HGP or PK)	DC*
No. of volunteers inoculated	26	75	213	251
No. getting colds ..	13 (50%)	34 (45%)	78 (37%)	77 (31%)
Incubation period (days):				
Mean	3·3	3·2	2·1	2·1
Range	2–4	2–5	1–5	1–4
Duration (days):				
Mean	7	6	9	10
Range	3–18	2–17	3–19	2–26
Maximum No. of handkerchiefs used daily:				
Mean	23	21	14	18
Range	8–105	8–120	3–38	3–60
Malaise (%)	46	47	28	25
Headache (%)	85	53	56	56
Chill (%)	31	18	28	15
Pyrexia (%)	23	21	14	18
Mucopurulent nasal discharge (%)	0	62	83	80
Sore throat (%) ..	54	79	87	73
Cough (%)	31	44	68	56
No. of volunteers with colds of indicated severity:				
Mild	10 (77%)	24 (71%)	63 (80%)	36 (47%)
Moderate	2 (15%)	7 (20%)	12 (15%)	28 (36%)
Severe	1 (8%)	3 (9%)	4 (5%)	13 (17%)

* Virus was administered only as nasal washings.

The statistical probability of some of the features of the colds due to 229-E virus n relation to colds due to other cold viruses are shown below.

(1) *t*-test on incubation periods	229-E : B814	$0{\cdot}3 > P > 0{\cdot}25$
	229-E : Rhino type 2	$0{\cdot}005 > P > 0\ 001$
	229-E : DC	$0{\cdot}05 > P > 0{\cdot}025$
	DC : Rhino type 2	$0{\cdot}498 > P > 0{\cdot}495$
(2) *t*-test on duration of colds	229-E : B814	$0{\cdot}15 > P > 0{\cdot}10$
	229-E : Rhino type 2	$0{\cdot}10 > P > 0{\cdot}05$
	229-E : DC	$0{\cdot}20 > P > 0{\cdot}15$
	B814 : Rhino type 2	$0{\cdot}10 > P > 0{\cdot}05$
	B814 : DC	$0{\cdot}01 > P > 0{\cdot}005$
	DC : Rhino type 2	$0{\cdot}95 > P > 0{\cdot}90$

Discussion

The fact that of the six isolations of this virus made by Hamre and Procknow five were from patients with clinical colds and only one from a healthy subject suggested strongly that the virus caused colds. Our results supplement these observations and show that after serial passage in tissue culture the virus can multiply in human respiratory epithelium in vitro and in vivo and can cause the common cold syndrome. Infection and disease occurred even when the serum contained substantial titres of neutralizing antibody, a phenomenon that has also been found on administering parainfluenza and respiratory syncytial virus to volunteers (Reichelderfer *et al.*, 1958 ; Tyrrell *et al.*, 1959 ; Kravetz *et al.*, 1961). The phenomenon might be due to lack of antibody in the nasal secretion of some persons with serum antibody, as appears to be the case with experimental infections with parainfluenza 1 virus (Smith *et al.*, 1966), but the possibility was not investigated in our studies.

There was no evidence of lower respiratory tract infection in our volunteers, but since the virus appears to infect children, as judged by the occurrence of serum antibody, it is nevertheless possible that the lower respiratory tract may be susceptible at that age and more serious disease may then be produced.

It is known that human sera often neutralize mouse hepatitis virus (Gledhill, personal communication). Furthermore, paired sera from 12% of Servicemen suffering from acute respiratory diseases have shown increasing antibody titres against mouse hepatitis virus (Hartley *et al.*, 1964), and it is possible that this occurred because some viruses of the avian-infectious-bronchitis-like group infect a significant proportion of such cases in the general population and induce the formation of antibody against the related virus. However, preliminary experiments have shown that our viruses are serologically distinct from avian infectious bronchitis and mouse hepatitis viruses on the basis of neutralization tests (Bradburne, Gledhill, and Berry, unpublished). There were no antibody rises against 229-E in sera from volunteers who developed colds after inoculation with B814, and the isolates of McIntosh *et al.* (1967) were also serologically distinct from 229-E. It therefore seems likely that we are dealing with members of a group in which individual viruses are very species-specific and in which those strains that infect man belong to a number of distinct serotypes. However, further studies are being made on these and related problems, and the results will be reported later.

Summary

A virus, 229-E, which morphologically resembles avian infectious bronchitis virus has been passed serially four times in man. Colds were produced in 13 out of 26 inoculated volunteers. There was a significant association between the presence of virus in the nose and the development of colds. Seven of the 13 volunteers who developed colds showed rising titres of antibody against this virus. The colds showed significantly longer incubation periods than did colds due to rhinoviruses, but no longer than those of colds caused by the related virus B814. The colds were also shorter and were associated with more nasal discharge than rhinovirus colds, but many of the differences are not statistically significant.

Of 215 sera collected from children and adults in Britain in the past 10 years 29% contained neutralizing antibody.

It is concluded that the virus can cause colds and probably circulates to a significant extent in this country.

We would like to thank the volunteers for their co-operation ; Miss E. M. Bullock for help with the clinical observations ; Dr. D. Hamre for providing the virus and serum ; Mr. S. Peto for advice on statistical problems ; and Mrs. P. K. Brown and Miss N. Frost for preparing the tissue cultures.

REFERENCES

Almeida, J. D., and Tyrrell, D. A. J. (1967). *J. gen. Virol.*, **1**, 175.
Andrewes, C. H. (1948). *J. roy. Soc. Arts*, **46**, 200.
Hamre, D., and Procknow, J. J. (1966). *Proc. Soc. exp. Biol. (N.Y.)*, **121**, 190.
Hartley, J. W., Rowe, W. P., Bloom, H. H., and Turner, H. C. (1964). Ibid., **115**, 414.
Hayflick, L., and Moorhead, P. S. (1961). *Exp. Cell. Res.*, **25**, 585.
Hoorn, B. (1966). *Acta path. microbiol. scand.*, Suppl. No. 183.
Kravetz, H. M., *et al.* (1961). *J. Amer. med. Ass.*, **176**, 657.
McIntosh, K., Dees, J. H., Becker, W. B., Kapikian, A. Z., and Chanock, R. M. (1967). *Proc. nat. Acad. Sci. (Wash.)*, **57**, 933.
Reichelderfer, T. E. *et al.* (1958). *Science*, **128**, 779.
Smith, C. B., Purcell, R. H., Bellanti, J. A., and Chanock, R. M. (1966). *New Engl. J. Med.*, **275**, 1145.
Tyrrell, D. A. J. (1965). *Common Colds and Related Diseases.* London.
—— and Almeida, J. D. (1967). *Arch. ges. Virusforsch.* In press.
—— and Blamire, C. J. (1967). *Brit. J. exp. Path.*, **48**, 217.
—— and Bynoe, M. L. (1965). *Brit. med. J.*, **1**, 1467.
—— —— Petersen, K. B., Sutton, R. N. P., and Pereira, M. S. (1959). Ibid., **2**, 209.

Acute Exudative Arthritis in Leprosy—Rheumatoid-arthritis-like Syndrome in Association with Erythema Nodosum Leprosum

A. B. A. KARAT,* M.B., B.S., B.SC., M.R.C.P., M.R.C.P.ED.; S. KARAT,† M.B., B.S., F.R.C.S.
C. K. JOB,‡ M.D., B.SC., M.C.PATH.; M. A. FURNESS,§ M.C.S.P.

Brit. med. J., 1967, **3**, 770–772

Erythema nodosum leprosum is a fairly common complication of lepromatous leprosy and is variously reported to occur in 30 to 40% of all patients with lepromatous leprosy on sulphone treatment (Buu Hoï and Basset, 1963; Cochrane, 1964; Job *et al.*, 1964). As yet there is no satisfactory explanation of the mechanism of production of erythema nodosum leprosum. Among the many hypotheses postulated, the concept of an immunological reaction as the fundamental basis of this rather dramatic complication is generally accepted (Aguas, 1963; Skinsnes and Tsang, 1963; Cochrane, 1964; Job *et al.*, 1964). There is some evidence to link up this phenomenon with autoimmunity, such as the presence of lupus erythematosus cell and rheumatoid factor in the sera of a proportion of these patients (Cathcart *et al.*, 1961; Bonomo *et al.*, 1965; Matthews and Trautman, 1965; Karat *et al.*, 1966). Pain in the joints (arthralgia) is a common and well-documented feature of erythema nodosum leprosum (Cochrane, 1964; Job *et al.*, 1964). Lele *et al.* (1965) described five cases of leprosy presenting as rheumatoid arthritis. Except for Case 4, none of their patients had erythema nodosum. The synovial biopsy was done in four out of the five cases, and the main histopathological finding was infiltration by round cells, epithelioid cells, and occasional giant cells. In the patient with erythema nodosum synovial biopsy did not reveal any significant change.

In the past two years at Schieffelin Leprosy Research Sanatorium we have seen 10 patients with lepromatous leprosy who developed acute painful exudative polyarthritis clinically similar to acute rheumatoid arthritis during the course of erythema nodosum leprosum. The polyarthritis cleared up completely when erythema nodosum subsided, leaving no residual signs of rheumatoid arthritis, clinical or radiological.

We present the case reports of two of these patients who, during the course of erythema nodosum leprosum, developed acute exudative polyarthritis clinically simulating acute rheumatoid arthritis; in both of them synovial biopsies were carried out during the acute phase. The nearest to the description of this condition we can find is that of Davison (1961) and of Wheate (1962). Wheate gives the case report of one patient who had a unilateral small effusion into the knee joint and "ganglion-like swelling of the synovia of both wrists on the dorsal aspects."

Case 1

A man aged 30 was admitted to hospital with a history of recurrent attacks of erythema nodosum leprosum for one year while on dapsone. He had had leprosy for four years. During the last two attacks of erythema nodosum leprosum he had noticed painful swelling of the small joints of the hands, knees, and ankles.

On examination he was seen to be ill with diffuse infiltration of the skin over the trunk, limbs, and face; slight enlargement of the ears; thinning of eyebrows; a normal nose; a large number of erythema nodosum leprosum lesions over the face, trunk, and limbs; and bilateral ulnar and lateral popliteal nerve enlargement. There was no motor paralysis, but sensory loss over the feet.

He had spindling of the proximal interphalangeal and metacarpophalangeal joints of the right hand and swelling of the right wrist, with palpable thickening of synovium (Fig. 1), and effusion into both knees (Fig. 2) and both ankle joints. All the affected joints were tender and there was painful limitation of movements of these joints.

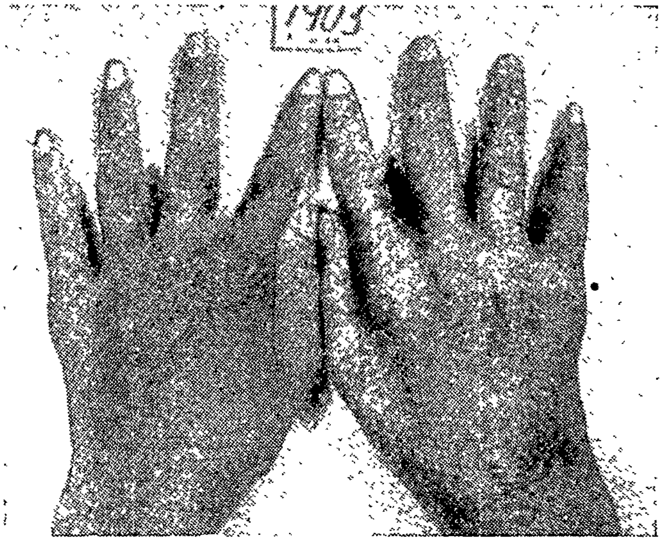


FIG. 1.—Case 1. Swelling of metacarpophalangeal and proximal interphalangeal joints of the right hand. Swelling of right wrist is also shown.

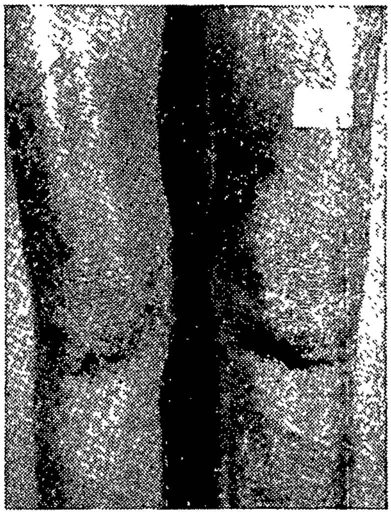


FIG. 2.—Case 1. Swelling of both knee joints, left more than right. There was effusion in both joints.

Investigations.—Haemoglobin 9 g./100 ml.; W.B.C. 21,000/cu. mm. (polymorphs 87%); erythrocyte sedimentation rate (Westergren) 32 mm. in first hour, 63 mm. in second hour; C-reactive protein four plus; antistreptolysin titre 333; Rose–Waaler test for rheumatoid factor (D.A.T.) 1:4; skin smears for acid-fast bacilli 1+ (Wade's method 0–6 scale); total plasma protein 7.3 g./100 ml. (gammaglobulin 1.6 g.); L.E. cells negative. *X*-ray examination of hands, wrists, knees, and ankles showed generalized osteoporosis. No subarticular erosions were seen. Synovial fluid: protein 1.8 g./100 ml. (globulin 0.78 g.); sugar 50 mg./100 ml.; W.B.C. 22/cu. mm. (polymorphs 75%). Direct smear: no organisms seen with Gram's stain and Ziehl–Neelsen stain. Synovial fluid was sterile on routine and acid-fast bacillus culture.

---

* Consultant Physician.
† Consultant Surgeon.
‡ Consultant Pathologist.
§ Physiotherapist.
Schieffelin Leprosy Research Sanatorium, B.O. Karigiri, via Katpadi, N.A. Dist., S. India.

Synovial Biopsy from Left Ankle.—On exploration of the ankle synovial membrane was found to be congested and thickened. There was villous hypertrophy. Clear straw-coloured fluid in the joint was aspirated and a synovial biopsy was taken. Histological examination showed numerous proliferating capillaries surrounded by inflammatory cells consisting of plasma cells and lymphocytes. There were focal collections of histiocytes and diffuse polymorphonuclear leucocytic infiltration. Acid-fast stain showed no bacilli (Figs. 3 and 4).

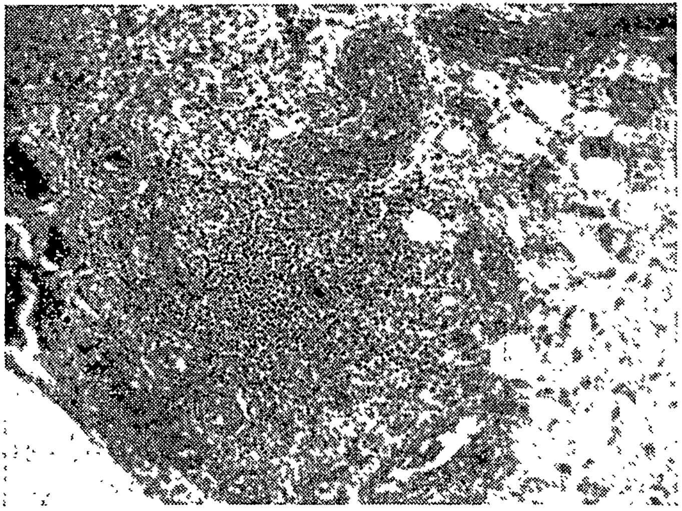


FIG. 3.—Case 1. Photomicrograph to show the synovial membrane densely infiltrated with inflammatory cells. There is marked increase in vascularity with proliferation of capillaries.

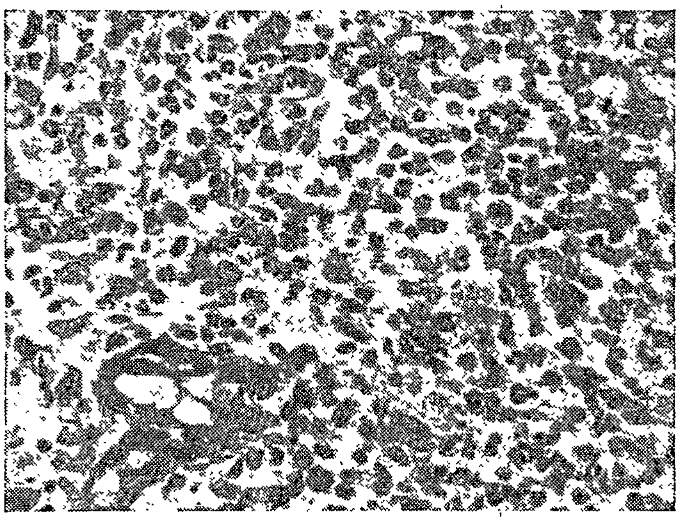


FIG. 4.—Case 1. High-power photomicrograph to show infiltration of synovial tissue with numerous polymorphs.

Case 2

A man aged 24 had had lepromatous leprosy for four years. He had been treated with dapsone for two years and during that time had had recurrent attacks of erythema nodosum leprosum. In the present attack he developed painful swelling of the metacarpophalangeal and interphalangeal joints of the hands, knees, ankles, and left elbow.

Examination revealed diffuse infiltration of the skin over the face, trunk, and limbs; erythema nodosum leprosum over trunk and face; loss of eyebrows; deformity of ears; partial collapse of the nose; enlargement of ulnar and lateral popliteal nerves on both sides with slight tenderness. There was no motor paralysis, but symmetrical loss of sensation in the feet.

He had spindling of proximal interphalangeal joints of fingers, and swelling of metacarpophalangeal joints, all of which were tender (Fig. 5); bilateral swelling of the knees, the right more pronounced than the left (Fig. 6); effusion into both the knee joints; painful limitation of movements of the knees; and painful swelling of and effusion into the right ankle joint (Fig. 7).

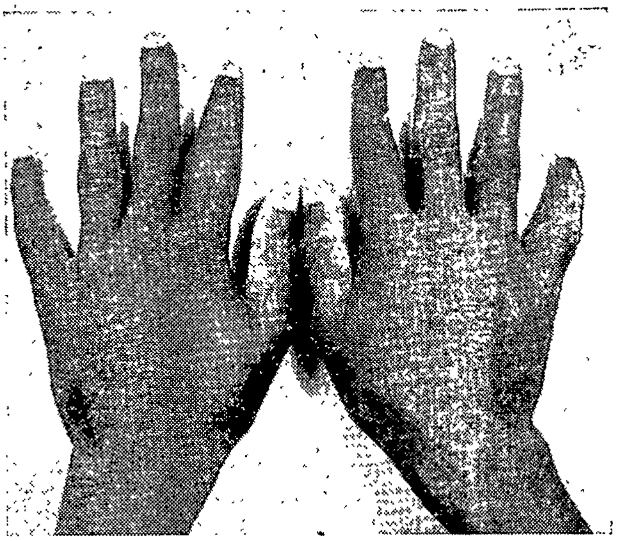


FIG. 5.—Case 2. Similar to Fig. 1. Spindling of fingers, more marked on the right. The right wrist is also swollen.

Investigations.—Haemoglobin 8.25 g./100 ml.; W.B.C. 11,000/cu. mm. (polymorphs 74%); erythrocyte sedimentation rate (Westergren) 116 and 138 mm. (first and second hours); C-reactive protein five plus; Rose–Waaler test for rheumatoid factor (D.A.T.) 1:32; skin smears for acid-fast bacilli 1.25+ (Wade's method 0–6 scale); total plasma protein 8.6 g./100 ml.; serum gammaglobulin 4.8 g./100 ml. (by paper electrophoresis method). No L.E. cells found on repeated examination. *X*-ray examination of hands, knees, ankles, and feet showed generalized osteoporosis. No erosions seen. Synovial fluid: W.B.C. 270/cu. mm., of which 45% were polymorphs; direct smear on Gram's stain did not show any organisms; Ziehl–Neelsen stain showed a number of acid-fast bacilli, most of which were granular. Synovial fluid was sterile on culture for routine organisms and acid-fast bacilli.

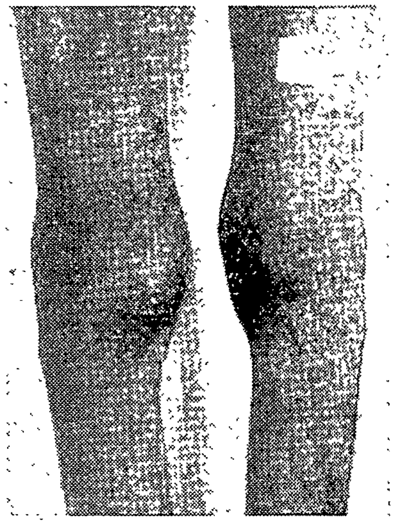


FIG. 6.—Case 2. Swelling of knees, the right more than the left.

Synovial Biopsy from Right Knee.—On exploration of the right knee the synovial membrane appeared thickened and congested. The synovial fluid was dark straw-coloured and opalescent. Histological examination of synovial tissue showed fibro-fatty tissue with marked increase in vascularity and an exudate consisting of fibrin and numerous polymorphonuclear leucocytes. There was marked tissue oedema. Acid-fast stain did not show any bacilli in the synovial tissue, but there were fragmented bacilli in a nerve present in the tissue. The entire appearance was typical of acute arthritis.

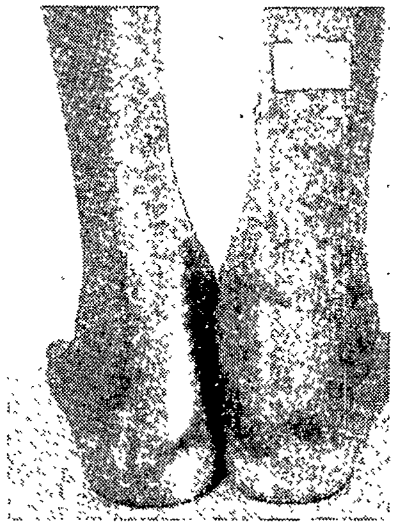


FIG. 7.—Case 2. Marked swelling of right ankle due to effusion into the joint.

Clinical Course and Management

The clinical course correlated very well with that of erythema nodosum leprosum—the acute arthritis either coincided with the onset of crops of erythema nodosum leprosum or followed its appearance in 24 to 48 hours. The joint manifestations cleared up 7 to 14 days after the subsidence of erythema nodosum leprosum. The usual measures, such as intravenous administration of 1% potassium antimony tartrate and oral chloroquine, were adequate to deal with the erythema nodosum leprosum, as well as the arthritis, at each subsequent episode of recurrence.

During the acute phase of arthritis local heat in the form of wax baths to the hands was very helpful in relieving pain as well as increasing the range of movement. Except during these periods of active physiotherapeutic measures, the affected limbs were immobilized in functional splints and maintained in elevation. Active exercises were encouraged as soon as the acute phase of the arthritis cleared up, to prevent flexion deformity and stiffness of the fingers.

Comment

General.—Arthralgia has been well recognized as a clinical manifestation of "reaction" in leprosy (Cochrane, 1964; Job *et al.*, 1964). An acute exudative polyarthritis occurring in association with these exacerbated phases has not been well documented. The clinical manifestations of this polyarthritis in leprosy closely simulate the acute phase of rheumatoid arthritis and may be mistaken for the latter. Unlike rheumatoid arthritis, the clinical manifestations in the joints clear up when the erythema nodosum leprosum resolves, without any residual damage or manifestations in the affected joints—as seen so far during a two-year follow-up of most of these patients. The synovial fluid, which had the biochemical features of a transudate, was sterile on culture, both for pyogenic organisms and for acid-fast bacilli. The Rose–Waaler test for rheumatoid factor was positive in one of the two cases described here and in 6 of the 10 patients we have so far observed. The joints most commonly affected were the small joints of the hands—the metacarpophalangeal and the proximal interphalangeal joints—the knees, and the ankles. Effusion into the knees and ankles was common.

Age and Sex.—Both patients (Cases 1 and 2) were young men. We have seen this syndrome in 10 patients, of whom only one was female. This is in striking contrast with the usual higher incidence of rheumatoid arthritis among young women (Robinson, 1963). On the whole, erythema nodosum leprosum occurs less commonly in women and is usually not as severely disabling as in men (personal observation). This may explain the rarity of the syndrome among women leprosy patients.

Disease and Its Complications.—All the patients had lepromatous leprosy of longer than three years' duration. In all of them the "rheumatoid syndrome" occurred only after recurrent episodes of erythema nodosum leprosum. We have not seen this syndrome during a first attack, nor in association with mild erythema nodosum leprosum. In all the patients there was involvement of skin and the subcutaneous tissues in the erythema nodosum leprosum process. Every one of them had systemic manifestations of fever, anorexia, and general malaise.

Histopathology of the Synovium.—In the affected joints this is of considerable interest and helps to substantiate the suggestion that this acute exudative "leprous" polyarthritis is different from acute rheumatoid arthritis. In this condition there is well-marked infiltration of the synovial membrane with polymorphonuclear leucocytes, and the joint cavity shows an exudate of fibrin with numerous polymorphs entangled in it. The acute inflammatory reaction in the synovial membrane is very similar to that seen in the coexistent erythema nodosum lesions found elsewhere in the body. This is in contrast with the lymphocytic and plasma cell infiltration of synovium which characterizes rheumatoid arthritis (Anderson, 1957).

It is interesting to note that none of our cases—the two reported here and the other eight cases we have so far observed—had lupus erythematosus cells. Whether these joint manifestations are "autoimmune" is open to debate. It seems as though the pathogenesis of these acute joint manifestations is linked with that of erythema nodosum leprosum, and elucidation of one should help in the understanding of the other.

Summary

The clinicopathological features of exudative polyarthritis simulating acute rheumatoid arthritis occurring in two lepromatous leprosy patients in association with erythema nodosum leprosum is, so far as we are aware, described for the first time.

It is suggested that erythema nodosum leprosum and the exudative polyarthritis occurring together may be aetiologically determined by an immunological phenomenon.

We gratefully acknowledge the continued financial support from the Leprosy Mission, London, and the American Leprosy Missions Inc., New York. We are also grateful to Mr. Japes Fowler, Mr. Cyril Prathapkumar, and Mr. Paul Rajasingh for technical assistance; to Mr. Christopher Dorairaj for the photographs and *x*-ray films; to Dr. Grace Koshy, Associate Professor of Bacteriology, Christian Medical College and Hospital, Vellore, for estimating the antistreptolysin titre and C-reactive protein; and to Mrs. L. Furness for secretarial assistance.

REFERENCES

Aguas, J. T. de las (1963). *Int. J. Leprosy*, **31**, 538.
Anderson, W. A. D. (1957). *Pathology*, 3rd ed., p. 1258. St. Louis.
Bonomo, L., Tursi, A., Trimigliozzi, G., and Dammacco, F. (1965). *Brit. med. J.*, **2**, 689.
Buu Hoï, N. P., and Basset, A (1963). *Int. J. Leprosy*, **31**, 536.
Cathcart, E. S., Williams, R. C., Ross, Hilary, and Calkins, Evan (1961). *Amer. J. Med.*, **31**, 758.
Cochrane, R. G. (1964). In *Leprosy in Theory and Practice*, 2nd ed., edited by R. G. Cochrane and T. F. Davey, pp. 336, 337. Bristol.
Davison, A. R. (1961). *Int. J. Leprosy*, **29**, 29.
Job, C. K., Gude, S., and Macaden, V. P. (1964). Ibid., **32**, 177.
Karat, A. B. A., Pulimood, B. M. P., Job, C. K., and Karat, S. (1966). Unpublished observations.
Lele, R. D., Sainani, G. S., and Sharma, K. D. (1965). *J. Ass. Phycns India*, **13**, 275.
Matthews, L. J., and Trautman, J. R. (1965). *Lancet*, **2**, 915.
Robinson, W. D. (1963). In *Cecil-Loeb Textbook of Medicine*, 11th ed., edited by P. B. Beeson and W. McDermott, p. 1468. London.
Skinsnes, O. K., and Tsang, D. T. S. (1963). *Int. J. Leprosy*, **31**, 539.
Wheate, H. W. (1962). Ibid., **30**, 387.

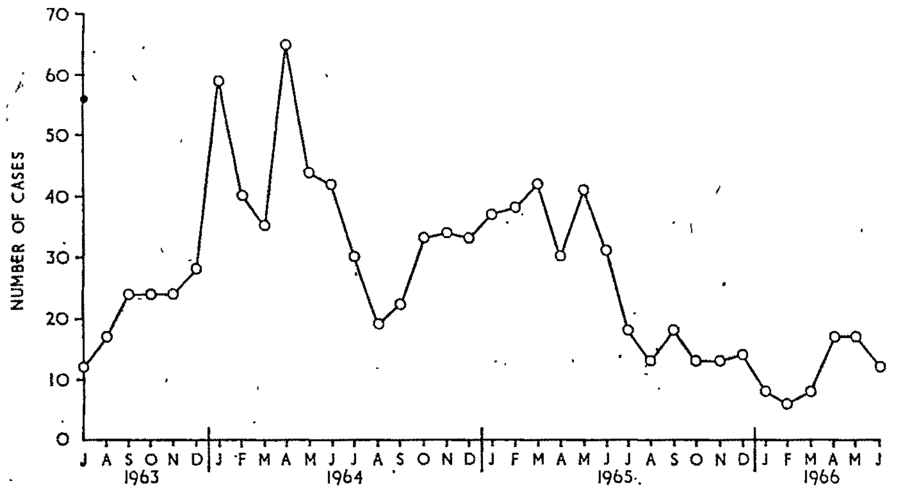
Infectious Hepatitis in Leicester 1963-6

C. BURNS,[*] M.B., CH.B., D.C.H., D.P.H.

Brit. med. J., 1967, 3, 773–776

During the latter part of 1962 the Leicester City Health Department became aware of an increasing incidence of infectious hepatitis among schoolchildren, and on 1 July 1963 the disease was made notifiable in Leicester by an order under Section 147 of the Public Health Act, 1936. This order was to run initially for a three-year period, ending on 30 June 1966, but has been extended for a further three years.

A marginal punch card was devised in conjunction with Kalamazoo Limited to record details of cases, and full information regarding each notified case was obtained at special home visits carried out by health visitors or clinic nurses. During the three-year period 961 cases were notified, and this paper presents an analysis of the epidemiological features of the outbreak. A preliminary analysis of information collected during the first 16 months has already been published (Burns, 1965).



Monthly incidence of infectious hepatitis in Leicester, July 1963 to June 1966.

Epidemic Pattern

General Course of Outbreak

The accompanying Chart shows the monthly incidence of the disease over the three years from 1 July 1963, and indicates that notifications continued at a high level throughout 1964 and during the first half of 1965, but began to fall in the second half of 1965 and remained low throughout the remainder of the period.

Long-term variations in the incidence of the disease with epidemic periods similar to that in Leicester, separated by intervals of several years of low incidence, have been reported from many areas, notably by Mosley *et al.* (1963) in Des Moines, Iowa, and on a national scale by the U.S. Department of Health, Education and Welfare (1964a, 1964b, 1964c). The Chief Medical Officer to the Ministry of Health (1965) showed a similar pattern for the Eastern Region of England and Wales, where the disease has been notifiable since 1943.

Seasonal Variation

A seasonal variation in incidence was, as the Chart shows, well marked in both 1964 and 1965, with maximum notifications in late winter and high incidence continuing into the spring. A seasonal trend has often been remarked on in this disease (Mosley *et al.*, 1963 ; Bothwell *et al.*, 1963).

Age and Sex Variations

In this as in other outbreaks (Bothwell *et al.*, 1963 ; Ward and Krugman, 1962) the disease affected the sexes more or less equally. There was a marked preponderance of cases in the 5–14 age groups, 73.2% of the cases being children in this group. This also is in line with many previous reports (Bothwell *et al.*, 1963 ; U.S. Department of Health Education and Welfare, 1963), though a predominance of cases in adults has been reported in outbreaks occurring in Denmark (W.H.O. Secretariat, 1964) and in Canada (Bothwell *et al.*, 1963).

Table I shows that the proportion of cases in children under the age of 15 years fell markedly during the final 12 months of the three-year period, coincident with a substantial fall in the number of notified cases as compared with the two previous years. A similar trend has been noted by other observers (U.S. Department of Health Education and Welfare, 1963 ; W.H.O. Secretariat, 1964). It would appear that this pattern is related to the fact that, in epidemic periods, children under the age of 15 number about three-quarters of the cases, and when a sufficient proportion of them have been infected either clinically or subclinically, and presumably acquired immunity, the incidence of the disease falls to non-epidemic levels, to rise once more when a new generation of susceptibles appears.

Geographical Distribution

During the three-year period cases occurred in all parts of the city. At various stages of the epidemic sizable local aggregations of cases were apparent in particular areas. These formed fairly well defined localized outbreaks, extending over periods of perhaps six to nine months. These local outbreaks tended to involve densely populated parts of the city, of relatively low socio-economic status. The south-eastern quarter

TABLE I.—*Percentage of Patients Aged Less Than* 15 *Years Related to Total Notifications*

Period	Total Cases	No Aged Under 15 Years	Percentage Aged Under 15 Years
1/7/63–30/6/64 ..	414	325	78·5
1/7/64–30/6/65 ..	390	324	83·1
1/7/65–30/6/66 ..	157	105	66·9
Total ..	961	754	78·5

---

[*] Divisional Medical Officer, St. Albans Division, Hertfordshire County Council; late Deputy Medical Officer of Health for the City of Leicester.

of the city, which comprises the more favoured residential suburbs, was almost completely spared. Table II shows the 961 cases notified, broken down into quarterly notifications in each of the city's electoral wards, together with certain additional information derived from the 1961 census report, regarding the ward population and the density of occupation of living accommodation.

Correlation coefficients were calculated between the attack rates per thousand based on the 1961 population figures and the two indices of population density derived from the same source, and gave figures of 0.784 between the attack rate per thousand and the percentage of persons living at more than 1.5 per room and 0.778 between the attack rate per thousand and the average number of persons per room. Both these coefficients are highly significant.

This procedure is, of course, imperfect and open to the dual criticism that neither the population figures from which the attack rates are calculated nor the indices of density of occupation are precisely contemporaneous with the occurrence of the cases. Examination of the annual records of numbers of electors registered in the 16 wards shows, however, that, allowing for alterations in ward boundaries, changes during the period concerned are small in relation to the correlation coefficients, and it is safe to draw the conclusion that the incidence of the disease is closely related to household congestion. Mosley *et al.* (1963) made similar observations on the association of high incidence of the disease with large congested households of low socio-economic status, and it is significant that in Leicester the largest number of cases and the highest attack rate occurred in Ward 16, which at the 1961 Census had the highest occupation densities. This ward consists almost entirely of a single large council estate, populated in the main by large families of low socio-economic status.

A further possible criticism is that as almost three-quarters of the cases occurred in the age group 5–14 years the apparent correlation between attack rates and domestic congestion may merely be a reflection of the possibility that the wards with the highest indices of overcrowding were also those with the highest proportions of children in their populations. Attack rates for the age group 5–14 years were therefore calculated for each of the 16 wards from data from the 1961 census, and the correlations between these rates and the congestion indices are respectively: (*a*) with the percentage of the population living at greater density than 1.5 per room, 0.877 ; (*b*) with the average number of persons per room, 0.524. Both these correlations remain significant, and in particular the high correlation between attack rates in the 5–14 age group and the percentage of the population living at more than 1.5 per room reinforces the conclusion that infectious hepatitis is a disease associated with overcrowding and underprivilege.

Mode of Transmission

The epidemiological pattern indicated direct person-to-person transmission as the mode of infection. This is the mode of spread in the majority of epidemics—for example, in Bristol (Bothwell *et al.*, 1963) and Des Moines, Iowa (Mosley *et al.*, 1963). Outbreaks have, however, been described in which both food and water have been the apparent vehicle of spread (*Lancet*, 1962, 1964 ; *Brit. med. J.*, 1964). In the U.S.A. clams and oysters have been incriminated in a number of outbreaks (U.S. Department of Health, Education and Welfare, 1964a, 1964b).

While no general attempt was made, except as regards food-handlers who were family contacts of known cases, to detect anicteric or subclinical cases, it was evident that such cases were a frequent source of infection to others. MacCallum (1961) quotes estimates of the ratio of anicteric to icteric cases of up to 10:1. In the Leicester outbreak the part played by subclinical cases in transmitting the disease manifested itself when, as happened occasionally, one or more cases occurred in a family where the only history of contact with a previous known case of the disease was in another member of the family who did not suffer an overt attack. Another index of the important part played by asymptomatic and unrecognized cases in the spread of the disease was the fact that of the 961 cases 638 (66.4%) were unable to recall any contact with a known case of the disease.

Spread within the Family

The 961 cases occurred in 742 households. In the affected households 36.2% of the children and 9.6% of the adults contracted clinical attacks of the disease. These figures compare very closely with those of Bothwell *et al.* (1963), who found in the Bristol outbreak that 39% of children and 10.3% of adults in affected households fell ill.

The secondary attack rate among child family contacts was 11.8% and among adults 1.9%. Mosley *et al.* (1963) reported a secondary attack rate of 10% among family contacts not protected with gammaglobulin.

School Spread

There are 185 schools in the city and cases occurred in 115 of them. In 62 schools there were fewer than five cases, 25 had more than 10 cases, and nine had more than 20 cases. These nine schools between them produced 267 cases—that is, more than a quarter of the total number of cases in the city and more than one-third of the cases among schoolchildren.

TABLE II.—*Distribution of Cases by Electoral Wards*

Period	No. of Cases in Ward:																Whole City
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	
1/7/63–30/9/63	2	—	—	—	—	—	2	4	2	2	10	31	—	—	—	—	53
1/10/63–31/12/63 ..	4	—	1	—	4	—	1	3	2	1	36	9	2	6	5	2	76
1/1/64–31/3/64	3	6	17	3	6	3	1	7	3	3	58	2	4	11	5	2	134
1/4/64–30/6/64	2	4	5	9	13	2	2	19	5	4	14	8	2	49	11	2	151
1/7/64–30/9/64	3	2	6	6	4	7	—	10	2	2	3	4	3	12	4	3	71
1/10/64–31/12/64 ..	1	1	—	6	3	1	1	7	8	8	5	4	9	10	8	28	100
1/1/65–31/3/65	1	2	1	2	3	2	6	5	12	2	—	3	5	9	11	53	117
1/4/65–30/6/65	—	—	8	2	—	1	1	6	14	3	—	—	4	10	13	40	102
1/7/65–30/9/65	—	9	9	—	3	—	2	2	2	1	—	2	2	6	5	6	49
1/10/65–31/12/65	—	4	5	—	2	3	4	9	—	—	—	1	—	4	3	5	40
1/1/66–31/3/66	—	—	2	—	2	—	1	9	2	—	1	—	—	1	4	—	22
1/4/66–30/6/66	—	—	2	1	—	—	—	35	—	—	1	1	—	2	2	2	46
Total ..	16	28	56	29	40	19	21	116	52	26	128	65	31	120	71	143	961
Population (1961 census)	9,858	13,194	13,035	14,557	12,181	9,355	17,639	25,774	23,699	17,605	20,827	19,385	18,162	18,559	21,969	17,671	273,470
% of persons at more than 1·5 per room (1961 census)	1·7	2·3	3·7	4·4	8·3	4·2	1·9	4·9	2·4	2·1	5·3	1·6	0·7	6·6	2·3	11·6	4·0
Av. No. of persons/room (1961 census)	0·56	0·55	0·57	0·55	0·60	0·56	0·53	0·73	0·66	0·59	0·68	0·63	0·52	0·65	0·65	0·74	0·62
Attack rate/1,000 (based on 1961 population figures)	1·62	2·12	4·30	1·99	3·28	2·03	1·19	4·50	2·19	1·48	6·15	3·35	1·71	6·47	3·23	8·09	3·51

The fact that more than half of the affected schools produced fewer than five cases each and 17 (14.8%) of them produced only one case is in striking contrast to the high incidence in the relatively small number of schools in which substantial outbreaks occurred. The reason for the great differences in the epidemiological pattern of the disease observed in different schools is obscure, but it does not appear to be related to factors within the school, such as adequacy of sanitary or washing facilities. The wide variation in the natural history of school outbreaks makes the evaluation of preventive measures, such as mass gammaglobulin administration or the institution of stringent hygienic measures as described by Schofield (1964), extremely difficult, and underlines the need for carefully controlled trials before conclusions are drawn regarding the efficacy of such measures and the circumstances in which they should be applied.

As already stated, the great majority of cases were children of school age. Within this group, however, there was a marked difference between the primary and secondary age groups. All nine schools with sizable outbreaks were primary schools, and when cases occurred in primary schools a substantially larger proportion of the children tended to fall ill than in a secondary school. At schools where cases occurred the overall attack rates were: primary 2.8%, secondary modern 1.2%, and grammar 0.5%. The difference between secondary modern and grammar school attack rates is striking, and a number of factors, including smaller classes in grammar schools, the presence in them of a proportion of young people aged 16 years and over with a less tendency to the disease, and, of course, differences in socio-economic background, may have contributed to this.

Outbreaks of infectious hepatitis have often been associated with schools and have characteristically smouldered on for several months, with shorter periods of explosive incidence within the outbreak. Tilley (1960), Flanagan and Lister (1962), Schofield (1964), and Yarrow (1964) have described such outbreaks in recent years, while Pickles (1939) stressed the role of school contact in the occurrence of outbreaks. On the other hand, Mosley *et al.* (1963) stated that in the outbreak in Des Moines, Iowa, examination of the role of the school indicated that the school, particularly the classroom, was not the primary source of infection, and that closer social and personal contact was necessary for transmission of infection to occur than was afforded by casual classroom association.

In the Leicester outbreak a close examination was made of 43 cases occurring at an infant school of 508 pupils, giving an attack rate of 8.44%. In these 43 cases the apparent source of infection was: known classroom contact, 34.9%; family/household contact, 22.1%; probable subclinical class contact, 10.5%; unidentified, 32.5%. In addition, all cases occurring in the families of these 43 children were examined, and of the 61 cases involved the apparent source of infection was: known classroom contact, 27.9%; family/household contact, 31.2%; probable subclinical class contact, 6.6%; unidentified, 34.3%.

The small numbers and the high proportion of cases of unidentified origin do not permit the drawing of conclusions on the relative importance of classroom as opposed to family contact in the transmission of the disease, but it does seem clear, in contrast with the findings of Mosley *et al.*, that contact in the classroom was a factor of considerable importance.

School Meals

The possibility of school meals being implicated in the spread of the disease was thoroughly investigated and there was no evidence that they were a factor. Of the 776 cases occurring among schoolchildren 336 (43.3%) took school meals, while of the total of 37,941 pupils in the schools where cases occurred 19,966 (52.6%) took school meals. Of the 19,966 children taking meals 336 (1.7%) suffered attacks, while of the 17,975 not taking meals 440 (2.5%) suffered attacks.

Clinical Features and Prognosis

Jaundice occurred in 91% of notified cases. Reference has already been made to the substantial numbers of anicteric cases and symptomless excreters of virus which are believed to occur during any outbreak, the present one being no exception. It was obvious that many anicteric cases were occurring among both school and family contacts, but no general attempt was made to search for them. The absence of any specific serological or virological test for the presence of infection is a most serious handicap in detecting such cases. The use of tests for the presence of bilirubin in the urine has been suggested (*Brit. med. J.*, 1963b) as a means of detection, and a number of such tests were carried out in the current investigation in family or school contacts who displayed symptoms but no clinical jaundice. The results were all negative: 44 (4.6%) of the cases required admission to hospital and 31 (70.5%) of these were between the ages of 5 and 14 years, while 9 (20.5%) were aged over 20 years. Three of the cases were fatal. An Indian immigrant woman aged 32 died in hepatic coma after a three-weeks illness; a schoolboy aged 5 years died of subacute liver failure after a six-weeks illness; and a 9-year-old boy died in hepatic coma after eight days. These three deaths represent a mortality rate of 3.1 per thousand.

Sherlock (1963) stated that the mortality in large outbreaks of infectious hepatitis has been generally quoted as one to two per thousand. In the Bristol outbreak (Bothwell *et al.*, 1963) there were three deaths in 2,107 cases. Occasionally, however, outbreaks have been reported with higher mortality. The *Lancet* (1962) referred to an outbreak in New Jersey in 1961 where there were 2,095 cases with 34 deaths.

There is some evidence (*Brit. med. J.*, 1963a) that cirrhosis may occasionally follow infectious hepatitis, but Sherlock (1963), reviewing the question of long-term sequelae, concluded that rapid and complete recovery is the rule, and while transition to cirrhosis does occur it is infrequent. Bothwell *et al.* (1963) reported that early follow-up studies of their cases appeared to confirm the rarity of prolonged ill-health or cirrhosis.

Discussion

Infectious hepatitis has been described as one of the biggest unsolved problems in medical virology (*Brit. med. J.*, 1964). The epidemiological features of the disease have been studied extensively in the United States, where the Department of Health, Education and Welfare has published a series of surveillance reports since April 1960, and in a number of European countries. In 1964 a symposium on viral hepatitis sponsored by the W.H.O. Regional Office for Europe was held in Prague. Seventeen countries including the U.K. were represented at this symposium, at which the clinical, laboratory, epidemiological, and control problems presented by the disease were reviewed and the setting up of detailed surveillance programmes in the different European countries was recommended.

So far as the United Kingdom is concerned, the disease is not generally notifiable, so that the magnitude of the problem it presents is unknown, and no information regarding its epidemiological pattern on a national scale is available. Local studies, including that carried out in East Anglia under the Jaundice Regulations, 1943 (MacCallum *et al.*, 1951), the reports by Bothwell *et al.* (1963) on 2,101 cases which occurred in Bristol in 1961–2, and by Clayton (1967) on his survey at Coventry, together with numerous reports of local outbreaks in schools or other communities (Tilley, 1960; Flanagan and Lister, 1962; Schofield, 1964; Yarrow, 1964; Pollock, 1964), and, of course, the classical studies of Pickles (1939), clearly indicate that in this country a considerable amount of ill-health is being caused by this infection, more especially among schoolchildren, and that an unknown though probably small amount of permanent liver damage also results from it.

The control of the disease presents peculiarly difficult problems. Not only do large numbers of anicteric or subclinical cases occur which, though remaining undiagnosed, are nevertheless infectious, there is evidence (MacCallum *et al.*, 1951; Ward and Krugman, 1962) that patients are infectious during the incubation period, about 20 days before the onset of jaundice. The incubation period itself is long and variable—up to six or eight weeks, and cases may follow each other in a family, separated by this interval. Furthermore, there is evidence that some patients continue to excrete virus for long periods after clinical recovery. Ward and Krugman (1962) quoted evidence of the finding of virus in the stools up to 15 months after the onset of illness. Despite the work of Rightsel *et al.* (1961) there is no simple laboratory method of detecting the presence of virus and no specific test for the carrier state. In food- or water-borne outbreaks, if the source can be traced and appropriate measures taken, good results may be obtained. In contact-spread outbreaks, on the other hand, it is doubtful whether at the present time effective control measures are possible.

The epidemiological features already referred to, together with the absence of any specific laboratory test for the carrier state, clearly render quarantine of contacts of no practical value, and this is confirmed by the work of Kostrzewski and Szmunes (1964). It seems reasonable to keep contacts who are food-handlers under surveillance for a period, and in Leicester such surveillance is maintained until six weeks has elapsed after the onset of illness in the last case in the family. Bothwell *et al.* (1963) excluded food-handlers in the school meals service for a period of one month if they were well; but this seems arbitrary and difficult to justify in view of the facts stated above. In Leicester these persons are kept under surveillance, their urine is tested weekly with the Ictotest tablet, and blood is taken for serum alanine aminotransferase estimation.

Schofield (1964) described an outbreak affecting two primary schools which was apparently abated by the introduction of stringent measures of hygiene, including special supervision of the children's handwashing, and disinfection thrice daily of all W.C. seats, flush-handles, washbasin taps, and door-handles. Similar measures were used at schools in Leicester where outbreaks occurred, but without noticeable effect.

Evidence is available (Ward and Krugman, 1962; Mosley *et al.*, 1963) of the efficacy of gammaglobulin in the U.S.A. in providing passive protection against a clinical attack of infectious hepatitis and similar claims have been made in respect of British gammaglobulin. However, properly controlled trials have hitherto been lacking in this country, and the need for caution in drawing conclusions from uncontrolled trials in view of the wide variations in the natural history of school and other institutional outbreaks has already been referred to. A controlled trial at present being carried out by the Epidemiological Research Laboratory, Colindale, will, it is hoped, clarify this question.

Future progress in the control of this disease would appear to lie in two directions. Firstly, the introduction of a simple and reliable test for the presence of the virus, and, secondly, the production of an effective vaccine. In the meantime there is a good case for general notifiability, at least for a period, in order to extend knowledge of the incidence and epidemiological pattern of the disease in this country, and so to provide the facts on which the use of improved control measures can be based when they become available. The whole problem may acquire much greater urgency if the suggestion made by Stoller and Collmann (1965) of an association between infectious hepatitis and Down's syndrome should be substantiated.

Summary

During the three years 1 July 1963 to 30 June 1966 961 cases of infectious hepatitis were notified to the Leicester City Health Department. The peak of the epidemic occurred during the first two years of that period. A well-marked seasonal trend, with maximum incidence in late winter and spring, was observed. Over the whole period more than three-quarters of the patients were aged under 15 years, children in primary schools being the most heavily affected group. As the intensity of the epidemic waned the proportion of child cases tended to fall. There was a significant association between high incidence of the disease and domestic overcrowding and poor living standards. There was evidence that anicteric and subclinical cases played a large part in the spread of the disease. The overall secondary attack rate among family contacts was 5.44%. Among children the rate was 11.8% and among adults 1.9%.

Cases occurred in 115 of the 185 schools in the city, but in the great majority of schools no extensive outbreak developed. The natural history of the disease as it affected schools showed wide variations, and there was no means of distinguishing in advance the small minority of schools in which the initial cases were followed by a sizable outbreak from those where only a small number of cases occurred. This makes the evaluation of both the efficacy of preventive measures, such as the administration of gammaglobulin, and the circumstances in which they should be used very difficult. Both family and school contact were important in transmitting the disease; there was no evidence, however, that school meals were a factor. Most of the cases had illnesses of mild or moderate severity, but three (3.1%) died.

I wish to thank Dr. B. J. L. Moss, Medical Officer of Health, City of Leicester, for his encouragement; the health visitors and clinic nurses of the Leicester City Health Department for their work in carrying out the domiciliary inquiries; and the clerical staff of the department for their indefatigable help with the analysis and tabulation of the data. Gratitude is also due to Mr. A. Lawrence, of the Leicester University Mathematics Department, Miss K. Wolfendale and Mr. G. Raymont, of the Leicester College of Technology, and Mr. V. A. Dickinson, of the Hertfordshire County Health and Welfare Department, for advice and assistance with statistical analysis.

REFERENCES

Bothwell, P. W., Martin, D., Macara, A. W., Skone, J. F., and Wofinden, R. C. (1963). *Brit. med. J.*, **2**, 1613.
Brit. med. J., 1963a, **1**, 5.
—— 1963b, **2**, 1602.
—— 1964, **2**, 69.
Burns, C. (1965). *Roy. Soc. Hlth J.*, **85**, 144.
Chief Medical Officer, Ministry of Health. (1966). *Annual Report 1965*, p. 45. H.M.S.O., London.
Clayton, T. M. (1967). *Med. Offr*, **117**, 195.
Flanagan, K. T., and Lister, J. (1962). *Brit. med. J.*, **2**, 376.
Kostrzewski, J., and Szmunes, W. (1964). *W.H.O. Report on European Symposium on Viral Hepatitis*, p. 75.
Lancet, 1962, **2**, 491.
—— 1964, **1**, 422.
MacCallum, F. O. (1961). In *Virus and Rickettsial Diseases of Man*, 3rd ed., edited by S. P. Bedson, A. W. Downie, F. O. MacCallum, and C. H. Stuart-Harris, p. 221. London.
—— McFarlan, A. M., Miles, J. A. R., Pollock, M. R., and Wilson, C. (1951). *Spec. Rep. Ser. med. Res. Coun. (Lond.)*, No. 273.
Mosley, W. H., Speers, J. F., and Chin, T. D. Y. (1963). *Amer. J. publ. Hlth*, **53**, 1603.
Pickles, W. N. (1939). *Epidemiology in Country Practice.* Bristol.
Pollock, G. T. (1964). *Med. Offr*, **111**, 301.
Rightsel, W. A., Keltsch, R. A., Taylor, A. R., Boggs, J. D., and McLean, I. W. (1961). *J. Amer. med. Ass*, **177**, 671.
Schofield, R. (1964). *Med. Offr*, **111**, 299.
Sherlock, S. (1963). *Diseases of Liver and Biliary System*, 3rd ed. Oxford.
Stoller, A., and Collmann, R. D. (1965). *Lancet*, **2**, 1221.
Tilley, J. H. MacD. (1960). *Brit. med. J.*, **2**, 1354.
U.S. Department of Health, Education and Welfare (1963). *Hepatitis Surveillance Report*, No. 17.
—— (1964a). Ibid., No. 18.
—— (1964b). Ibid., No. 19.
—— (1964c). Ibid., No. 20.
Ward, R., and Krugman, S. (1962). *Progr. med. Virol.*, **4**, 87.
World Health Organization Secretariat (1964). *Report of Symposium on Viral Hepatitis in Europe.* Annex 11, p. 19.
Yarrow, A. (1964). *Lancet*, **1**, 485.

Natural History of Refsum's Syndrome in a Gloucestershire Family

A. M. G. CAMPBELL,* D.M., F.R.C.P. ; E. R. WILLIAMS,† M.A., M.B., M.R.C.P.

Brit. med. J., 1967, 3, 777–779

Thirty-nine cases of Refsum's syndrome (Refsum, 1946) or heredopathia atactica polyneuritiformis have now been reported (Carrell *et al.*, 1966). The neurological features—namely, a mixed sensory and motor peripheral neuropathy, atypical retinitis pigmentosa with night blindness and constricted visual fields, cerebellar ataxia, and nerve deafness—are well attested and have been recently reviewed (Alexander, 1966), while abnormalities occurring outside the central nervous system include ichthyosis, epiphysial dysplasia, and cardiomyopathy (Gordon and Hudson, 1959). The disease is inherited as an autosomal recessive (Refsum, 1946) and most cases have occurred in consanguineous families.

The discovery of an excess of phytanic acid (3, 7, 11, 15-tetramethylhexadecanoic acid) in the serum and tissue lipids of these patients (Klenk and Kahlke, 1963 ; Eldjarn, 1965) has opened several exciting fields of speculation regarding the natural history of this disease, the aetiology of which is now partly understood. This has led us to investigate further a family living in the Forest of Dean area of Gloucestershire. Two members of this family have Refsum's syndrome and have been followed by one of us (A. M. G. C.) since 1958 and 1960 respectively.

We wish to report the results of a clinical and biochemical survey of three generations of the family, to record abnormalities in phytanic acid content of the cerebrospinal fluid (C.S.F.) in one of the patients, and to comment on the marked fluctuation in the clinical course of the disease, which was paralleled by variations in levels of C.S.F. protein.

Case 1

The patient, a man now aged 28, was first seen in 1958 at the age of 19, complaining of weakness of the limbs and unsteadiness and difficulty in walking, which had become worse after a febrile illness.

Since the age of 7 he had been noticed to be unsteady and had never been able to play games at school. At 14 he saw an orthopaedic surgeon because of pes cavus, and his mother stated that his feet had been deformed since he started to walk ; at this time he first noticed deafness. In September 1957 he had "Asian" influenza and a fortnight later developed weakness, numbness, and tingling of the limbs and slurred speech. He was admitted to a near-by hospital and was first thought to have an infective polyneuritis, as the C.S.F. protein was over 300 mg./100 ml.

When first seen he was found to have a severe peripheral neuropathy with absent reflexes, marked wasting of the hands and lower legs, and a glove-and-stocking anaesthesia to all sensory modalities. He also had bilateral nerve deafness, ataxia and intention tremor, clawing of the feet, and atypical retinitis pigmentosa (Fig. 1) with some degree of optic atrophy. The pupils were small, but reacted to light and accommodation. The visual acuity was 6/9 R and 6/6 L and there was a generalized constriction of the visual fields.

The patient has been followed over the past eight years and his disease has taken a variable downhill course. Over this period he has been extensively investigated ; haemoglobin, white blood count, erythrocyte sedimentation rate, serum electrolytes and urea, fat balance, xylose excretion, electroencephalogram, urinary porphyrins and amino-acids, urinary ketosteroid excretion, and skull and chest radiographs had all been normal. The serum cholesterol was 150 mg./100 ml., serum lipids were 0.71 g./100 ml., and serum α_2-globulin just increased at 0.9 g./100 ml. (liver-function tests were otherwise normal). The electrocardiogram was normal in 1958, but by 1966 there were flat T waves over the lateral chest leads. Foot radiographs (Fig. 2) showed metatarsal dysplasia with an equinovarus deformity and shortening of all the metatarsals except the second. Electromyography revealed only changes associated with a reduced muscle mass, and muscle biopsies showed fibrosis. The C.S.F. was at normal pressure with no increase in cells, and was

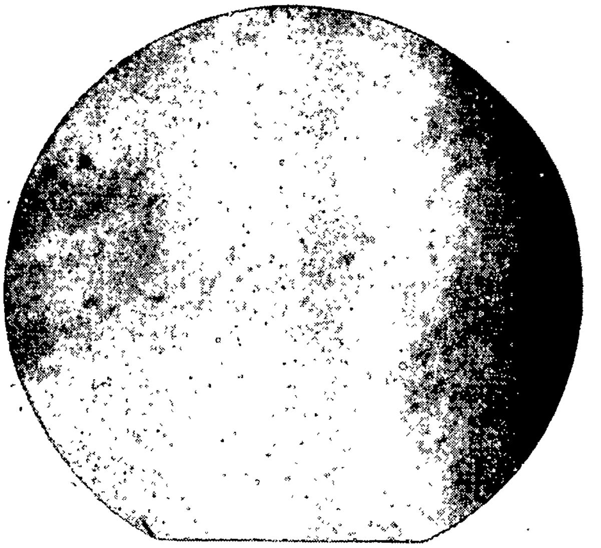


FIG. 1.—Case 1. Fundus photograph showing atypical retinitis pigmentosa.

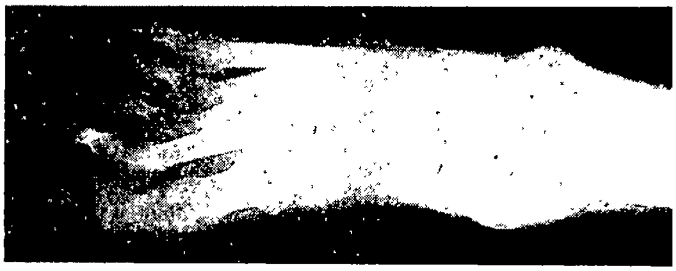


FIG. 2.—Case 1. Radiograph of foot.

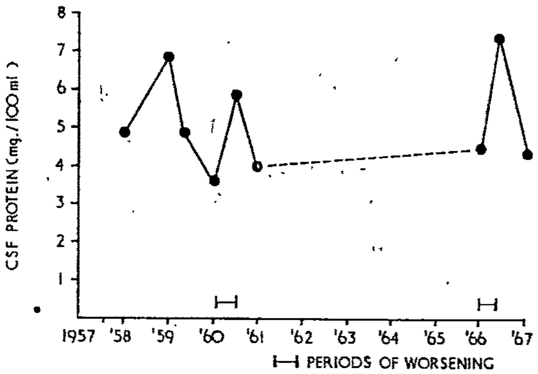


FIG. 3.—Case 1. C.S.F. protein plotted against time.

---

* Neurologist, Bristol Royal Infirmary.

† Late Medical Registrar, United Bristol Hospitals. Present appointment: Senior Medical Registrar, Bath United Hospital.

a pale yellow; the protein was consistently greatly raised, ranging from 368 to 732 mg./100 ml. A great excess of globulin was present. It seemed possible that exacerbations of the disease were associated with a rise in C.S.F. protein (Fig. 3).

Between February and August 1966 he worsened steadily and became unable to walk at all in spite of being on a low phytol diet, but between October 1966 and February 1967 there was a great improvement, particularly in motor power peripherally, so that he was able once more to write and type, and could walk without assistance and control his invalid motor vehicle. During this period the only dietary reduction imposed was the avoidance of green vegetables and fat meat.

Case 2

A married sister, aged 33, of the previous patient had a healthy childhood and adolescence, though mild deformity of the feet was noted by her mother. At the age of 20 she developed an acute weakness of the limbs and unsteadiness, again following a febrile illness. She was thought to have poliomyelitis and was admitted to hospital, where she was found to have weakness of the right arm and both legs, absent tendon jerks, ataxia of all limbs, and impaired vibration sense in the legs. A diagnosis of infective polyneuritis was again made, supported by a C.S.F. protein level of 400 mg./100 ml. She slowly improved; at the age of 22 she married and has two daughters, aged 6 and 8. During both pregnancies she thought she was noticeably weaker and more ataxic. In 1963, when aged 30, she had a total hysterectomy for menorrhagia with conservation of the right ovary. After this she again became weak and unsteady but improved in a few months, and since 1964 has remained well able to cope with her household duties, and feels that she has steadily improved. Neither this patient nor her brother has shown any mental deterioration.

When examined in 1966 she was a good deal better than when we saw her in 1960. She had bilateral cerebellar signs, bilateral drop-foot with absent ankle jerks and mild wasting of the hand and foot muscles, and claw-feet similar to her brother's, with the same atypical retinitis and nerve deafness. The C.S.F. protein had dropped to 83 mg./100 ml., radiographs of the tarsal bones were normal, and her disease was clearly not so severe as that of her brother.

Family Study

The family tree of the three generations studied is given in Fig. 4. The family are of yeoman stock and live in a small Gloucestershire town. There is no history of any other familial disease and no suggestion of consanguinity; while I 1 traces his ancestry back through four generations of Forest of Dean dwellers, I 2 is a native of Cheltenham. There is no consanguinity in any of the spouses of the sibs of the propositi.

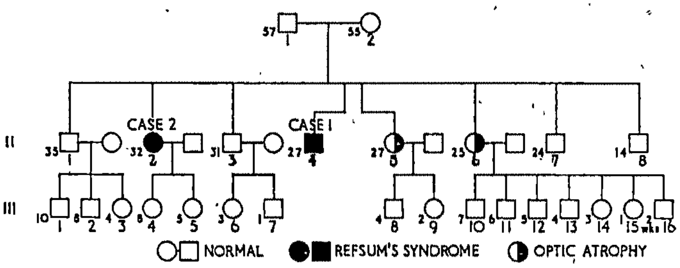


FIG. 4.—Family tree.

All the subjects shown in the family tree were examined. Two sisters (II 5 and 6) were found to have a mild optic atrophy and II 6 had a retinal cyst. No abnormality was found in any others, and in particular none of the third generation had retinitis pigmentosa, ataxia, or clinical evidence of bone disorder.

Serum from everyone in the family was examined for the presence of phytanic acid, but with the exception of the propositi this was absent in all of them. Creatine phosphokinase activity and serum caeruloplasmin levels were also estimated in the propositi and eight relatives (see Table). It can be seen that the creatine phosphokinase is raised in both the propositi, as might be expected in any wasting disease (Gubbay *et al.*, 1966). The serum caeruloplasmin was raised in Case 1 and also in his younger sister (II 6), who had optic atrophy, though not in his twin sister.

Biochemical Findings

	Age	Phytanic Acid (% of Total Fatty Acid)	Creatine Kinase (i.u.)	Caerolo-plasmin (mg./100 ml.)
I 1	57	0	11	5·3
I 2	55	0	16	13·1
II 1	35	0	20	10·6
II 2 (Case 2) ..	32	15·6	90	18·9
II 3	31	0	15	10·5
II 4 (Case 1) ..	27	34·7	68	26·0
II 5	27	0	13	8·8
II 6	25	0	8	32·8
II 7	24	0	18	5·0
II 8	14	0	56	10·6
Normal controls		0	Males up to 66 Females up to 43	14·25

Phytanic Acid

The propositus (Case 1) was shown to have a very high level of phytanic acid in the serum. This was estimated by gas-liquid chromatography in Oslo (Eldjarn, personal communication, 1966) to be 90 mg./100 ml. of serum, a value among the highest so far found in this condition by these workers. An aliquot of the same sample was found to contain phytanic acid in a concentration of 34.7% of total serum fatty acids by Professor J. N. Cumings. A sample of serum taken in 1960 and freeze-dried contained 12% of the total fatty acids as phytanic acid.

In Case 2 the serum contained 15.6% of the total of fatty acids as phytanic acid (July 1966) and 14.3% when re-estimated in February 1967.

C.S.F. samples from both propositi were also examined. A freeze-dried specimen taken from Case 1 in 1960 contained phytanic acid in a concentration of 10% of total fatty acids. A specimen taken in August 1966, when the disease had progressed considerably, contained 19.4%. No phytanic acid was demonstrated in the C.S.F. in Case 2, however. These 1966 C.S.F. specimens were also subjected to phospholipid estimation and protein electrophoresis and showed markedly raised total phospholipid, lecithin, and globulin values.

Discussion

The elevated phytanic acid levels here reported are in accordance with previous studies (Kahlke, 1964; Eldjarn, 1965; Rake and Saunders, 1966), and it now seems established that the clinical features of the disease are associated with an impairment of oxidative degradation of this branched-chain fatty acid (Eldjarn *et al.*, 1966). Though an excess of phytanic acid has been found in many tissues, including liver, kidney, brain, nerve, skeletal muscle, and urine (reviewed by Rake and Saunders, 1966), C.S.F. levels have not previously been recorded.

The family study shows that the inheritance demonstrated is compatible with an autosomal recessive mode of transmission. Kahlke and Richterich (1965) found higher amounts of phytanic acid in the serum of the apparently healthy mother of a patient with Refsum's syndrome than the serum of the patient; this raises the possibility of a biochemical abnormality being demonstrable in heterozygous carriers of the disease, a situation akin to that in thalassaemia or in glucose-6-phosphatase deficiency—Von Gierke's disease (Cori and Cori, 1952). This would be of importance in genetic counselling, but we found no phytanic acid in the serum of any relatives, confirming the findings in the parents of two Norwegian cases of Refsum's syndrome (Eldjarn, personal communication, 1966).

The remarkable variability of the clinical course of Refsum's syndrome is now well known. Of Refsum's original cases, one presented after an acute febrile illness, and one apparently began as a sequel to the physical exertion of fishing near the Lofoten Islands. In both cases the worsening immediately after a febrile episode had led to their first hospital admission. Another of Refsum's cases relapsed regularly in the springtime; in the light of our present knowledge it is tempting to speculate that this might have been associated with seasonal dietary variations. A member of one of Refsum's original families has recently been reported to have improved after long-term mental hospital admission, possibly again associated with low vegetable intake (Eldjarn *et al.*, 1966). Following preliminary reports on the value of a diet low in phytanic acid Eldjarn *et al.*, 1966) in the condition, this diet was given to our Case 1, but without improvement. Because of the patient's intolerance the diet was relaxed, and on moderate restriction he was at the time of writing showing steady improvement.

A fluctuation in C.S.F. protein was evident in our cases, and reference to Fig. 3 might suggest that there was a relation between the activity of the disease and the C.S.F. protein in Case 1 over the nine-year period of study. The C.S.F. protein in Case 2 has dropped from 400 mg./100 ml. in 1958 to 83 mg./100 ml. in 1966. Since 1964, a year after her hysterectomy, she has improved markedly and steadily. This is of interest as it might indicate that an alteration in hormone balance after hysterectomy may have favourably influenced the course of the disease.

The only biochemical abnormality consistently described so far in Refsum's syndrome is that of phytanic acid accumulation. While the C.S.F. phospholipid, lecithin, and globulin increases here recorded may simply reflect this abnormality, abnormalities of copper metabolism in the condition have been reported by several workers (Richterich *et al.*, 1965; Rake and Saunders, 1966). In Case 1 and a sib with optic atrophy (II 6) the caeruloplasmin was raised (see Table). The significance of this finding is at present obscure.

Continued follow-up of patients with Refsum's syndrome, with phytanic acid estimations being compared to clinical state, would seem a fruitful field for study. While alteration in phytanic acid intake may well affect the disease process, there may be physiological factors influencing the metabolic pathways of phytanic acid breakdown which also affect the course of the disease. Such a hypothesis would fit the observations above regarding the effect of intercurrent illness and improvement in a woman after the child-bearing period.

Summary

The results are reported of a clinical and biochemical study of two sibs with Refsum's syndrome who have been studied over a period of nine years. Three generations of the family were investigated, and no significant evidence of biochemical abnormality was found in any of the unaffected members. The serum phytanic acid level was raised in both patients, and high levels of phytanic acid in cerebrospinal fluid were present in one.

Fluctuations in the severity of the condition are compared with C.S.F. protein levels, and possible explanations for this characteristic variation discussed.

REFERENCES

Alexander, W. S. (1966). *J. Neurol. Neurosurg. Psychiat.*, **29**, 412.
Carrell, R. W., Scott, P. J., and McLellan, G. H. (1966). *N.Z. med. J.*, **65**, 766.
Cori, G. T., and Cori, C. F. (1952). *J. biol. Chem.*, **199**, 661.
Eldjarn, L. (1965). *Scand. J. clin. Lab. Invest.*, **17**, 178.
—— *et al.* (1966). *Lancet*, **1**, 691.
Gordon, N., and Hudson, R. E. B. (1959). *Brain*, **82**, 41.
Gubbay, S. S., Walton, J. N., and Pearce, G. W. (1966). *J. Neurol. Neurosurg. Psychiat.*, **29**, 500.
Kahlke, W. (1964). *Klin. Wschr.*, **42**, 1011.
—— and Richterich, R. (1965). *Amer. J. Med.*, **39**, 237.
Klenk, E., and Kahlke, W. (1963). *Hoppe-Seylers Z. physiol. Chem.*, **333**, 133.
Rake, M., and Saunders, M. (1966). *J. Neurol. Neurosurg. Psychiat.*, **29**, 417.
Refsum, S. (1946). *Acta psychiat. scand.*, Suppl. No. 38, p. 9.
Richterich, R., van Mechelen, P., and Rossi, E. (1965). *Amer. J. Med.*, **39**, 230.

Medical Memoranda

Perforated Duodenal Ulcer Presenting as Acute Respiratory Failure

Brit. med. J., 1967, 3, 779–780

Respiratory failure in patients with chronic bronchitis and emphysema is usually part of a generalized cerebral depression from hypoxia and hypercapnia. It may come on suddenly, however, as a result of bronchial blockage from plugs of inspissated secretions (Simpson, 1962). In the following case a generalized peritonitis induced acute respiratory failure in a severely emphysematous patient.

CASE REPORT

A man aged 48 was admitted to hospital with bronchopneumonia and congestive cardiac failure complicating his long-standing chronic bronchitis and emphysema. His blood gases at the time of this admission were: *p*H 7.35 units, $P\text{CO}_2$ 72.5 mm. Hg, base excess +8 mEq/l., standard bicarbonate 31 mEq/l., and $P\text{O}_2$ 79 mm Hg. Chest *x*-ray examination showed appreciable generalized emphysema with bullous formation affecting both left and right apical zones together with recent inflammatory shadowing at the left base. After a period of bed rest associated with diuretics, digoxin, and antibiotic therapy, he made a satisfactory recovery but was still considerably disabled by his emphysema. His blood gases on 19 April 1966—that is, the day before his discharge—showed an established ventilatory insufficiency as well as impaired alveolar-arterial gas exchange (see Table).

He was advised to stop smoking, as this was considered the only thing likely to delay progression of his emphysema.

On 6 May at 4.15 p.m. he was readmitted in acute respiratory failure with complete apnoea. Emergency treatment in the casualty department consisted of endotracheal intubation with positive-pressure oxygen respiration, intravenous infusion of 7.5% bicarbonate, and hydrocortisone also administered by the intravenous route. The *p*H on admission was 7. Treatment was continued in the intensive care unit, where the patient was put on an East-Radcliffe respirator. Two hours later his general condition improved and he regained consciousness. By this time he had received 1 litre of 7.5% bicarbonate and was on tetracycline 100 mg. intramuscularly six-hourly. Investigations produced the following results: P.C.V. 60%; Hb 128%; serum electrolytes—Na 137 mEq/l., K 4.7 mEq/l., Cl 81 mEq/l.; blood urea 83 mg./100 ml. The blood gases at 6.30 p.m. are shown in the Table.

He now complained of severe abdominal pain and was found to have a rigid and silent abdomen. A previous long-standing history of dyspepsia suggested the diagnosis of a perforated peptic ulcer. This was confirmed by the presence of free gas under the right diaphragm shown on an *x*-ray film of the abdomen.

At laparotomy a perforated anterior duodenal ulcer was found with established generalized peritonitis. The perforation was closed with three chromic catgut sutures and an omental patch. After toilet of the peritoneal cavity, it was drained by tubes in the right subphrenic space and in the pelvis. After a further 14 hours on the respirator he was transferred to an oxygen tent. Tracheostomy was decided against, as he was by this time breathing well and was able to cough satisfactorily.

Table Showing Blood Changes

Date	Time	Treatment	*p*H	P_{CO_2} (mm. Hg)	Base Excess (mEq/l.)	Standard bicarbonate (mEq/l.)	P_{O_2} (mm. Hg)
19/4/66			7·33	72·5	+8	31	58
6/5/66	4.15 p.m.		7·0				
6/5/66	6.30 „	E.R. respirator. Bicarb. 1 litre	7·42	65·0	+13		300
7/5/66	11 a.m.	O_2 tent	7·34	80·0	+10·5	33·0	56
8/5/66	12 noon	O_2 „	7·34	68·5	+6·0	29·0	53
9/5/66	4.00 p.m.	O_2 „	7·34	72·0	+8·5	31·0	58

The Table indicates the blood gases during the immediate postoperative days. The patient showed steady improvement, but on the sixteenth postoperative day had a complete dehiscence of his abdominal wound. This was resutured under general anaesthesia without complications affecting the respiratory system. Ten days later he developed Friedlander's pneumonia and despite all attempts at resuscitation he died on 3 June. Unfortunately a post-mortem examination was refused.

COMMENT

There are two main types of respiratory failure: (1) ventilatory failure in which the P_{CO_2} is increased, and (2) impaired alveolar-arterial gas exchange with decreased oxygen saturation but without hypercapnia (Fletcher, 1962). The most severe cases of respiratory failure are usually encountered in patients with advanced emphysema and bronchitis. These patients usually show a composite picture of both underventilation and impaired alveolar-arterial gas exchange.

The above patient had advanced chronic respiratory insufficiency and was relying on his diaphragmatic movements for his tidal exchange. The duodenal perforation with its attendant peritonitis "splinted" his diaphragm and thus precipitated an acute respiratory failure. On 9 May 1966, three days postoperatively, he was breathing spontaneously and his blood gases gave almost identical values to those carried out on 19 April—that is, the accepted normal for him (see Table).

A pronounced increase in arterial P_{CO_2} causes cerebral vasodilatation and increased intracranial pressure (Comroe *et al.*, 1962). It is possible that hypercapnia might have been a contributory cause towards the perforation of a duodenal ulcer in this case; the CO_2 engendered raised intracranial pressure, stimulating the vagus centre with consequent gastric hyperacidity. Also hypercapnia stimulates release of adrenaline from the adrenal medulla.

We would like to think Mr. J. Moroney, under whose care this patient was admitted, for permission to treat and publish this case.

A. CUSCHIERI, M.D., F.R.C.S.ED.
K. F. EDWARDSON, M.B., CH.B., B.SC., F.R.C.S.

Broadgreen Hospital,
Liverpool.

REFERENCES

Comroe, J. H., Forster, R. E., Dubois, A. B., Briscoe, W. A., and Carlsen, E. (1962). *The Lung: Clinical Physiology and Pulmonary Function Tests*, 2nd ed., p. 157. Chicago.

Fletcher, C. M. (1962). *Proc. roy. Soc. Med.*, **55**, 565.

Simpson, T. (1962). Ibid., **55**, 569.

Lupus-like Syndrome Induced by Procainamide

Brit. med. J., 1967, 3, 780–781

Many drugs have been associated with the onset of a syndrome resembling systemic lupus erythematosus. Among the drugs implicated are hydrallazine; sulphonamides; anticonvulsants of the phenytoin group, and troxidone; penicillin; phenylbutazone; tetracycline; streptomycin and isoniazid; griseofulvin; thiouracil derivatives; and procainamide.

Since the first description of a syndrome closely mimicking, if not identical with, systemic lupus erythematosus, and occurring after the administration of procainamide (Ladd, 1962), 13 cases have been reported—12 in patients receiving the drug for cardiac disease (Hahn, 1964; Colman and Sturgill, 1965; Kaplan *et al.*, 1965; Paine, 1965; Carabia and Fortney, 1965) and one in a patient with dystrophia myotonica (Prockop, 1966). All previous reports have appeared in the American literature.

CASE REPORT

A 50-year-old widow attended hospital in May 1965 with symptoms suggestive of angina of effort, and was subsequently found to be hypertensive, with a blood pressure of 260/150 mm. Hg. Investigation showed no cause for this, and a diagnosis of essential hypertension was made. She was initially treated with antihypertensive drugs, but these were withdrawn when she had a myocardial infarction. In September 1965 she developed paroxysmal ventricular tachycardia and was given quinidine sulphate, but because of a drug rash occurring within 24 hours this was replaced by procainamide 500 mg. q.i.d.

In January 1966 she was readmitted to hospital complaining of left-sided pleuritic pain of sudden onset. She had no cough, sputum, or haemoptysis. She had a pleural rub at the left costophrenic angle and signs of a small left-sided pleural effusion. Her pulse was in sinus rhythm and her blood pressure was 160/100 mm. Hg. E.S.R., blood picture, and blood urea were within normal limits. Serum aspartate aminotransferase and serum lactate dehydrogenase were also normal. *X*-ray examination showed a small pleural effusion at the left costophrenic angle and marked cardiac enlargement. Though there was no obvious source of emboli, an initial diagnosis of pulmonary embolism was made and anticoagulation was started. Procainamide was continued as prophylaxis against further cardiac arrhythmia.

Initially there was some improvement, but three weeks after admission the patient began to complain of severe pain in the small joints of both hands and in the muscles around the shoulder girdles. Subsequently she had a further episode of left-sided pleuritic pain, followed by pain and a pleural rub on the right side. *X*-ray examination showed an increase in the left-sided pleural effusion and the presence of fluid at the right base. The E.S.R. was 70 mm. in one hour and the serum gammaglobulin 1.5 g./100 ml. The most likely diagnosis was thought to be multiple pulmonary emboli, and the oral anticoagulants were supplemented by high doses of intravenous heparin. However, no clinical improvement was noted.

The possibility of a collagen disease—a procainamide-induced lupus syndrome—was then considered. Positive L.E.-cell preparations were found on several occasions, the L.E. latex fixation and Jones tests were positive, and the antinuclear factor was demonstrated.

Therefore the procainamide was withdrawn and replaced by propranolol 20 mg. q.i.d. The effect was dramatic. The myalgia and arthralgia subsided; the chest symptoms and signs abated, and *x*-ray examination showed a clear right lung field within one month, followed by a gradual resolution of the effusion on the left side; the E.S.R. fell to 10 mm. in the hour in two months; L.E.-cell preparations were negative after six weeks, and the antinuclear factor was negative five months later.

When seen in October 1966 the patient was well, and was able to do light housework and take mild exercise.

COMMENT

In the 14 cases reported previously, in which similar reactions occurred, procainamide was given in a dosage of 1–5 g. daily. Symptoms of the lupus syndrome appeared after three weeks to 22 months of therapy. The commonest manifestations were polyarthralgia (14 cases), positive L.E.-cell preparations (13 cases), pleuropulmonary symptoms (nine cases), and the presence of antinuclear factor (in all five cases examined). Our patient took 2 g. of procainamide daily for five months before the appearance of chest symptoms.

Apart from two cases that were followed for only seven or eight weeks after procainamide was stopped, all have shown complete recovery within two years. This may represent a difference from the similar syndrome precipitated by hydrallazine, in which hypergammaglobulinaemia or antinuclear factor antibodies were found five years after discontinuation of the drug and disappearance of symptoms (Alarçon-Segovia *et al.*, 1965). Recrudescence has been found to follow re-exposure to the drug, but it was not attempted in this case.

There is still much controversy surrounding the mechanism giving rise to this drug-induced syndrome. Some authors Alarçon-Segovia *et al.*, 1965; Lee *et al.*, 1966) feel that the drug unmasks a predisposition to develop lupus erythematosus. Studies in patients with the "hydrallazine syndrome" have shown that symptoms and signs possibly due to S.L.E. were present before the drug was given. Patients who at one time had developed clear-cut drug-induced S.L.E. have occasionally been observed to have apparently spontaneous recurrence of the disease years later. There is, however, as yet no case reported of spontaneous recurrence or chronic S.L.E. induced by procainamide.

There are two other possibilities. Firstly, the symptoms could be a manifestation of drug toxicity or hypersensitivity—that is, a lupus–drug reaction. In favour of this a case has been reported (Prockop, 1966) of a patient with established S.L.E. who received full doses of procainamide for 15 months for a myotonic illness with no exacerbations of S.L.E., though there were episodic symptoms long before and long after the period of drug administration. This may be evidence that the lupus-like drug reaction differs from the disease. Secondly, the appearance of S.L.E. during drug administration might be coincidental, but the increasing number of cases reported makes this unlikely.

A review of the cases would suggest that procainamide is used in circumstances—for example, atrial fibrillation, paroxysmal atrial tachycardia, ventricular ectopics—in America where other drugs would be the first choice in Britain. It was only because this patient, with recurrent ventricular tachycardia, was hypersensitive to quinidine that procainamide was used. It would seem that this drug should be prescribed on a long-term basis only when there is no less potentially harmful alternative.

We wish to express our thanks to Professor O. L. Wade for permission to publish this case, and for advice on the manuscript.

D. G. McDEVITT, M.B., M.R.C.P., M.R.C.P.I.
J. F. T. GLASGOW, M.B., B.SC., M.R.C.P., M.R.C.P.I.
Department of Therapeutics and Pharmacology,
Queen's University, Belfast

REFERENCES

Alarçon-Segovia, D., Worthington, J. W., Ward, L. E., and Wakin, K. G. (1965). *New Engl. J. Med.*, **272**, 462.
Carabia, A. G., and Fortney, T. G. (1965). *J. Tenn. med. Ass.*, **58**, 287.
Colman, R. W., and Sturgill, B. C. (1965). *Arch. intern. Med.*, **115**, 214.
Hahn, A. L. (1964). *Missouri Med.*, **61**, 19.
Kaplan, J. M., Wachtel, H. L., Czarnecki, S. W., and Sampson, J. J. (1965). *J. Amer. med. Ass.*, **192**, 444.
Ladd, A. T. (1962). *New Engl. J. Med.*, **267**, 1357.
Lee, S. L., Rivero, I., and Siegel, M. (1966). *Arch. intern. Med.*, **117**, 620.
Paine, R. (1965). *J. Amer. med. Ass.*, **194**, 23.
Prockop, L. D. (1966). *Arch. Neurol. (Chic.)*, **14**, 326.

Hypoparathyroidism and Malabsorption

Brit. med. J., 1967, **3**, 781–782

The association of secondary hyperparathyroidism with osteomalacia caused by malabsorption has often been noted (Davies *et al.*, 1956). There also seems to be a connexion between hypoparathyroidism and the malabsorption syndrome.

Bennett *et al.* (1932), in describing 15 cases of "idiopathic steatorrhoea," suggested that five may have had secondary hypoparathyroidism, in view of the finding of a raised serum inorganic phosphorus level. Several cases of idiopathic hypoparathyroidism associated with malabsorption and generalized moniliasis have been described (Collins-Williams, 1950; Salvesen and Böe, 1953a; Clarkson *et al.*, 1960). A few other cases of idiopathic hypoparathyroidism coexisting with malabsorption alone have been documented in recent years (Lowe *et al.*, 1950; Case Records of Massachusetts General Hospital, 1954; MacGregor and Whitehead, 1954; Jackson *et al.*, 1956; Williams and Wood, 1959; Cochrane *et al.*, 1960; Taybi and Keele, 1962). In a case reported by Clarkson *et al.* (1960) a flat small-bowel mucosa was found on biopsy, and correction of the hypoparathyroid state converted to normal most of the demonstrated abnormalities of absorption.

CASE REPORT

An unmarried woman aged 58 was admitted to hospital for investigation of an iron-deficiency anaemia which had been present for nine months and had failed to respond to treatment. She gave a history of a "nervous breakdown" followed by depression at the age of 22. A year later she had noticed a progressive deterioration of vision, and was found to have bilateral cataract, one of which was successfully removed at operation.

Clinical examination revealed a pale, nervous woman, with finger-clubbing. A postmature cataract was present in the left eye. Neurological examination showed a positive Trousseau's sign, but a negative Chvostek's sign.

Investigations showed a serum calcium level of 5.7 mg./100 ml. and a serum inorganic phosphorus of 6.1 mg./100 ml. Alkaline phosphatase was within the normal range. The serum albumin and serum iron were low, but serum vitamin B_{12}, folic acid, and cholesterol were normal. Tests for faecal occult blood were consistently negative. Faecal fat collection showed a level of 15 g./day, but D-xylose excretion test gave an equivocal result. Radiology showed no bony change, and small-bowel meal and barium enema were normal. Electrocardiogram was also normal. Biopsy of the small-bowel mucosa by the peroral method, using the Crosby capsule (Crosby and Kugler, 1957), showed marked villous atrophy with inflammatory changes and epithelial degeneration. The phosphate excretion index (Nordin, 1962 ; Nordin and Smith, 1965) gave results consistent with hypoparathyroidism.

The patient was treated with calcium supplements and vitamin D_2. After three months the biochemistry was normal, and repeat biopsy of small-bowel mucosa showed minimal damage and a marked improvement from the previous appearances.

DISCUSSION

Hypoparathyroidism and malabsorption have been reported together in more cases than would reasonably be expected by chance. Jackson (1957) thought that the association was well enough documented to be regarded as a "syndrome." There is, however, a lack of uniformity in the principal features of the reported cases. In some the symptoms of malabsorption are dominant, and in others the features of hypoparathyroidism. In most cases the symptoms give no clear indication of the primary condition.

Several possible explanations for the association have been postulated. Salvesen and Böe (1953b) suggested that intestinal moniliasis may have been the cause in their case, and perhaps in others. This seems unlikely to account for more than a few instances. They also suggest that patients with malabsorption have a relative parathyroid insufficiency due to malabsorption of a substance necessary for the continuation of normal parathyroid activity. There is, however, no evidence favouring the existence of such a substance. Hypocalcaemia may occur with either hypoparathyroidism or malabsorption. The serum inorganic phosphorus is raised in the former, and normal or low in the latter, the depression being caused by compensatory overactivity of the parathyroid gland. There is no evidence that this overactivity will eventually lead to hypofunction of the gland, or any definite evidence that hypoparathyroidism causes intestinal dysfunction and malabsorption. In the present case, if malabsorption were the primary disorder, the serum inorganic phosphorus would be expected to be low, or within the normal range ; this would be so if the patient was responding normally to the low serum calcium level due to poor absorption. In fact, however, the level is high, as in most of the cases reported. This suggests that the hypoparathyroidism may be the primary abnormality in many of the reported cases.

In the present case there is abundant evidence favouring a long-standing hypoparathyroidism. The development of bilateral cataract so early in life, together with mental symptoms (Clark *et al.*, 1962 ; Denko and Kaelbling, 1962), suggests that the condition was present 35 years ago. It is also known that hypoparathyroidism, whatever the cause, may remain latent for many years (Bull and Dillihunt, 1965). It seems likely that this patient's malabsorption was not of very long standing, as the symptoms of anaemia and possibly other deficiencies would have occasioned her attendance at hospital earlier. In addition, the treatment given in an attempt to improve parathyroid function resulted in an improvement in absorptive capacity of the small bowel, together with considerable restoration towards normal of the mucosal appearances. For these reasons, and the high serum phosphorus level, there is a possibility that parathyroid hypofunction has caused damage to the mucosa of the small bowel. None of the cases reported in the literature are incompatible with this hypothesis. This patient may therefore fall into the secondary coeliac syndrome group postulated by Hindle and Creamer (1965a, 1965b). They found that 36% of patients with a flat jejunal mucosa had some associated disease in addition to the symptoms of malabsorption. The primary disease may have been present for many years before malabsorption developed. They found it impossible to differentiate between primary and secondary coeliac syndrome groups on the basis of the deficiencies present and in the response to treatment. In some cases the mucosal changes were reversible with treatment of the underlying disease.

A wide list of conditions have been described as being associated with malabsorption and a flat jejunal mucosa. These include carcinoma (Creamer, 1964), malignant lymphoma (Gough *et al.*, 1962), diabetes mellitus (Mailman, 1958 ; Ellenberg and Bookman, 1960 ; Vinnik *et al.*, 1962), ulcerative colitis (Goulston, 1964 ; Salem *et al.*, 1964), infectious hepatitis (Astaldi *et al.*, 1964), tuberculosis and sarcoidosis (Hindle and Creamer, 1965a, 1965b), hepatic cirrhosis (Salem *et al.*, 1964), uraemia and congestive cardiac failure (Lochry and Creamer, 1966), and the dermatoses (*Lancet*, 1965). Hypoparathyroidism may therefore be regarded as one more disease which can cause the secondary coeliac syndrome.

I wish to thank Dr. Hugh Conway for permission to report this case, and for the helpful criticism which he made on reading the manuscript.

R. I. RUSSELL,* M.B., CH.B., M.R.C.P.ED., M.R.C.P.GLASG.,
Royal Alexandra Infirmary, Paisley.

---

* Present address: Gardiner Institute of Medicine, Western Infirmary, Glasgow W.1.

REFERENCES

Astaldi, G., Grandini, U., Poggi, C., and Strosselli, E. (1964). *Amer. J. dig. Dis.*, **9**, 237.
Bennett, T. I., Hunter, D., and Vaughan, J. M. (1932). *Quart. J. Med.*, **25**, 603.
Bull, D. M., and Dillihunt, R. C. (1965). *J. Amer. med. Ass.*, **193**, 308.
Case Records of Massachusetts General Hospital (1954). *New Engl. J. Med.*, **251**, 442.
Clark, J. A., Davidson, L. J., and Ferguson, H. C. (1962). *J. ment. Sci.*, **108**, 811.
Clarkson, B., Kowlessar, O. D., Horwith, M., and Sleisenger, M. H. (1960). *Metabolism*, **9**, 1093.
Cochrane, W. A., Morse, W. I., and Landrigan, P. (1960). *Amer. J. Dis. Child.*, **100**, 544.
Collins-Williams, C. (1950). *Pediatrics*, **5**, 998.
Creamer, B. (1964). *Brit. med. J.*, **2**, 1435.
Crosby, W. H., and Kugler, H. W. (1957). *Amer. J. dig. Dis.*, **2**, 236.
Davies, D. R., Dent, C. E., and Willcox, A. (1956). *Brit. med. J.* **2**, 1133.
Denko, J. D., and Kaelbling, R. (1962). *Acta psychiat. scand.*, **38**, Suppl. No. 164.
Ellenberg, M., and Bookman, J. J. (1960). *Diabetes*, **9**, 14.
Gough, K. R., Read, A. E., and Naish, J. M. (1962). *Gut*, **3**, 232.
Goulston, K. J. (1964). Ibid., **5**, 490.
Hindle, W., and Creamer, B. (1965a). *Brit. med. J.*, **2**, 455.
—— —— (1965b). Ibid., **2**, 458.
Jackson, W. P. U. (1957). *Lancet*, **1**, 1086.
—— Hoffenberg, R., Linder, G. C., and Irwin, L. (1956). *J. clin. Endocr.*, **16**, 1043.
Lancet, 1965, **2**, 69.
Loehry, C. A., and Creamer, B. (1966). *Brit. med. J.*, **1**, 827.
Lowe, C. U., Ellinger, A. J., Wright, W. S., and Stauffer, H. M. (1950). *J. Pediat.*, **36**, 1.
MacGregor, M. E., and Whitehead, T. P. (1954). *Arch. Dis. Childh.*, **29**, 398.
Mailman, R. H. (1958). *Ann. intern. Med.*, **49**, 190.
Nordin, B. E. C. (1962). *Scot. med. J.*, **7**, 74.
—— and Smith, D. A. (1965). *Diagnostic Procedures in Disorders of Calcium Metabolism.* London.
Salem, S. N., Truelove, S. C., and Richards, W. C. D. (1964). *Brit. med. J.*, **1**, 394.
Salvesen, H. A., and Böe, J. (1953a). *Acta med. scand.*, **146**, 290.
—— —— (1953b). *Acta endocr. (Kbh.)*, **14**, 214.
Taybi, H., and Keele, D. (1962). *Amer. J. Roentgenol.*, **88**, 432.
Vinnik, I. E., Kern, F., and Struthers, J. E. (1962). *Gastroenterology*, **43**, 507.
Williams, E., and Wood, C. (1959). *Arch. Dis. Childh.*, **34**, 302.

Schizophrenia in a Male Pseudohermaphrodite

Brit. med. J., 1967, **3**, 783–784

There now exists a considerable literature concerning intersex states in humans. Money (1952), reviewing the literature and studying a personal series of cases, found only one case with coexistent schizophrenia. Subsequently a further patient in this group was also diagnosed as schizophrenic (Money, personal communication). No further cases seem to have been reported in the interim.

CASE REPORT

A man aged 44 was admitted to hospital for investigation in March 1964, his only complaint being of fatigue, which he felt was related to poisons circulating in his blood stream after an attack of " chorea " at the age of 14.

He stated that at birth he had been registered as a girl and had been reared as such until the age of 14, when he was admitted to the local mental hospital suffering from " chorea with mania." While in hospital it was decided that he was in fact male, and on discharge he was re-registered. He seemed to adjust to the change quite rapidly and believed that the event was only a " nine-days wonder " in his village.

He left school at 18 and studied engineering, qualified in 1945, and subsequently worked regularly until 1961, changing his job frequently but always for promotion.

He married in 1947 (his wife was aware of his anatomical abnormality as a result of premarital love play). In 1950 they adopted a son, and a second in 1958. In 1960 the family moved from Scotland to London and the patient claimed that his wife found it impossible to settle down. She left him in 1961, taking the elder boy with her, and since then he has had no contact with her. At that time he became interested in spiritualism and began to take instruction in mediumship.

In 1962 he had his first recognized psychotic breakdown, while on holiday in Northumberland. He was thought to be deluded and possibly hallucinated, and a diagnosis of schizophrenia was made. He was admitted to hospital and given electric convulsion therapy and chlorpromazine, recovering in six weeks. He returned to London, but did not resume his work. In September 1963 he again went on holiday and took his young son with him. They camped in the Wye Valley, but after a few days he found an empty cottage, which he broke into, and set up home. This led to his appearing before local magistrates and being placed on probation. His son was taken into care. While on probation he moved to Oxford, claiming that he had friends in the neighbourhood, though in fact he knew no one. He found himself a flat, but made no attempt to get work, and remained at home doing almost nothing for six months. This led to his probation officer asking for psychiatric opinion, and the patient's subsequent admission to hospital.

Family History.—Father aged 76, alive and well. Mother died at age 66, said to have had chronic heart disease. Brothers: one aged 46, married with one son with congenital absence of auditory pinna ; another aged 42, also registered as a girl, redesignated as male after medical examination when in the A.T.S. There was no family history of mental illness.

Mental State.—On admission he was pleasant and co-operative, with no mannerisms. He gave a coherent account of his life up to the previous two years, but he was vague about recent events, in contrast to the detailed account of the rest of his life. He did not show gross thought disorder at that time, but there was some flattening of affect. He denied having any special powers of healing as he had claimed on his previous admission, but expressed the idea that his fatigue was due to toxins which circulated in his blood and caused scratches to appear on his arms. These ideas had little affective loading, and sank into the background when he was told that his blood tests were normal. He did not seem to be hallucinated, but admitted hearing voices in the past. He was unable to recognize the voices or to state what they said to him. From the psychosexual aspect he stated that he always felt awkward as a girl and that he was " a big clumsy tomboy." He was glad to change his role, and claimed it was little problem for him. His sexual orientation had been exclusively heterosexual. He claimed that he and his wife achieved mutual satisfaction by digital manipulation. He thought the greatest problem resulting from his genital abnormality had been his inability to pass urine in a standing position.

Physical Examination.—He was of normal male build and appearance (Fig. 1), and on examination all systems were normal apart from the genitourinary tract. There was a reducible left inguinal hernia, and a mass which was thought to be a testicle passed freely through the inguinal ring. There was a backward-pointing phallus about 1 in. (2.5 cm.) long. The scrotum was unfused, giving the appearance of labia majora and minora. Posteriorly there was a dilated urethral orifice which permitted the passage of one finger to the depth of 1 in. (2.5 cm.) (Fig. 2). No prostatic tissue was palpable. By digital stimulation of the hypospadic

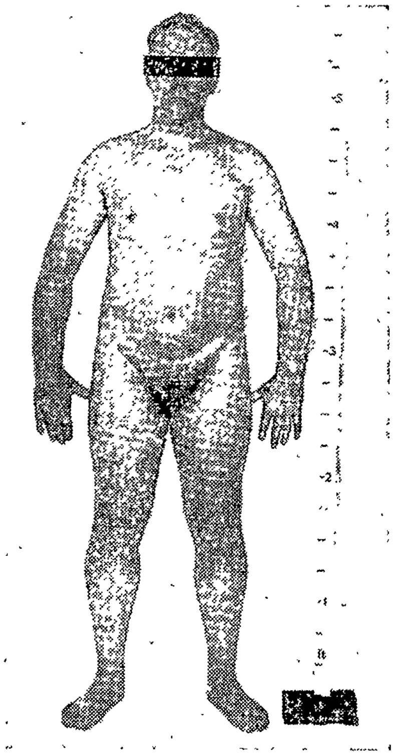


FIG. 1

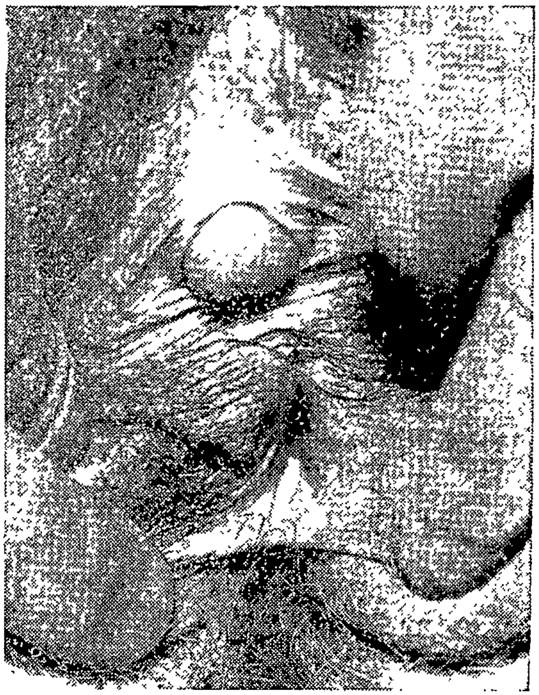


FIG. 2.—External genitalia showing phallus and external urinary meatus.

penis the patient was able to produce a few millilitres of fluid from this orifice. This fluid did not contain any spermatozoa.

Investigations.—Hb 96%; E.S.R. 2 mm. in one hour; Wassermann reaction and Kahn test negative; 17-ketosteroids 10.4 mg. in 24 hours; buccal smear showed no Barr bodies. I.V.P.: no suggestion of prostatic indentation of urethra.

Psychometry.—The Minnesota multiphasic personality inventory scales were within normal limits whether scored as a male or a female. The score on the Epstein test was within normal limits.

He was diagnosed as having schizophrenia and his physical state as one of cryptorchidism with a gross hypospadias. This was later confirmed at operation.

He was given no specific treatment, but after a few weeks he found himself a job with an engineering firm and left hospital, remaining in employment for 10 months. While in hospital he was referred for surgical opinion and subsequently had a series of operations; firstly, for repair of a left inguinal hernia, and, secondly, for a plastic operation to enable him to urinate in a standing position.

Since he left hospital he has shown more floridly schizophrenic symptoms. He believes that he is in communication with two people on Mars, and they are dictating a book on spiritualism to him. His communication with them is at times interrupted by other "spirit voices," which sometimes swear at him or pass insulting remarks. He is undertaking a process of "spiritual cleansing" which requires him to bath as often as possible, and he spends much of his spare time in the bath.

He does not speak of any of these ideas other than during psychiatric interview, but then it is difficult to interrupt the flow of his ideas. So far his delusions have not interfered with his work, though his employers describe him as slow and lacking in initiative. He feels extremely well and can see no reason for taking any form of medication.

His mental condition has remained unchanged since his plastic operation, but his mood has been one of mild elation since he was first referred for a surgical opinion, and he was grateful for the operation enabling him to urinate standing up. Until his admission he had never sought medical help for this problem.

COMMENT

Since Freud many analysts have stressed the aetiological importance in schizophrenia of patients' uncertainty about their sexual role. Organically orientated workers have also attempted to implicate gonadal malfunction in the aetiology of schizophrenia, but the weight of evidence suggests that such changes in structure or function as have been shown are either coincidental or the result of the disease (David, 1957).

Were either theory correct it would be anticipated that people with so marked abnormality of their sexual organs as to lead to incorrect sex assignment would have a high incidence of schizophrenia. In fact this association seems to be extremely rare.

I wish to thank Dr. B. M. Mandelbrote for permission to publish this case, and Professor G. Harris for permission to use the photographs, which were taken in the department of anatomy, University of Oxford.

K. L. K. TRICK, M.B., B.S., D.P.M.,
Senior Research Registrar.
Littlemore Hospital,
Oxford.

REFERENCES

David, G. B. (1957). In *Schizophrenia: Somatic Aspects*, edited by D. Richter. London.
Money, J. (1952). Unpublished Doctoral Thesis. Harvard University.

Haemorrhage from Base of Tongue

Brit. med. J., 1967, 3, 784

When a patient presents with expectoration of blood its source is usually obvious. The history alone will often indicate the site of haemorrhage. We describe the case of a patient admitted to hospital with apparent haemoptysis who was found to be bleeding from the rupture of an enlarged vein at the base of the tongue. Enlarged, or varicose, veins have been noted in this area before, but little attention has been paid to them (Eggston and Wolff, 1947). It has been suspected that they could be the cause of bleeding, but we have been unable to find any previous description of a patient in whom this had actually been shown.

CASE REPORT

A man aged 58 was admitted to hospital after he had expectorated blood continuously for three days. During the previous week an exacerbation of his bronchitis had caused repeated coughing. On admission it was assumed that he had haemoptysis, but careful questioning suggested that the blood was coming from above the larynx. He had noted that he could produce heavily blood-stained saliva without coughing. There was no history of any abnormal bleeding.

General and oral examination showed nothing abnormal, apart from the presence of blood in the oropharynx. Chest *x*-ray picture, platelet count, and prothrombin time were normal, but the haemoglobin, which was 14.6 g./100 ml. on admission, fell to 9.6 g./100 ml. during the next five days.

Indirect laryngoscopy, performed the day after admission, showed an enlarged vein at the right side of the base of the tongue which extended over the anterior part of the epiglottis. There was a pool of blood around this vein. These findings were confirmed on examination under general anaesthesia, and it was then obvious that the haemorrhage was caused by a rupture of this vein in the glosso-epiglottic fold. Diathermy was applied to the bleeding-point and haemorrhage stopped completely. The patient returned home four days later.

COMMENT

Spontaneous haemorrhage from the throat is rare, but it must be considered when one of the usual causes of expectoration of blood cannot be found. If the site of haemorrhage is not visible on ordinary examination there should be no delay in using a laryngeal mirror to inspect the base of the tongue, hypopharynx, and larynx.

Our patient had a large vein at the base of the tongue, and it is probable that it had ruptured during a bout of coughing. It is stated that varicose veins in this area may occur in association with gout, cirrhosis of the liver, and influenza (Thomson and Negus, 1955), though no reason for this is given. In the above case the only associated condition was chronic bronchitis.

We wish to thank Dr. Maxwell Telling for permission to report this case and Mr. C. P. Mills for his advice and help.

J. H. WETHERILL, M.B., M.R.C.P.,
Senior Registrar in Medicine.
A. G. GANDHI, M.B., D.L.O., F.R.C.S.ED.,
Senior Registrar, Ear, Nose, and Throat Department.
The General Infirmary at Leeds.

REFERENCES

Eggston, A. A., and Wolff, Dorothy (1947). *Histopathology of the Ear, Nose, and Throat*, p. 967. Baltimore.
Thomson, St. C., and Negus, V. E. (1955). *Diseases of the Nose and Throat*, 6th ed., p. 520. London.

Current Practice

TODAY'S DRUGS

With the help of expert contributors we publish below notes on a selection of drugs in current use.

Tolnaftate

Tolnaftate is marketed by Glaxo Laboratories Ltd. under the name Tinaderm.

Although the use of griseofulvin has revolutionized the treatment of some types of fungus infections of the skin and its appendages, there still remains a great need for a really efficient topical fungicide. Over the years a large number of preparations have been introduced, many of which have a potent in-vitro action, but in clinical practice they have been found to have little advantage over the other preparations, and indeed benzoic acid ointment *B.N.F.* is still one of the most commonly prescribed preparations.

Tolnaftate was synthesized by a group of Japanese workers[1] and has been used in the U.S.A. for the past four years; the clinical results seem promising.

Chemistry and Pharmacology

Tolnaftate is the approved name for 0-2-naphthyl *N*-methyl-m-tolylthiocarbamate. It is a colourless and odourless compound, soluble in organic solvents but almost insoluble in water. Most of the original clinical work was carried out with 1% solution in polyethylene glycol, but tolnaftate is now marketed as a 1% cream and 1% powder under the name of Tinaderm.

The in-vitro activity has been the subject of a number of reports.[2 3] The minimum inhibiting concentration in µg./ml. is between 0.08 and 0.008 for four common ringworm fungi, *Trichophyton mentagrophytes*, *T. verrucosum*, *Epidermophyton floccosum*, and *Microsporum canis*, and it is 3.0 for *T. rubrum*. There is no significant effect against *Candida albicans*, some species of aspergillus, or bacteria.

Massive doses in animals have shown no toxicity,[4] and Goldman and Lasser[5] could not demonstrate any adverse effects in seven patients treated for seven consecutive days with 1% tolnaftate lotion applied to 90% of the body surface. Rostenberg[6] was unable to sensitize 54 subjects, and the clinical reports do not mention cases where sensitization or a primary irritant effect has been noted.

Clinical Studies

Robinson and Raskin[7] treated 185 patients with superficial fungus infections and reported improvement in 173 after two to four weeks' treatment. This included 128 cases with *T. rubrum* infection, 124 of which were improved, but it is noted that cases with palmar and plantar lesions did not clear completely. Many other trials have been carried out, including those of Leer,[4] who described 520 patients with 73% showing clearing or improvement, Neuhauser,[8] who treated 100 patients with 86% clearing or improved, and Erve[9] reporting 176 cases, 25 of which had *T. rubrum* infection, and 23 of these showed a good response. Gould[10] treated 86 patients, including 40 in a double-blind study; twice as many sites cleared with tolnaftate cream as with the placebo. A double-blind technique was als used by Adam and Craig[11] on 29 patients, 82% of whon showed clearing or great improvement after three weeks' treatment.

Discussion

From all these reports it seems that tolnaftate is effective i the common ringworm fungus infection of the toes and groin and skin elsewhere. It has no worth-while action on nail ringworm and it is doubtful whether it helps much in scalp ringworm. The clinical results in tinea versicolor (*Malassezi furfur*) are good. It has no effect on *Candida albicans* infections, and this limitation will need stressing, as otherwise it wil be used in chronic paronychia and other conditions associate with this fungus. It would thus seem that many of the case where tolnaftate is most effective are those which usuall respond readily to the older fungicidal applications. However *T. rubrum* infections have often proved difficult to clear, an tolnaftate may well have an important place in their management, particularly in the toe-web and groin infections. Th widespread scaling of hands and feet which this fungus infection sometimes causes does not respond so readily, and Wethered Heeler, and Warin[12] in a double-blind paired comparison i such patients were unable to demonstrate any clinical or mycological effect after treatment with tolnaftate cream for on month. Another important aspect of management of fungu infection is the tendency to recurrence after treatment is discontinued. Erve[9] reports no recurrence during 10 months observation, but Robinson[3] mentions two cases which recurre after apparently successful treatment with tolnaftate. Th period of treatment required in each type of case is likely to b determined only when more experience of the drug has bee obtained. In most of the clinical reports two to four weeks treatment has been sufficient, but some conditions may wel require longer.

Dosage and Cost

Tolnaftate is available as Tinaderm in 1% powder 1% cream It should be applied once or twice a day.

The basic N.H.S. cost of 15 g. of cream is 3s. 9d. and of 50 g of powder is 4s. 6d.

REFERENCES

[1] Noguchi, T., *Second Interscience Conference on Antimicrobia Agent and Chemotherapy, Abstract 34*, 1962. Chicago.

[2] Weinstein, M. J., Oden, E. M., and Moss, E., *Antimicrob Ag. & Chemother.*, 1964, p. 595.

[3] Robinson, H. M., ibid., 1964, p. 608.

[4] Leer, J. A., ibid., 1964, p. 615.

[5] Goldman, L., and Lasser, A. E., ibid., 1964, p. 602.

[6] Rostenberg, A., ibid., 1964, p. 606.

[7] Robinson, H. M., and Raskin, J., *J. invest. Derm.*, 1964, 42, 185.

[8] Neuhauser, I., *Antimicrob. Ag. & Chemother.*, 1964, p. 613.

[9] Erve, J., van de, *J. S. C. med. Ass.*, 1964, 60, 351.

[10] Gould, A. H., *Dermatolog. Trop.*, 1964, 3, 255.

[11] Adam, J. E., and Craig, G. E., *Canad. med. Ass. J.*, 1965, 93, 1004.

[12] Wethered, R. R., Heeler, W. R., Warin, R. P., *Brit. J. Derm.*, 1967, in press.

ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Phenylketonuria in Adults

Q.—*Is there any likelihood that the institution of dietary measures could improve mental defect in a young adult suffering from phenylketonuria who has had no previous treatment? Is the diagnosis of the disease in an older person made by the same tests as in infancy?*

A.—There is little likelihood that any worthwhile improvement in intelligence would result from giving a low phenylalanine diet to a young adult with phenylketonuria. Occasionally, however, treatment produces some improvement in behaviour or in epilepsy.

In affected females who become pregnant dietary treatment should be given throughout pregnancy to prevent damage to the foetal brain, which will result from the high level of phenylalanine in the foetal blood produced secondarily by the high level in the mother's blood.

The diagnosis of the disease in an older person is made by exactly the same tests as are used in infancy.

Diet and Hypochlorhydria

Q.—*Should patients with primary hypochlorhydria be given specific advice on diet, and, if so, what should it be?*

A.—Hypochlorhydria, if demonstrated by the augmented histamine test, implies that atrophic gastritis is present.[1] No specific diet or other treatment is indicated for this condition or for the accompanying failure of gastric acid secretion. However, atrophic gastritis and hypochlorhydria are associated with gastric ulcer,[2] gastric carcinoma,[3] and iron-deficiency anaemia.[4] Total gastric atrophy and achlorhydria are features of pernicious anaemia.

A barium meal examination and full blood count are advisable when hypochlorhydria has been demonstrated, and specific dietary or other treatment may be needed if any of these associated conditions are found.

REFERENCES

[1] Bock, O. A. A., Richards, W. C. D., and Witts, L. J., *Gut*, 1963, **4**, 112.

[2] du Plessis, D. J., *Lancet*, 1965, **1**, 974.

[3] Shearman, D. J. C., Finlayson, N. D. C., Wilson, R., and Samson, R. R., ibid., 1966, **2**, 403.

[4] Davidson, W. M. B., and Markson, J. L., ibid., 1955, **2**, 639.

Electric Toothbrushes

Q.—*What are the merits of electric toothbrushes?*

A.—It is to be expected that the rapid movements of the heads of electric toothbrushes would enable the teeth to be cleaned and the gingivae massaged more expeditiously, even when the heads are small. The use of a small head would enable the brushing to be more accurately controlled. Three types of brush movement are used in electrical toothbrushes. There is some evidence that an arcuate movement is less effective than plain horizontal or vertical movements in cleaning surfaces of teeth which are readily accessible.

Many clinical trials to evaluate the effectiveness of electrical toothbrushes have been undertaken. In general, they seem to indicate that electrical toothbrushes are equally as effective as conventional ones or may sometimes be more effective when the patient has not been given precise instructions on toothbrushing techniques.[1] In studies in which the electrical toothbrush has been used, after instruction, over a defined period of time sufficient for a conventional toothbrush to clean the teeth adequately—for example, three minutes—an electrical toothbrush is not usually more effective than a conventional one.

In brief, it would seem that the merits of electrical toothbrushes lie in their speed of action and possibly in more precise control. Children, aged about 5 and over, can usually handle them well after instruction and are attracted by their novelty. Many handicapped patients are able to clean their mouths more effectively than they would with a normal toothbrush.

REFERENCE

[1] Chaikin, B. S., Goldman, H. M., Schulman, S. M., and Ruben, M. P., *Periodontics*, 1965, **3**, 200.

Oedema with Disc Lesions

Q.—*I have observed oedema of the fingers in association with cervical disc protrusions and oedema of the foot with lumbar disc lesions. Have these observations been recorded, and what is the explanation? Is it possible for oedema of the contralateral foot to occur?*

A.—I am unaware of observations of oedema in cervical or lumbar disc lesions. I have not made this observation myself, though I have seen a very large number of patients with both conditions.

The only observation that I have made, and on only one occasion in a lumbar disc lesion, was a cyanotic, slightly swollen foot. This stemmed from the degree of paralysis below the knee which gave a problem similar to that of polio. In polio cyanosis and oedema occur from the lack of the "muscle pump," and that was the explanation in this patient. However, it would not be the explanation in most cases of lumbar disc lesion, and I would say never in the case of cervical disc lesions.

Headwear and Baldness

Q.—*Does tight, close-fitting headwear aggravate premature baldness in men or women?*

A.—The development of the common male-pattern baldness is dependent almost exclusively on hereditary factors and the degree of androgenic stimulation to which the hair follicles are subjected. Follicles are usually maximally stimulated in the adult male. The development of male-pattern alopecia in the female may be induced by normal female levels of androgen in those heavily predisposed genetically, but the incidence and severity are increased if androgen levels are raised.

For centuries tight close-fitting headwear has been blamed for aggravating male-pattern alopecia in both sexes, but there is no evidence whatever that it does so.

Notes and Comments

Gaucher's Disease and Pregnancy.—Dr. N. R. M. BUIST (Department of Pediatrics, University of Oregon Medical School, U.S.A.) writes: Your expert is in error in answering a question about the inheritance of Gaucher's disease ("Any Questions?" 8 July, p. 97). He states that a parent suffering from the recessive form of this disease has a 25% risk of producing an affected child. In fact the risk is much less. Since the incidence of autosomal recessive Gaucher's disease is not known, it is impossible to compute accurately the risks in this case. However, if one calculates the disease frequency of this form of Gaucher's disease to be 1/10,000, which is certainly an overestimate, then the heterozygote incidence is 1/50, and the chances of an affected homozygote producing an affected child would be 1/200. The figure of 25% chance of a child being affected is only applicable when both parents are known to be heterozygotes for a recessive condition.

OUR EXPERT replies: I was wrong not to point out that the incidence of 25% was to be expected only when both parents were heterozygotes for the recessive form of Gaucher's disease. As Dr. Buist points out, it is not possible to calculate the risks with any degree of accuracy in the case of one parent being a homozygote when the incidence of autosomal recessive Gaucher's disease is not known, but he is right to emphasize the decreased risk.

Tropical Ulcer.—Dr. J. N. MEIN (Milton, New Zealand) writes: Though I would agree that the regimen set out in the answer ("Any Questions?" 24 June, p. 818) is sound, it is probably impracticable and expensive in small, isolated hospitals, such as the one in Nigeria where I worked, and especially not appropriate for clinic use.

I found that a generous layer of B.I.P.P. (bismuth, iodoform, and paraffin paste) on gauze, covered with cotton-wool and a gauze bandage, could be applied even to a dirty ulcer and changed at weekly intervals, with no restrictions of activity apart from keeping the dressing as dry as possible. A large proportion of ulcers healed on this treatment, though larger ones certainly required a split skin graft. I found that I could get a good granulating area for grafting by using B.I.P.P. on an outpatient basis until the day before operation, then a few dressings of eusol or saline as the final preparation. I never used antibiotic cover postoperatively, and achieved a take-rate of about 80%. I avoided pinch grafts because of keloid formation at the donor site.

OUR EXPERT replies: I would agree with Dr. Mein's comments. He writes from personal experience in Nigeria. The treatment of tropical ulcers is bound to vary from area to area, depending essentially on funds available, the number of patients attending, as well as the number of medical attendants. Basic principles, however, remain esentially the same.

NEW APPLIANCES

Apparatus for Warming Blood for Transfusions

Dr. PATRICK J. BENNETT, senior registrar, the Middlesex Hospital, and London Chest Hospital, and Mr. F. ALLADINE, heart-lung machine technician, London Chest Hospital, write: The factors responsible for the harmful effects of rapidly transfused cold blood are now well recognized (Mollison, 1967). The blood is cold (4° C.) and acidotic ; it has an excess of disodium hydrogen citrate, which interferes with the ionization of serum calcium ; and it contains an excessively high serum potassium level.

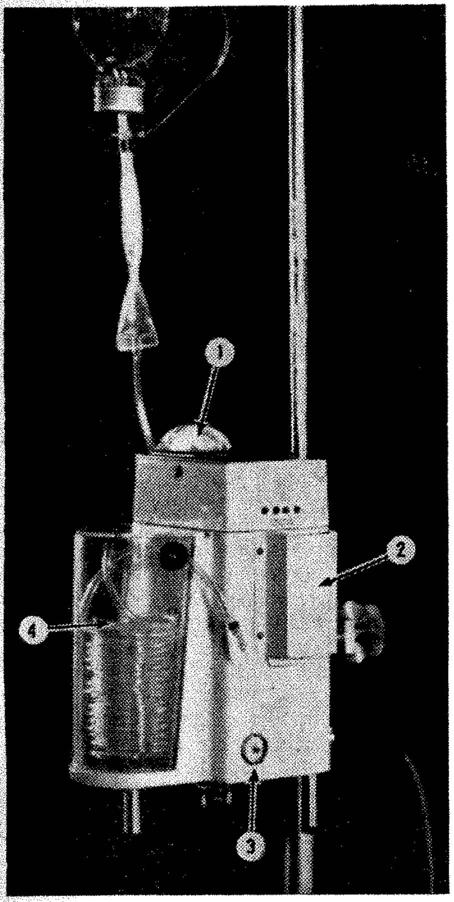


FIG. 1.—The apparatus.

There is evidence that the temperature of the transfused blood is an important factor in the morbidity associated with massive transfusion (Boyan and Howland, 1961). As the temperature of the heart approaches 30° C. there is an increasing risk of ventricular fibrillation, and it may be that the heart is more sensitive to the other factors—for example, raised potassium level of the transfused blood—as the temperature is lowered. Boyan (1964) reported a decrease in mortality from 58.3 to 6.8% using warmed blood in two matched series of patients receiving at least 3 l. of blood at a minimum rate of 50 ml./min.

Apparatus to warm blood has been described, but there has not been any general recognition of the part played by cold blood in operation mortality. Consequently, such apparatus has either been imported, with the result that its high cost has been a deterrent, or individual hospital departments have made their own.

It was decided, therefore, to construct a commercially available model in the hope of making transfusion of warm blood a reasonable prospect in other centres. It was designed with the object of economy in mind, and the simplest and cheapest method of warming blood is to add an extra length of tubing to the intravenous set, and place this in a water-bath maintained at 38° C.

Such an apparatus is of no value unless it is convenient to use. It was decided, therefore, that it should be compact enough to be attachable to a drip stand ; that blood should drip through readily without pumping ; and, ideally, that the extra tubing should be a " drop in " coil, ready at a moment's notice.

Description of Apparatus.—Simply, the apparatus is a 3-pint (1.7-l.) water-bath maintained at 38° C. by a 500-watt heater governed by a preset fine thermostat (Fig. 1, 1) which responds to a change of temperature in the water-bath of $\frac{1}{4}$° C. A second safety thermostat (Fig. 1, 2) automatically cuts off the electricity supply should the bath temperature rise above 40° C. for any reason. A small thermometer set in the base of the apparatus provides a final visual safeguard against overheating (Fig. 1, 3). The water is continuously circulated by a water-pump in the main housing to eliminate local temperature gradients. A 20-ft. (6.1-m.) coil of extension tubing fits into the small chamber at the front of the apparatus (Fig. 1, 4), made of perspex, to permit continuous observation. The unit weighs 11 lb. (5 kg.) and measures 12 by 7 by 7 in. (30 by 18 by 18 cm.).

Performance.—After switching on the apparatus takes about three minutes to achieve its operative temperature. Fig. 2 shows the temperature of blood leaving the blood-warmer at varying rates. It was felt that the performance with 1 pint (570 ml.) in five minutes was satisfactory, as this is generally acceptable as a level of rapid transfusion. It is possible to improve on these figures, but the additional length of tubing required impedes the free flow of the drip.

The apparatus has been in use for six months at both the Middlesex Hospital and the London Chest Hospital for warming blood in operations involving lung bypass, hypothermia, and arterial surgery. It has performed satisfactorily and has been found to be convenient enough to be used regularly by others, and no hazards have been uncovered.

Blood would take 30 minutes or so to traverse the heating coil at a transfusion rate of 1 pint (570 ml.) in four hours—a situation unlikely to occur when warming the blood as indicated, and, though there is evidence that blood may be incubated under sterile conditions for up to four hours without harmful effect on the red blood cells (Jandl and Tomlinson, 1958), it would seem both unwise and pointless to use any blood-warming apparatus except when transfusion is likely to be rapid.

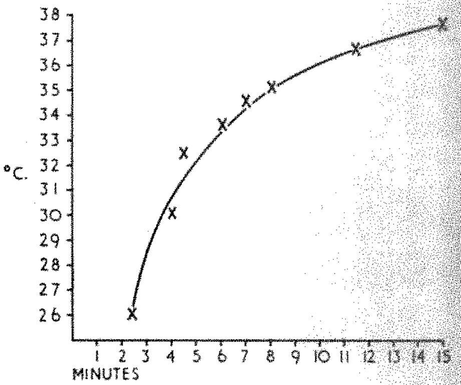


FIG. 2.—Temperature of 1 pint (570 ml.) of blood leaving the unit against time to pass through apparatus.

At present the extension tubing, sterilized by gamma-irradiation, is supplied as a loose coil in a plastic pack and has to be hand-wound to fit the apparatus. It is expected in the near future to have " drop in " coils prepared commercially in individual sterile packs ready for instant use in this unit.

We are indebted to Dr. H. Churchill Davidson, of St. Thomas's Hospital, for his advice on this project, and to the photographic department, the Middlesex Hospital, for the photograph.

The apparatus was manufactured by the South East Engineering Co., 93 Victoria Road, Romford, Essex, from whom these units and extension tubes can be obtained.

REFERENCES

[1] Boyan, C. P. (1964). *Curr. Res. Anesth.*, **43**, 304.

[2] —— and Howland, W. S. (1961). *Anesthesiology*, **22**, 559.

[3] Jandl, J. H., and Tomlinson, A. S. (1958). *J. Clin. Invest.*, **37**, 1202.

[4] Mollison, P. L. (1967). *Blood Transfusion in Clinical Medicine*, 4th ed. Oxford.

Book Reviews

Science and the Drinker/Driver

Alcohol and Traffic Safety. Proceedings of the Fourth International Conference on Alcohol and Traffic Safety. (Pp. 353+xiii. $10.00.) Bloomington, Indiana: Department of Police Administration, Indiana University. 1966.

The fourth international conference on alcohol and traffic safety was held in Indiana in December 1965, but the proceedings have only recently become available. They run to fifty papers contributed by specialists from many countries. Together they declare an academic insistence on comprehensiveness and on the value of knowledge for its own sake. Yet it can also be said that this material could conveniently be offered as a series of short books written for different specialists—sociologists, pharmacologists, clinical pathologists, psychiatrists, lawyers, and criminologists—such are the consequences of man's discovery of alcohol and what he regards as its desirable effects.

In the hands of such a team of specialists there is scarcely any limit to the permutations that can be devised with alcohol as one factor and human behaviour as the other; and the sponsors of this conference evidently agreed to the relevance of "Alcohol Effect on Latency of Caloric Nystagmus," "Biochemical Investigation of the Enzymatic Metabolism of Ethanol-Acetaldehyde in the Brain Cortical Substance," and "the Influence of Glucocorticoid on the Rate of Disappearance of Ethanol from the Blood of the Dog." These academic exercises at the periphery of the subject will doubtless attract the applause that is due to diligence and erudition; but the concern of the general public (activated by horse-sense rather than esoteric niceties) over the growing menace of road traffic, inevitably shifts attention to the man at the wheel.

Amidst a welter of scientific literature there is a danger that the stark realities of the situation may become obscure. The adverse effects of alcohol on behaviour and dexterity have been recognized for thousands of years. The danger of travelling at high speeds on congested roads is increasingly apparent, and it is perfectly plain that the hazards must be increased by the presence of intoxicated drivers. These generalizations have been confirmed so often by elegant and elaborate surveys that—in Dr. Ira Cisin's words: "We might almost say, 'Hold, enough. Do we really need further convincing on this point?'" Nevertheless, as Dr. Cisin points out, within this situation there are matters that call for closer definition and action. There is a whole range of degrees of "being under the influence of alcohol"; there are wide variations in the demands made upon the judgement of the motorist—drunk or sober; and there is the disconcerting observation "that people with a little alcohol in them are relatively lower risks than the people with no alcohol at all" (p. 51).

The last of these statements—far from justifying smugness among self-styled "moderate drinkers"—may in fact have little relevance to the problems inherent in drinking. The relatively poor record of the total abstainers may be due to the presence in this company of many good folk who suffer from mild obsessional disorders which tend to impair their skill and judgement when driving. In other words, the claim that a little of what you fancy does you good must be reviewed in the light of experiments where the individual acts as his own control (that is, with and then without alcohol) and not by comparison with people of a very different psychological make-up.

Dr. Cisin emphasizes the distinction to be made between social drinkers and problem drinkers—a matter to which Dr. Howard Pyle (President of the National Safety Council) also refers (p. 330) in his address at the Banquet Meeting. There appear to be three main types of drinker/drivers.

". . . the problem of the alcoholic," says Dr. Cisin, "is *not* that he drives after drinking excessively but that he does everything after drinking excessively, and our target with the chronic alcoholic is not to get him to stop driving after drinking but to get him to stop or control his drinking. Driving is only one of the things he does badly, and our objective is to treat his disease, alcoholism, on the safe presumption that, if we succeed, the driving will take care of itself."

The sociopathic driver who happens to drink; ". . . the man who characteristically goes through the school zones at fifty miles an hour . . . a destructive menace primarily because of his driving . . . His problem is not that he drives after drinking but the fact that he is permitted to drive at all.

". . . people who drink normally and who drive normally, but who on certain occasions find themselves in a position where the two acts are performed in temporal juxtaposition. . . . this group of normal persons is the group at which our propaganda must be aimed."

Even if we define the problem in this way, what are the chances of success in reducing the hazard created by the intoxicated driver? Dr. John Birrell, who is police surgeon at Melbourne, Australia, says: ". . . the sociologists have found that very few people are influenced toward change in behaviour by what they read in newspapers or see on television. People are influenced most by the standards of the groups to which they belong; within these groups are what the research people call 'opinion leaders,' whose influence on the attitudes and habits of their friends is quite decisive. . . . So probably we haven't got a public at all; we have a number of publics with quite different needs. We must do much more talking with community groups, no matter how small they are, because we then influence the influentials among them in their attitudes and often unconscious efforts on our behalf."

Incidentally, among a large number of excellent papers in the proceedings, Dr. Birrell's on public education and mass communication aspects is outstanding in revealing his insight into the specific problem and into human nature. He is surely right to urge the conference to "take up your pens and write for the layman and for the schools, for the schools particularly." Dr. Birrell's paper is itself worth ten dollars for its entertainment value. He writes with such gusto and humour that he is obviously the man to prepare a pamphlet on the subject of the drinker/driver which might be issued to every boy and girl when 15 years of age in the schools of the British Commonwealth.

STANLEY ALSTEAD.

Frontiers of Medicine

Lectures in Medicine. By C. W. H. Havard, M.A., D.M.(Oxon), M.R.C.P.(Lond.). (Pp. 381+xiii; illustrated. 63s. Paper 40s.) London: Staples. 1967.

I would like to have written this book. It is the kind of book for which any physician interested in explaining the frontiers of medicine would be proud to claim credit. It consists of a series of lectures to medical students in their final year on subjects which are of current interest to the practising physician but which are difficult to come by in the standard texts.

The topics discussed are inborn errors of metabolism (with a commendably broad classification), chromosomal abnormalities, evaluation of new drugs (containing some sensible words on clinical trials), corticosteroids, drug-induced disease, autoimmunity, cardiac arrest, respiratory failure, malabsorption, potassium depletion, and radioisotopes. A lecture on psychosomatic disorders seems at first sight out of place among so many recent advances in scientific knowledge, but it is as well that students are reminded that the majority of patients suffer from symptoms which cannot be adequately quantitated and yet require careful assessment if they are to be properly managed. The last three chapters are written by distinguished colleagues—viruses and disease (J. E. Stark), statistics (M. P. Curwen), and computers (L. C. Payne).

The exposition is clear and authoritative, at the same time avoiding dogmatism, and there are frequent summaries throughout the chapters. There is a selected bibliography for further reading, but this does not include the lecture on computers, an omission that needs remedying. The book is attractively produced and printed. Although primarily intended for medical students, I can think of others who would benefit from reading these lectures—for example, that relatively new educational phenomenon, the post-registration nurse. And it should not be despised by the postgraduate doctors who qualified when many of these subjects were being developed, for, as Payne says, " Human memory is like a vapour trail ; it attenuates with time."

A. Paton.

Uveal Tract Disease

System of Ophthalmology. Vol. 9. Diseases of the Uveal Tract. By Sir Stewart Duke-Elder, G.C.V.O., F.R.S., and Edward S. Perkins, Ph.D., M.D., F.R.C.S. (Pp. 978 +xvi ; illustrated. £11.) London : Henry Kimpton. 1966.

Volume 9, the sixth of the 15 volumes of this monumental work covering the whole field of ophthalmology, has now become available, and, like its predecessors and no doubt its successors, is a truly remarkable achievement. Professor E. S. Perkins has co-operated with Sir Stewart Duke-Elder in the compilation of the seven chapters covering diseases of the uveal tract, and to anyone unconnected with the specialty it may well seem incredible that nearly 1,000 pages are required for adequate coverage of the text and illustrations of the various diseases which can involve the middle layer of such a comparatively small, though very important, organ as the eye.

In the middle years of the twentieth century there has been much research and discussion on the problems of uveitis, which used to be responsible, either directly or indirectly by causing cataract or glaucoma, for perhaps most of the blindness during the years between childhood and old age. Though the causes of some varieties such as syphilis, leprosy, and tuberculosis are proved, the origin of others, including the common serous and comparatively mild ones, are still mysterious. In days gone by tuberculosis or a septic focus far from the eye were thought without much evidence to be the factors precipitating an inflammatory reaction in the uveal tract, but now other possibilities such as allergy and autoimmunity are more often invoked. Since the aetiology so often remains obscure, therapy must be to a great extent empirical. But though we still cannot claim to be able to treat the cause in every case research has now provided us with a weapon which at least subdues the inflammation and controls the exudation which is so damaging to a complex optical organ, much of which is composed of central nervous tissues in which damage is incapable of repair. The advent of corticosteroid preparations for focal or systemic application has provided a therapeutic weapon for which the older ophthalmologists must have longed and which has completely altered the outlook for intraocular inflammations. Though corticosteroids have their dangers and do not actually cure the disease, they do at least protect the delicate ocular tissues until the inflammatory stage is passed.

The authors have, so far as possible, confined their attention to diseases of the uveal tract, though not forgetting that these may have a profound effect on other ocular structures, including the retina. Various chapters deal in great detail with circulatory disturbances, inflammations, degenerations, cysts and tumours, and the uveal manifestations of systemic diseases. The text is admirably comprehensive and written in excellent English. The illustrations, though possibly less copious than in some other volumes, are adequate and of high quality.

A work of this size must necessarily be mainly a reference book, and as such it succeeds in its object. It is an essential component of any ophthalmic library and of outstanding value to any English-speaking ophthalmologist.

Harold Ridley.

Cardiac Pathology

Cardiac Pathology. By Robert Lannigan, M.D., M.C.Path. (Pp. 385+vii ; 226 illustrations. £5 16s.) London : Butterworth. 1966.

This excellent, comprehensive book bridges the gap that has existed between the usual single chapter devoted to cardiovascular pathology in the student textbooks and the extensive reference volumes which are available on the subject. It contains 14 chapters, of which 12 are by the author.

Throughout, one is aware that this text has been written by someone with knowledge and great personal experience. Emphasis has been laid intentionally on morphological aspects. Facts are stated briefly and concisely. The incidence of different lesions from the literature is reviewed and supplemented by the author's own figures. Theories on controversial subjects—for example, the " nature of the tissue changes in rheumatic heart disease " or the " nature of myxoma " —are presented with clarity, and the author gently guides the reader to the currently accepted view. One of the outstanding chapters is that on diseases of the coronary artery. It contains beautiful descriptions of early and late lesions of atherosclerosis, and the theories related to aetiology and pathogenesis have been skilfully condensed into a few pages. The handling of some of the rare diseases such as virus and rickettsial endocarditis, thrombotic thrombocytopenic purpura (Moschcowitz's syndrome), and indeed the whole chapter devoted to the heart in diffuse connective tissue diseases deserves special mention.

Naturally, a book of this size cannot deal with every subject in great detail, nor does the author claim to do so. The section on myocardial infarction is at first glance surprisingly brief, yet it manages to give the important facts, including some histochemical findings. The book does not deal only with morphological aspects, and there is a chapter by Dr. Paul Davidson on the physiological aspects of normal cardiac output and cardiac failure. The final chapter is on heart diseases in childhood, by Dr. A. H. Cameron. For a book of this size it is understandable that only the more common congenital abnormalities could be included, and the interested reader is referred to classical references on the various subjects.

The entire book is well endowed with references. Photographs are excellent and include many on electron-microscopy. It will be an excellent aid for the postgraduate student in pathology or medicine and also for the practising pathologist. The hope is expressed in the preface that the undergraduate will also find it useful, and I believe that he will.

E. G. J. Olsen.

Cytogenetics

Human Population Cytogenetics. By W. M. Court Brown. (Pp. 107+xii ; illustrated. 40s.) Amsterdam : North-Holland. 1967.

Dr. Court Brown and his colleagues of the M.R.C. Clinical Effects of Radiation Research Unit have done more than any other body of investigators to elucidate human population cytogenetics. Thus this book, based on a series of lectures given in the University of London in 1966, deserves the attention of everyone interested in the subject. A prerequisite is that the reader must start with a working knowledge. One must not believe the editor's preface that this particular volume conforms to type in the series, *Frontiers of Biology*, in providing something on a wide and non-specialized basis. The author is more correct in saying that human cytogenetics is essentially in a descriptive phase and he jumps in at the deep end to describe, without a glossary of the sophisticated jargon.

To your reviewer, who is no pundit in cytogenetics but a haematologist who has had to live with them for the last decade during the exponential growth phase of this particular aspect of the subject, there were no terminological problems. I had only admiration for the fascinating accounts of chromosome studies on the general population, the identity of the chromatin-positive male, the Y chromosome, and the structural heterozygosity of the autosomes. I was left wondering, however, from the short introduction on lymphocytes, whether the author was concerned more in painting a realistic picture than in striving for precision of brushwork. This may be a legacy from the original presentation as lectures.

John F. Loutit.

Gynaecology for Students

A Short Textbook of Gynaecology and Obstetrics. By G. D. Pinker, M.B., F.R.C.S.(Ed.), F.R.C.O.G., and D. W. T. Roberts, M.Chir., F.R.C.S., F.R.C.O.G. (Pp. 188+xii ; illustrated. 25s. Paper 16s.) London : English Universities Press. 1967.

One author is from St. Mary's Hospital and the other from St. George's. The students of both hospitals and elsewhere should be pleased with this short textbook, for it is well written and the few line drawings by Mr. Emanual Lee illustrate the text well.

The approach is from clinical practice, and therefore pathology, psychology, endocrinology, and detailed consideration of such subjects as chromosomal abnormalities are dealt with very briefly indeed. Within these obvious limitations imposed by the authors on themselves, and by the series of University Medical Texts of which this is one volume, the book can be recommended both as an introduction to obstetrics and gynaecology and as revision reading. It is to be hoped that no student will believe that there is enough here to see him through his final examinations without attendance diligently at clinical and pathological sessions. He will also need more than a nodding acquaintance with some larger textbook where the inevitable dogmatic statements required by the format of this book can be seen to need qualification and modification.

PHILIP RHODES.

Reviews on Neuroendocrinology

An Introduction to Clinical Neuroendocrinology. Edited by Eörs Bajusz. (Pp. 573+xv; illustrated. sFr./DM.115.) Basel and New York: S. Karger. 1967.

This book is a difficult one to review because it can scarcely be regarded as a coherent whole. The title is misleading in that it implies a carefully graded introduction to the principles of the subject, whereas the book consists in reality of a series of independent reviews and papers on a rather heterogeneous series of subjects. Too wide a field is included under the general heading. The term neuroendocrinology can be justified for experimental work done on the controlling functions of the hypothalamus and basal nuclei, but it can scarcely be justified for many clinical aspects reviewed here such as secondary amenorrhoea or cerebral vascular disease.

The book is in fact a series of 24 separate articles by a total of 34 authors. Works of multiple authorship always require strong editorial guidance if they are to achieve a homogeneous whole. Here there is evidence of weak editorial control and of inadequate subediting. The systems of references in the texts are not uniform, some being numbered, others not. A marked Continental influence persists in many of the sections, not only in the lines of thought but even in the style of English. The specific weight of urine is referred to, for example, and in one article only 38% of the references given are in English, and in another only 36%. Some reviews are thorough, such as the section on the histology of the hypothalamo-neurohypophyseal system, but others are too narrowly specialized like the section on the physiology and pathology of this system, which confines itself almost entirely to posterior pituitary hormones and to a thorough survey of the diagnosis and treatment of diabetes insipidus. A comprehensive review of what is known about anencephaly is followed by one on the electroencephalogram in thyroid deficiency.

Some contributions are clear and concise surveys such as those on endocrine function in anorexia nervosa, and on the effects of sex hormones on human sexual behaviour. Others are essentially accounts of personal researches such as the paper on the assay of urinary A.C.T.H., or that on the effects of emotional stimuli on catechol amine excretion in urine. These stimuli range from industrial and office stress to the viewing of horror and of pornographic films by both sexes, the latter films having been borrowed from the Swedish Public Prosecutor. I am among those who feel that original results should not be published in this way, but should be submitted to the orthodox scientific journals which employ a referee system.

There are many good articles in this book, and the final section is a review of progress in basic and clinical neuroendocrinology by the editor Bajusz himself. If this last section had been considerably expanded it could have made by itself a more logical and coherent book than the present very assorted series of articles included in the volume.

C. L. COPE.

Satisfaction in Work

A Fortunate Man. The Story of a Country Doctor. By John Berger. Photographs by Jean Mohr. (Pp. 158; illustrated. 30s.) London: Allen Lane, The Penguin Press. 1967.

This book is an interesting blend of speculative essay and subjective biography. Berger has chosen for his central character a country doctor with the fictitious name of John Sassall. The working life of Sassall is depicted clearly and skilfully while his private and family life remain to a large extent concealed. Most of the biographical data are presented pictorially and almost half the book consists of photographs of Sassall, his patients, and the area in which they live.

Sassall practises a high standard of medicine. He is responsible for the domiciliary care of all his patients and for the treatment of many of those who require admission to hospital. He attends most of the births and deaths that occur in his practice and is fully aware of the various relationships, both family and social, that exist among his patients. We are shown photographs of him aspirating a chest, manipulating a spine, and taking an E.C.G. We are informed that he reduces simple fractures and is prepared to devote an hour after supper to patients whom he thinks might benefit from psychotherapy. These are procedures normally undertaken by many country doctors, and it is not because he applies these basic skills that Berger considers him to be a particularly good doctor. His primary quality is described as an ability to meet the deep but unformulated expectation of the sick for a sense of fraternity. He does this by encouraging his patients to recognize aspects of themselves in their doctor.

The impression I receive is that Sassall is not a particularly happy or contented man. He is often restless and periodically becomes deeply depressed. He is epitomized by Berger as fortunate because he finds a basic purpose and meaning to life in the work he does. He has become an integrated member of the community in which he lives and has established a very definite, individual, and intimate relationship with his patients. It is concerning the nature and significance of this relationship that Berger likes to speculate and generalize. I find some of the basic premises offered by Berger unacceptable—for example, that a strong element of superstition is always evident in "practical" common sense—but many of his ideas are interesting and worth reading.

I enjoy most biographies, and this one conforms to the general rule. It is unusual in its choice of subject and form of presentation. The book has been issued as a hard-cover edition by the Penguin Press. Its format is pleasing and it can be read with ease in one evening.

W. D. REES.

Books Received

Review is not precluded by notice here of books recently received.

Atlas of Roentgenographic Measurement. 2nd edition. By Lee B. Lusted, M.D., and Theodore E. Keats, M.D. (Pp. 249; illustrated. 83s.) London: Lloyd-Luke. 1967.

Human Atheroma. With Particular Reference to Endocrine Aspects of Aetiology. By W. L. Ashton, M.B., M.R.C.P. (Pp. 82. 21s.) London: William Heinemann. 1967.

Mental Subnormality. Subnormality and Severe Subnormality. 3rd edition. By W. Alan Heaton-Ward, M.B., Ch.B., D.P.M. (Pp. 100. 8s. 6d.) Bristol: John Wright. 1967.

Second Thoughts. Selected Papers on Psychoanalysis. By W. R. Bion, D.S.O., B.A., M.R.C.S., L.R.C.P. (Pp. 173. 25s.) London: William Heinemann. 1967.

Accidents in the Home. By David Cargill. (Pp. 123. 18s. Paper 7s. 6d.) London: Hamish Hamilton. 1967.

Proceedings of the Seventh Canadian Cancer Research Conference, Honey Harbour, Ontario. (Pp. 432+vii; illustrated. £6.) Oxford: Pergamon. 1967.

Management of Emotional Disorders in Paediatric Practice. With a Focus on Techniques of Interviewing. By Jerome L. Schulman, M.D. (Pp. 307. 72s.) London: Lloyd-Luke. 1967.

How to Avoid a Coronary Thrombosis. By David Cargill. (Pp. 114; illustrated. 18s. Paper 7s. 6d.) London: Hamish Hamilton. 1967.

Food Disorders. Medical and Surgical Management. By Nicholas J. Giannestras, M.D. (Pp. 521; illustrated. £8 5s.) London: Henry Kimpton. 1967.

Surgery of Rheumatoid Arthritis. By Leonard Marmor, M.D., F.A.C.S. (Pp. 261; illustrated. £5 12s. 6d.) London: Henry Kimpton. 1967.

Respiratory Physiology. By N. Balfour Slonim, M.D., Ph.D., and John L. Chapin, Ph.D. (Pp. 199+xi; illustrated. 66s.) London: Henry Kimpton. 1967.

Gynecologic Pathology. By Frederick T. Kraus, M.D. (Pp. 504+ix; illustrated. £6 18s. 6d.) London: Henry Kimpton. 1967.

A Synopsis of Otolaryngology. 2nd edition. By John F. Simpson, F.R.C.S., Ian G. Robin, F.R.C.S., John C. Ballantyne, F.R.C.S., and John Groves, F.R.C.S. (Pp. 529+xv; illustrated. 52s. 6d.) Bristol: John Wright. 1967.

The Use of Lateral Thinking. By Edward de Bono. (Pp. 156; illustrated. 18s.) London: Jonathan Cape. 1967.

Practical Anaesthesia for Lung Surgery. By Ruth Mansfield and Richard Jenkins. (Pp. 193; illustrated. 50s.) London: Baillière, Tindall & Cassell. 1967.

Growth and Development of Children. 5th edition. By Ernest H. Watson, M.D., and George H. Lowrey, M.D. (Pp. 463; illustrated. 73s.) London: Lloyd-Luke. 1967.

Drug Responses in Man. Ciba Foundation Volume. Edited by Gordon Wolstenholme and Ruth Porter. (Pp. 257. 65s.) London: J. & A. Churchill. 1967.

Middle Articles

Orthopaedic Care of Children with Myelomeningocele: a Modern Programme of Rehabilitation

E. H. STRACH,* M.CH.ORTH., F.R.C.S.

Brit. med. J., 1967, 3, 791–794

> "A niche of usefulness and self-respect exists for every man, however handicapped, but that niche must be found for him."
> —JOHN GALSWORTHY.

An ever-increasing number of children suffering from congenital paraplegia due to myelomeningocele are being referred to the orthopaedic surgeon for treatment of skeletal deformities and for rehabilitation. The management of these children is often so complex that it presents a veritable challenge to the orthopaedic surgeon. The aim of this paper is to show some of the problems he has to deal with and to suggest some lines of management.

This study is based on personal experience with 173 patients (98 male, 75 female) who were referred for orthopaedic treatment during the past 10 years. They represent, therefore, a selected group of cases, but they are a typical cross-section of cases seen in the orthopaedic department.

I must emphasize that the intensive programme of rehabilitation described here is not accepted by all workers in this field.

The ages of the patients at the time of review or at the time of death were: under 5 years, 104+10 deaths; 5–10 years, 45+1 death; 10–17 years, 12+1 death. The primary myelomeningocele operation was performed in the first 24 hours in 81; at 2 to 7 days in 44; at 8 days to 6 months in 24; and later in 11. The timing of the operation in two patients was unknown and in 11 cases operation was not performed.

Hydrocephalus was present in 130 cases (75%). Ventriculo-atrial shunt operation was performed in the first month of life in 54 children and at a later date in 65 children. Spontaneous arrest occurred in 11 cases.

Paralysis of the legs was severe in 89 children (above the twelfth dorsal segment), moderate in 43 (above the fifth lumbar segment), slight in 15 (at or below first sacral segment), and spastic in 8. Paralysis was not present in 18 children.

Urinary diversion was performed in 23 cases.

Size of the Problem.—There is no increase in the number of children born with this malformation. With modern initial treatment of the myelomeningocele and the hydrocephalus many more children survive than formerly. The incidence of myelomeningocele in the United Kingdom is 2.5 to 3 per 1,000 live births. It has been estimated that in England and Wales 2,500 children are born every year with this malformation. Fifty per cent. will reach the age of 5 and a quarter of these will have no handicap and three-quarters will have a physical or mental defect. Eighty-four per cent. of all survivors are mentally normal.

Early Management

This is usually carried out by the paediatric surgeon in a neonatal surgical unit. Ideally, the myelomeningocele should be closed within 24 hours of birth to prevent infection and to preserve neural tissue. The frequent occurrence of hydrocephalus can be controlled by ventriculo-atrial drainage by means of a Holter valve. There are complications, but it is important to realize that the control of hydrocephalus is successful and without complications in two-thirds of the cases.

Orthopaedic Treatment

The aim is towards achieving independence of the congenitally paralysed child, notably to enable it to stand and to walk. There are cases where this aim is unobtainable; where there is severe mental deficiency, rehabilitation will fail. It is interesting to note than only 8% of all reviewed cases showed a severe degree of mental deficiency. Another 8% showed a milder degree, and in some of these rehabilitation was successful and even improved the child's mental capacity. It seems that physical improvement gives rise to an increased mental performance. Other factors militating against a successful rehabilitation are lack of determination of parents, a large head, and obesity.

Early Orthopaedic Management

In the first few weeks of life the orthopaedic management will take second place to the treatment of the spinal defect and hydrocephalus. However, an assessment of the neurological lesion and deformities should be done on the day of birth and repeated during the first few weeks of life. Muscle charting of the neonate is not an easy matter and often only a rough estimate of the activity of muscle groups is possible. Electromyography has been used but so far has proved of only academic interest. With experience, muscle testing becomes easier. Sharrard (1964) has rightly pointed out that the normal neonate moves his limbs freely while awake, and failure to move the legs spontaneously indicates a severe degree of paralysis. It is important to differentiate between spontaneous and reflex movements. The latter occurs in the isolated cord syndrome below the level of the lesion and is quite a common occurrence.

The neurological lesion is often segmental, and paralytic deformities occur according to the level of the lesion. For example, if innervation is intact down to the fourth lumbar segment and absent below it, the hips will be flexed and adducted, the knees will be extended, and the feet dorsiflexed.

Besides paralytic deformities there may be concomitant truly congenital deformities such as hemivertebrae, rib abnormalities, severe club-feet, and congenital dislocation of the hip. In the earlier stages these deformities can be controlled by conservative means, such as repeated moulding, retentive strapping, and plaster slabs or splints. There is, of course, a danger of sores developing in these insensitive legs, but a well-padded plaster or splint can be applied with impunity.

---

* Consultant Orthopaedic Surgeon, St. Helens and Whiston Hospitals (Liverpool Regional Hospital Board).

Later Treatment

When the child reaches the age of 14 to 18 months the orthopaedic surgeon's efforts will be directed towards ambulation. It is important that ambulation should be started at an early age, for it is physiological for the walking and standing reflex patterns to develop at that time. There will be a limited reflex pattern if lower-limb innervation is deficient or absent, but at least compensatory reflex action will be allowed to develop in the upper limbs and trunk. Theoretically, all paraplegics should be able to walk in one way or another, provided their legs are adequately supported and they can use their upper limbs. This applies to congenital paraplegia as much as to adult traumatic paraplegia. In the former there is no previous experience in walking; on the other hand, trophic sores are not as prone to develop as in adults. Early ambulation reduces the subsequent incidence of coxa valga and of trophic ulcers.

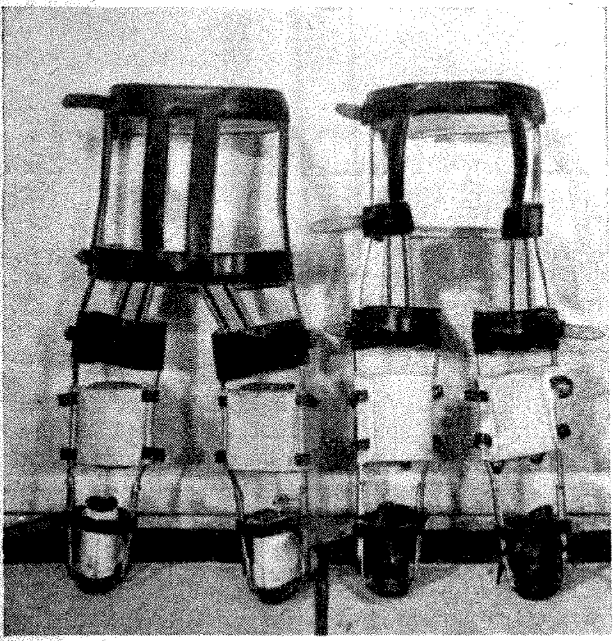


FIG. 1.—Two walking-appliances. The one on the right has a broad elastic sheet at the back to avoid pressure on any kyphosis.

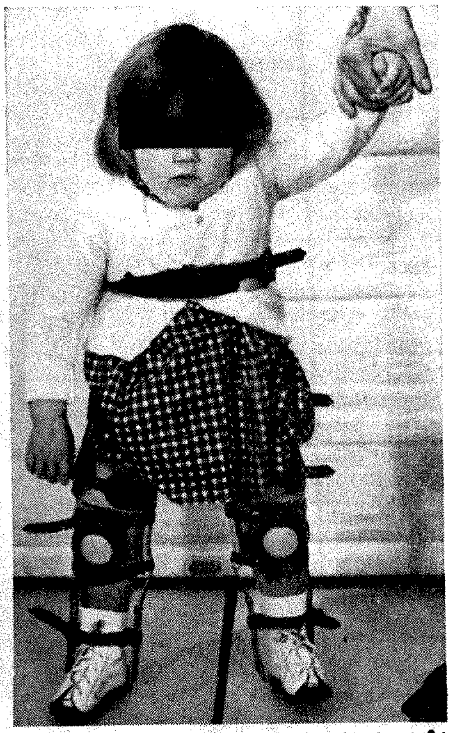


FIG. 2.—Complete paraplegia at the level of the eleventh dorsal segment in a child aged 3. Started to walk with the appliance at age of 15 months. Normally the trunk part of the appliance is hidden by her dress.

If there is complete and flaccid leg paralysis this task is simplified. There are no deformities, and all that is needed is to support the legs by an appliance which consists of two callipers joined to a body brace (Figs. 1 and 2). The children take to it readily and often protest when it is taken off. At first they are trained to stand in it for short periods. Additional support is given by holding their hands and allowing the children to grip so that they learn to use their hands purposefully for balancing and progression. They soon acquire a rocking type of gait. The appliance is worn for increasing periods during the day so that the skin can get used to the pressure. Sores are rare. The feet and any kyphosis are the areas at risk. It is useful to abduct the appliance at the level of the hips for several reasons. It gives a wider base and an increased side-to-side stability. It increases the excursion of the rocking movements during progression. If the hips tend to dislocate, the abducted position increases their stability. At times it was found useful to attach skis to the appliance, as this increases the front-to-back stability and gives the child confidence in the initial stages of walking.

As the child grows older a new appliance will have to be made, and this will contain hinges at the level of the hips to allow sitting. In some cases less rigid supports can be used as a lively splint in the form of a coil-spring appliance (Fig. 3). They allow the legs to swing at the hips. In all appliances a broad elastic strap passes over the buttocks to confer some extension to the hips. These straps may be extended to the heel in calf paralysis.

When the child is 5 knee hinges should be fitted to the appliance to allow more natural sitting, and, as the upper limbs become more efficient in balancing, the trunk part of the appliance can be replaced by a simple pelvic band.

Conventional callipers, the mainstay of the support in cases of poliomyelitis, are useless in spina bifida. They are used mainly for quadriceps paralysis, but in spina bifida isolated quadriceps paralysis is unknown. In a lesion at or above the second lumbar segment there will be quadriceps paralysis, but at the same time the glutei (which are innervated by the lower lumbar and sacral segments) will be paralysed, so that the calliper without a body brace will be insufficient. In a lesion at the fourth lumbar level the quadriceps will be working, so a calliper alone is unnecessary. The glutei will still be paralysed, and only a full appliance can replace the action of body support in these cases. Sharrard's posterior iliopsoas transfer is of immense value. It restores muscle balance around the hip and prevents dislocation, and if successful in restoring strong hip extension the child can keep the trunk upright and manage to walk without the full appliance.

Hip in Spina Bifida

(1) *Flexion deformity* is the most important hip deformity because it may severely hinder rehabilitation, thus making standing or walking impossible. It is caused by unequal muscle pull or by faulty posture. Most of these children attain a characteristic sitting posture with hips acutely flexed and externally rotated, with knees flexed, supporting themselves by the hands in front (Fig. 4). If they are allowed to sit like this while awake and to sleep on their sides with the hips bent, the flexion deformity will become fixed. It may yield to conserva-

tive treatment, but if present for a long time operative flexor release may be the only hope of enabling the child to stand upright. In this series flexion deformity was present in 25 hips of 16 children. Six hips required the flexor release operation.

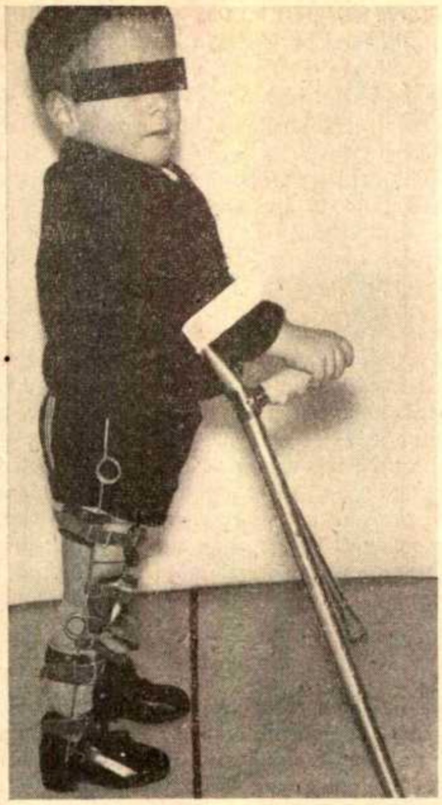


FIG. 3.—Child aged 4, with paralysis at third lumbar segment, using coil-spring appliance.

(2) *External rotation deformity* of the hips rarely interferes with ambulation and can be controlled by the appliance. Occasionally, one may have to transfer the sartorius to the outer side of the knee.

(3) *Abduction deformity* results from faulty sitting posture or from prolonged treatment of the dislocated hip, or it may be part and parcel of tightness of the tensor fasciae femoris. If postural it may respond to traction, but the tensor fasciae femoris was a potent cause of this deformity in 13 hips, and in five cases operative release was required. If associated with coxa valga it can be corrected by varus osteotomy.

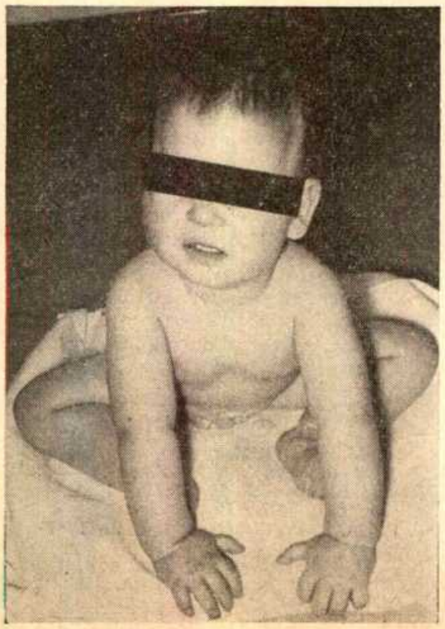


FIG. 4.—Typical sitting posture in severe congenital paraplegia (level ninth dorsal segment).

(4) *Dislocation of the hip* is common—103 dislocations or subluxations were found in 80 children (46% of all children were affected). There are four factors which can cause the dislocation:

(*a*) Laxity of the capsule is often present in any neonate but is much more pronounced if the hip muscles are paralysed. This factor was found in 24 cases.

(*b*) Unequal muscle pull is the most important single factor causing dislocation of the hip. In a lesion of the third or fourth lumbar segment the flexors and adductors are working while abductors and extensors are paralysed. The resulting adduction deformity leads to dislocation of the hip. In such cases the posterior iliopsoas transfer operation is the logical treatment of this muscle imbalance. It was present in 51 cases and in three cases of predominant spasticity.

(*c*) Coxa valga often occurs if the hip muscles are paralysed. It seems to be caused by the absence of the moulding force of the muscles and lack of weight-bearing. It predisposes to subluxation and later to a dislocation, which tends to occur in the slightly older child. It was present in 19 hips and in two cases with predominant spasticity.

(*d*) Severe dysplasia of the hip (Putti's embryonal dysplasia) was present in five cases. It was characterized by high dislocation present at birth and stiff hips, the picture resembling arthrogryposis. It was resistant to all forms of conservative treatment. In two cases open reduction of the hip was successful.

Treatment of Dislocated Hips

In the first few months a simple abduction splint, a modified Forrester-Brown splint, may be all that is required (Fig. 5). It was successful in 33 hips, though four of these were too recent to be sure about lasting success. In 28 hips dislocation recurred after such conservative treatment. In 29 cases adductor tenotomy was required. There were 16 psoas transfer operations ; nine of these also had a varus osteotomy (five of them at the time of the psoas transfer). All but one hip remained reduced, and in five cases of psoas transfer the full walking appliance was replaced by below-knee irons. Eighteen varus and rotation osteotomies were performed. Three open reductions were necessary.

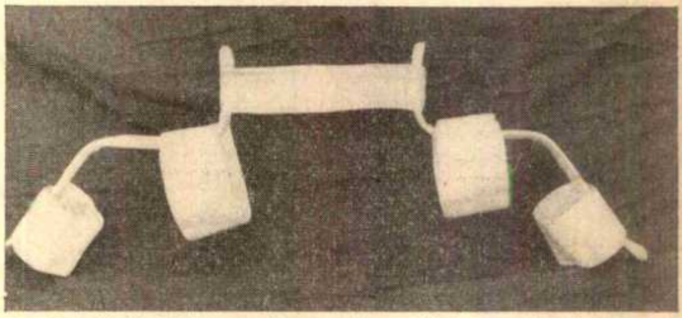


FIG. 5.—Modified Forrester-Brown splint. Vinyl-covered malleable steel bands. The connecting steel band lies in front of the abdomen, so that no pressure is exerted on the scar of the back. Velcro fasteners.

Foot Deformities in Spina Bifida

A deformity of one or both feet was present in 117 children. In addition, 25 had flail feet. The equinus element was present in 58 cases (91 feet), the calcaneus element in 54 cases (77 feet), the valgus element in 40 cases (58 feet), and the varus element in 35 cases (50 feet).

Most of the foot deformities were due to muscle imbalance, but the equinus deformity could not be explained by a segmental lesion. The equinus feet can result from spasticity or fibrosis of the calf, but in some cases it was due to an associated congenital club-foot deformity.

The conservative treatment should be started early, due care being taken to protect the skin. In cases of muscle imbalance correction of the foot deformities is easy, but relapse occurs readily; therefore a tendon transfer operation is required to restore muscle balance. This was done in 16 feet. Tendon transplants through the interosseous membrane were found particularly successful. There were four tibialis posterior transfers to the front and outer side of the foot for the varus deformity, and also six tibialis anterior transfers to the tendo achillis insertion for the common calcaneus deformity. Elongation of the tendo achillis was performed in 30 feet. In the severe congenital club-foot deformity a radical approach was adopted because weight-bearing on the deformed foot tended to cause pressure sores. A soft-tissue release was done on six feet, and wedge tarsectomy was performed in one " intrinsically vicious club-foot " at the age of 3.

If a child with only a mild paralysis develops an increasing varus deformity of the foot, or if the paralysis increases, one must suspect diastematomyelia. This happened in three children in this series. It was confirmed by myelograms, and the bony spur was removed, with arrest of the progressive paralysis.

Knee in Spina Bifida

The flexion deformity is important because it may hinder rehabilitation. It is not caused by muscle imbalance but by a faulty posture, spasticity, or fibrosis of the hamstrings. Conservative measures usually suffice, and up to 30° of flexion deformity can be compatible with ambulation if an appliance is to be worn. In other cases hamstring lengthening and preferably transfer to the patella was found satisfactory.

Genu recurvatum often occurs in lesions at the level of the fourth lumbar segment, when there is hamstring paralysis and a strong quadriceps. It can be prevented by splintage and does not interfere with walking. Elongation of the quadriceps was not found necessary.

Spinal Deformities

The scar overlying the myelomeningocele is usually quite healthy. There are often associated naevi or lipomata. In most cases the bony gap can be felt and frequently there is local kyphosis. This deformity makes the overlying skin or scar vulnerable to pressure and to avoid this the walking-appliance has to be fitted accordingly. Severe spinal deformities were present in 41 cases: 20 scoliosis, 11 kyphoscoliosis, and 10 kyphosis. Only conservative treatment was required, such as special braces and straps fitted to the walking-appliance. So far no spinal fusion or spinal osteotomies have been performed.

The lumbar lordosis was often combined with a flexion deformity of the hips and was relieved by the flexor-release operation of the hips. Any residual scar or swelling at the site of the myelomeningocele was protected by the lordosis.

Fractures in Spina Bifida

Fractures often occur in cases of myelomeningocele: they are often undetected, and they heal spontaneously with excess callus formation. They may be an incidental finding when an x-ray examination is carried out for some other reason. Prolonged plaster immobilization of paralysed legs causes profound demineralization of the skeleton, and this is often followed by fractures. Soon after removal of the plaster cast the affected limb swells, and this is usually the only clinical sign of a fracture. Both femora and tibiae can thus break after removal of a plaster spica, in spite of careful handling of the limbs. Such complications are rare after the use of splints; the little movements these splints permit seem to prevent the severe osteoporosis. Splints are therefore to be preferred to plaster, which should be kept on for the minimum possible time.

Epiphysial separations are less common, but have presented diagnostic difficulties. They may be mistaken for osteomyelitis or even bone sarcoma. The trauma is mild, an ill-fitting calliper may be the cause, bruising is absent, and there is no pain. The radiological signs may be unusual—widening of the epiphysial line, sclerosis, and debris in the soft tissues.

Treatment of fractures presented no problem; they healed readily, requiring protection by splints for only short periods. In this series 20 children had 36 fractures. One epiphysial separation healed slowly and with deformity.

Sores in Spina Bifida

Sores used to be a dreaded and almost inevitable complication in these cases. If insensitive skin is exposed to prolonged pressure, both from within (bony prominence) and from without (chair, bed, calliper, shoe), ischaemic necrosis will result, giving rise to the sore. Of all the factors operative in its formation, the time factor can be most readily altered. With active rehabilitation and early ambulation the endangered skin is exposed to pressure for short intervals. Sores are therefore not as common or as severe as in the bedridden or chair-fast child. In this series they were found at one time or another in 30 children.

Conclusion

An attempt has been made to elaborate the problems of the orthopaedic care and rehabilitation of this increasing group of congenitally paraplegic children. The question of schooling and training for employment is becoming acute. In the past the few educable survivors were absorbed into special schools, some entered ordinary schools, and many had no systematic education. At present there is a need for the speedy establishment of special schools for these children. The future may bring further advances in many fields, such as power-driven callipers, improved design of wheel-chairs, and electrical stimulation of the bladder. With all modern methods of treatment, of rehabilitation, and of education, it is hoped that many children will eventually be trained to be of some use in their homes and for some form of suitable employment. This may well bring self-respect and happiness to them and their families.

Summary

The orthopaedic problems of 173 cases of myelomeningocele are analysed. A plea is made for early ambulation with the help of a walking-appliance which is often successful even in the severest forms of paralysis. Such active treatment helps the physical and mental development of these children and often prevents complications such as fractures and sores.

My thanks are due to Mr. J. Atherton, of M. Masters & Sons Ltd., and Mr. S. Edney, of the Hamlin Surgical Appliances Co., for constructing the appliances and for many helpful suggestions; also to Mr. M. Bayliss for the photographic work.

BIBLIOGRAPHY

Eckstein, H. B., and Macnab, G. H. (1966). *Lancet*, **1**, 842.
Golding, C. (1960). *J. Bone Jt. Surg.*, **42B**, 387.
James, C. C. M., and Lassman, L. P. (1962). Ibid., **44B**, 828.
Jones, G. B. (1954). Ibid., **36B**, 375.
Mawdsley, T., Rickham, P. P., and Roberts, J. R. (1967). *Brit. med. J.*, **1**, 663.
Sharrard, W. J. W. (1964). *J. Bone Jt. Surg.*, **46B**, 426.
—— Zachary, R. B., Lorber, J., and Bruce, A. M. (1963). *Arch. Dis. Childh.*, **38**, 18.
Smithells, R. W. (1965). In *Proceedings of a Symposium on Spina Bifida*, p. 2a. London.
Soutter, Felicity E. (1962). *J. Bone Jt. Surg.*, **44B**, 106.

Twenty-first World Medical Assembly

STANLEY S. B. GILDER, T.D., B.SC., M.B., B.S.

Brit. med. J., 1967, 3, 795–796

It may seem strange that the most significant item of business at a World Medical Assembly should be the definition of death, but this was the case in Madrid last week. The second item of significance lay at the other end of the spectrum of human life, with part of the scientific sessions devoted to a consideration of the population problems of the world from medical, demographic, ethical, and legal points of view.

Madrid exercises a civilizing influence on its guests, and perhaps this, as well as the steadying influence of the Secretary-General of the World Medical Association, Dr. ALBERTO Z. ROMUALDEZ, was responsible for the civilized manner in which the business of the Assembly was conducted during the week of 10–17 September. An international group of doctors from 32 countries, some with firm views on such matters as ethics or medical economics, is usually good for some display of temper, but in the whole week the only flutter in the Spanish dovecotes was during the scientific sessions, when the exhausted interpreters claimed a break after over four hours on population problems, at a time when about 80 Spanish doctors were clamouring to join in a heated debate which, all euphemisms aside, was concerned with the legitimacy or otherwise of the famous contraceptive pill.

British doctors will be glad to know that when the results of elections for vacant seats on the council of the W.M.A. were declared Dr. DEREK STEVENSON, Secretary of the B.M.A., topped the poll with 57, as against 54 votes for an Uruguayan and 50 for the editor of the *Medical Journal of Australia*, Dr. RONALD WINTON. Also elected was the former French member of council, Dr. J. JONCHÈRES, who has had a busy year in his practice in the cognac country preparing a document designed to show how to define death. Let us hasten to add that this does not mean that doctors are no longer sure when their patients are dead. The trouble arises, as everyone in the profession knows but the laity may not appreciate, because we can now maintain circulation and respiration artificially and there comes a time when the doctor needs to know two things—can he switch the machines off because the patient is in irreversible coma, and can he let his surgical colleagues remove organs for grafting? This has already been well discussed in various meetings, notably the Ciba Foundation symposium in *Ethics in Medical Progress*, at a French meeting on medical ethics in Paris in 1966, by a working group nominated by the Royal Medical Board in Sweden and headed by Professor GUNNAR BIÖRCK, by participants at the International Congress of Medical Law in Ghent last August, and no doubt on a thousand and one other less famous occasions. Obviously the crux of the matter is to prove "neurological death," and about this there is still much argument. For how long must the electroencephalogram be silent before one can assume that brain function has gone for ever? The figures given vary between five minutes and 48 hours, so there is little wonder that the W.M.A. was unable to solve the problem at once. They are keeping the subject under study and will give some guidance as soon as they can.

Medical Education

The medical education committee had started their planning for another world conference on medical education, for the W.M.A. believes that this subject is the concern of all practising doctors and not merely medical educators. After the last conference in New Delhi last November there was a movement by some educators to take the matter out of W.M.A. hands, but W.M.A. feels, perhaps with some justification, that a teacher is not going to admit that his methods are poor unless those he taught tell him so. The next conference will take place somewhere in Europe in 1972 and its theme will be "Medical Education: the Problem of Collective Responsibility." Mr. J. R. NICHOLSON-LAILEY, former Chairman of B.M.A. Council, has been active in promoting this. However, when his committee suggested that at this conference the views of medical students and of patients should be heard there was a horrified reaction from Continental colleagues who had never heard of Mrs. Helen Hodgson and her Patients' Association and felt that patients should be seen but not heard. Nevertheless, they agreed that the conference should give some thought to the interests of patients in their deliberations.

FIG. 1.—The new President of the World Medical Association, Dr. Alfonso de la Fuente (Spain), taking the presidential oath.

There was a time when discussion of medical economics and its allied problems (still quaintly termed "socio-medical affairs" in W.M.A.) took up a large part of the time allotted to business. Now for some unknown reason the situation has changed. This Assembly devoted very little time to this matter, the most interesting part of the debate concerning the attitude of the medical profession to unacceptable social legislation. The industrious Dr. R. SCHLOEGELL (Germany), who is the expert in this field, presented a paper on this, based on answers to questionaries from 26 national associations. Nine happy associations (including Sweden, Denmark, and Ireland) foresaw no trouble with their Governments over unacceptable legislation. The rest had adopted a variety of methods of protesting, but were unanimous in condemning the strike method used by other labour forces, though they found it legitimate to refuse to do their work under unacceptable conditions. In disputes between doctors and the Governments, the answers to the questionary indicated a certain measure of public sympathy for the doctors, provided of course that the public were not involved in any protest action the doctors took and that they believed the doctors were fighting for principles, not cash. Replies suggested that an important aspect of the problem was comprehensive information of the public and the doctors themselves about the issues at stake.

A matter which will come up for study in this committee next year is medical malpractice. Actions for negligence in the U.S.A. have multiplied beyond all reason, and this plague shows signs of spreading elsewhere. It deserves study on a world scale.

At the ceremonial session Dr. JESUS TAMESIS, of the Philippines, handed over the presidency of the Assembly to Dr. ALFONSO DE LA FUENTE, of Madrid, a thoracic surgeon, who will hold office until August 1968, when the next Assembly meets in Sydney and the office passes to an old friend and former Chairman of Council of W.M.A., Sir LEONARD MALLEN, of Adelaide.

Scientific Sessions

The general theme chosen by our Spanish colleagues for the Assembly was "Humanismo," a word not exactly equivalent to humanism, which has now come to mean a secular movement in the Anglo-Saxon world. Within this framework there were three meetings, if one includes the medical writers' conference—which really amounted to a discussion of pathology in art as exemplified in the works of Velazquez, El Greco, and Goya, all intensely concerned with the human condition of their time. The scientific sessions proper dealt with the population explosion, and with medicine and society.

Family Planning

As could have been predicted, discussion of the population explosion and family planning, which went on for hours beyond the allotted time, generated more heat than light, though two contributions were outstanding for their objectivity and quality. The first was by Professor J. **BOTELLA**, professor of gynaecology in Madrid, who discussed the action of the oral contraceptives with particular reference to his own work on their effects on ovaries, endometrium, tubes, cervical mucus, and cervical cytology. He explained that, whereas family planning was not allowed in Spain and the Catholic doctor could not prescribe the pills for this purpose, they found legitimate use as therapeutic agents, and all his studies on patients had been in such cases. (My own information is that sales in Spain, presumably for these purposes, have risen rapidly.) Professor Botella also pointed out that the mechanism of action was of great interest to a Catholic doctor. He said: "Putting aside the question of what Rome will decide, contraception through anovulation is not the same as contraception through such a mechanism as that of progestogens alone, which sterilize by (1) killing the morula by impeding its transport through the tube; (2) stopping the sperm from passing through the cervix." Thus it might be licit to use sequential or combined therapy but never progestogens alone, since these were really very early abortifacients. However, until the exact mode of action of oral contraceptives was known—and it was likely a multiple one, with variations according to the preparation used—no further opinions could be expressed.

Demographic Problems

This honest paper was followed by an equally honest summary of the demographic problem by Professor **DEL CAMPO**, who has the chair of sociology in Madrid. He pulled no punches in stating the case for urgent action to avoid impending widespread famine. For the first time, he said, *Homo sapiens* has to assume responsibility for the environment in which he lives. The problem must be faced; the only question is how to solve it, for birth rates depend on a complex of biological and social factors. A husband and wife may think that they determine how many children they will have, but in fact biology and society decide this for them.

When Professor Del Campo left the platform the theme took off into areas where a humble doctor is lost. Two theologians, recognized international authorities on the subject, Fathers **SIGMOND** and **ZALBA**, performed a series of intellectual acrobatics, but they did make some very valid points. They were anxious, for example, that family planning should never be used for political ends, to keep the powerful nations in power, or to raise living standards without reference to individual happiness. Father Zalba, having laid down a series of norms for use of oral contraceptives, as, for instance, to correct menstrual irregularities or to prevent ovulation in a woman whose health demanded postponement of pregnancy but whose husband would not co-operate, finally expressed the hope that "medical science would find a solution to the population problem more humane than the antiovulatory pill."

FIG. 2.—A general view of the Assembly at the opening session.

The Assembly a day previously had approved a resolution endorsing family planning in principle, though of course it could give no guidance on details.

The last major contribution to the debate on family planning in the scientific session came from a Spanish lawyer, and was chiefly notable for an unfortunate excursion into the fields of statistics and medical science, in which a certain amount of mythology replaced scientific fact. The following quotation is a good example: "Everyone knows that an organ which does not carry out its function is a sick organ, and that sexual excitation without fertilization is responsible for numerous disorders, just as are masturbation and the use of chemical spermaticides; even condoms affect male virility." All in all, contraception took a lot of punishment during the subsequent discussion, though two participants swam against the stream. An American Catholic physician said that if he had a dollar for every woman who had asked him for the pill he would be rich, and another doctor said bluntly that he preferred contraception to abortion, and these were the two alternatives. Unfortunately the Spanish press printed on Sunday, 17 September, under the heading "Conclusions of the XXI World Medical Assembly," without confirmation from either Council or the Secretariat, a report which may give the impression that W.M.A. is against the use of oral contraceptives. This of course is not so.

FIG. 3.—The platform party at the opening session. (From left to right) Dr. Stanley Gilder, Editor of the *World Medical Journal*; Miss Margaret Natwick (W.M.A. Headquarters Staff); Dr. Alberto Romualdez, Secretary General of the W.M.A.; (mainly hidden), Dr. Garcia Orcoyen, the Spanish Director General of Health; Dr. Jesus Tamesis, of the Philippines, the retiring President of the W.M.A.; Dr. Gerald Dorman (U.S.A.), Chairman of the W.M.A. Council; and Dr. Ernst Fromm (West Germany), Treasurer of the W.M.A.

Medicine and Society

With the second session on medicine and society peace returned. Drs. **DE LA QUINTANA** and **DE CALDAS** made sweeping historical surveys to demonstrate how the evolution of social thought and of social structures had affected the practice of medicine. The doctor may think he is free within the limits of contemporary medical science, but he is not; what he does and how he does it are very much conditioned by what society thinks about sickness and health (witness the contrast between the Greeks, who were against the treatment of persons with basic physical or mental defects, and the early Christians, who regarded suffering as ennobling) and by how society is structured. The third lecture in this session looked at the problem from another angle. Professor **LOPEZ IBOR**, a psychiatrist of international reputation, looked at the influence of the changes in modern society on the training of the medical student. He felt that we needed a new type of doctor, but we must make our educational experiments slowly, with pauses to assess the results. As a psychiatrist he was of course concerned about the tendency to dehumanize medicine and the need to counteract it.

It was altogether a useful week, and there were welcome signs that W.M.A. is gathering steam. People worked harder and played less, and most significant was the fact that for the first time in many years the Treasurer, Dr. E. **FROMM** (Germany), could come to the rostrum and announce that last year W.M.A. balanced its budget with a little to spare. Even the publications business is looking up, for next year both the Canadian Medical Association and the Australian Medical Association are going to distribute the *World Medical Journal* to all their members, while other associations are looking into the possibility of following suit. Once more also the *British Medical Journal* is taking an active part by preparing a supplement to the standard reference book *World Medical Periodicals*.

Correspondence

Letters to the Editor should not exceed 500 words.

Mortality of the Ambulance Ride

SIR,—Your recent correspondence on the mortality of the ambulance ride (26 August, p. 560, and 9 September, p. 678) calls attention to a problem which has been of considerable concern to ambulance authorities for a long time, although perhaps it has not received a great deal of mention in the medical press. Few doctors have much experience of travelling by ambulance.

In the first place the sensation when travelling as a passenger is quite different from that experienced when travelling as a recumbent patient, and the problem of suspension in ambulances is one which has received considerable attention, but there are difficulties. It may not be generally realized that there is no chassis which is designed specially for an ambulance. Ambulances in this country are built by a small number of specialist firms who have shown considerable ingenuity and are always willing to try new methods, but there is the limiting factor that all their work has as its foundation the commercially available types of chassis. The present position is to a large extent governed by economics, but this may not always be the case. The Ministry of Health Working Party on Ambulance Training and Equipment (the Millar Committee)[1] has drawn up an outline specification for a new chassis which may well be looked at by some of the manufacturers (Appendix I, part 2). For economic reasons, however, this specification may not be taken up unless the chassis can be put to some other commercial use as well. Perhaps the finest special-purpose ambulance was the Daimler ambulance which was available from 1949. In spite of its fine appearance and high quality it was a very expensive vehicle not only to purchase—and one must remember that the cost would be considerably higher today—but also to run, and in urban conditions it did not have a high degree of manœuvrability. An ambulance which may be entirely satisfactory in urban conditions may well prove to be unsuitable for work in country districts.

One of your correspondents suggests that there are medical reasons why the patient should face forward, and this is something which is worthy of further investigation. It is interesting to note that the most comfortable ride for any ambulance patient is in a railway train. Probably the main factor in making this so is that the ride is smooth and free from frequent starts and stops. It is sometimes difficult to persuade hospital doctors that their patients are more comfortable on long journeys in a train than in an ambulance, but the patients themselves and those in attendance upon them have no doubt that this is true.

In common with other branches of the Health Service the financial aspect is a considerable element in this problem, and consideration has to be given to how much money can be diverted with good reason for this purpose. Even when the suspension is improved, as, for instance, by special suspension of the actual stretcher within the vehicle so that in theory the patient has an extremely smooth ride, one is faced with another problem, and that is that in spite of all the evidence that the ride is very smooth some of the patients suffer from travel sickness, and these are people who do not normally suffer from this when in an upright position. Our experience is that, while these suspension units undoubtedly absorb vibration, the free movement inevitably causes more swaying. An interesting theory has been put forward that the body, accustomed as it is to adjusting itself when in an upright position while travelling, is unable to readjust itself during the comparatively short time that the patient is in the recumbent position.

Finally, ambulance crews are taught to study the comfort of their patients and to realize the risks of a rough ride. Stress is laid in their teaching on the fact that, while speed may be vital in reaching the ambulance victim, once immediate life-saving action has been taken there is seldom the same need for undue haste in reaching the hospital.—I am, etc.,

A. B. STEWART,
Medical Adviser,
Greater London Council,
Inner London Education Authority.
County Hall,
London S.E.1.

REFERENCE

[1] *Report by a Working Party on Ambulance Training and Equipment*, 1967, Ministry of Health and Scottish Health and Home Department, H.M.S.O.

SIR,—I have always admired the French pragmatism in using well-sprung estate cars to move their invalids to hospital, while their dead go to the cemetery in a suitably ornate van. In England the comfort of the corpse merits a fine limousine, the medical needs of the severely sick a bone-shaker. The British ambulance, alias the French hearse, has brought some of our patients to the brink of the grave. May I join your previous correspondents (9 September, p. 678) in seeking a rapid research project to improve our devoted but antiquated ambulance service?—I am, etc.,

Derby. K. J. GURLING.

Thyrocalcitonin

SIR,—Your leading article on thyrocalcitonin (29 July, p. 256) mentions the discovery of the phosphaturic action of this hormone in the rat, which led Robinson *et al.*[1] to condemn the use of tests of parathyroid function based on phosphate excretion in man. Quite apart from the neglect of possible species differences, this conclusion is only partly justified. When a change in the secretion rate of parathyroid hormone occurs as a primary event, the thyrocalcitonin secretion would be expected to change in the same direction, and so to reinforce any change in phosphate excretion. This means, for example, that the diagnostic value of a normal test of phosphate excretion in excluding primary hyperparathyroidism has been strengthened.[2] On the other hand, when a change in the secretion rate of parathyroid hormone occurs as a secondary response to a change in plasma calcium from some other cause, thyrocalcitonin secretion would be expected to change in the opposite direction, and so to counteract any change in phosphate excretion. This is probably why the phosphate excretion index does not change in response to dietary calcium deprivation[3]; clearly the inference that this procedure does not stimulate the parathyroid glands[4] is invalid.—I am, etc.,

Department of Medicine, A. M. PARFITT.
University of Queensland,
Brisbane, Australia.

REFERENCES

[1] Robinson, C. J., Martin, T. J., and MacIntyre I., *Lancet*, 1966, 2, 83.
[2] Sanderson, C., *Lancet*, 1966, 2, 280.
[3] Nordin, B. E. C., Smith, D. A., and McCregor, J., in *The Parathyroid Glands*, edited by P. J. Gaillard, R. V. Talmage, and A. M. Budy, 1965, p. 125. Chicago.
[4] Nordin, B. E. C., and Smith, D. A., *Diagnostic Procedures in Disorders of Calcium Metabolism*, 1965. London.

Place of the Mentally Retarded

SIR,—The very stimulating paper by Professor T. McKeown and Dr. I. Leck (2 September, p. 573) and also your leader (same issue, p. 567) prompt me to raise some points, necessarily limited by space. I work jointly for a local health authority and in a hospital for subnormals, and believe that the individual subnormal (and that is what this is, or should be, all about) requires a continuum in which he can be cared for. Therefore before moving 326 subnormal children from one camp (health) to another (education) I would like to be certain that they are going to benefit, and I find cold comfort in the fact that, according to the authors, 162 educationally subnormal children (13.6% of the total E.S.N. children in Birmingham) are already awaiting admission to school. What educational and training facilities would be available to the group the authors wish to transfer to district general hospitals? Clinical experience leaves me in no doubt that this group requires as much attention educationally as those the authors wish to transfer to the education authority.

The massive transfer of about half the hospital population to the local authority for residential care must be considered in more detail. Presumably these cases cannot go home, otherwise they would already be there. Suitable foster-homes for subnormals are notoriously difficult to find in any quantity. I presume, therefore, that the vast majority would be housed in hostels, and, as the Ministry of Health's standard sets a maximum of 25 beds per hostel, and there is no mention of any existing hostel accommodation in Birmingham, approximately 30 hostels will have to be found or built. When applied on a national basis it is in my opinion quite unrealistic to contemplate money, let alone staff, becoming available on this kind of scale. This is not to say that much more money is not required for the service; I agree completely with the authors that an inadequate service should not be disguised as desirable because it is economical.

One way of obtaining improvement in the service is to avoid multi-authority responsibility and duplication of effort; we should close our ranks, pool our resources, and integrate. A single responsible authority derived from health and welfare, education, and hospital authorities could well be the basic essential ingredient of such a concept. The best use is thereby, I suggest, more likely to be made of the available finances, staff, and accommodation, and the controlling authority would have a sense of unified responsibility and purpose.—I am, etc.,

Broomfield,
Chelmsford, Essex.
M. E. YORK-MOORE.

SIR,—I noted with some surprise in a leading article dealing with this subject (2 September, p. 567) the dogmatic statement that "clearly no special search should be made to 'ascertain' the large number [of persons with intelligence quotients of 70 or less] or to make special provision for them." If this is correct then much of the work of school medical officers and educational psychologists is indeed being misdirected.

The ascertainment of mental subnormality is essential to the assessment of the educational needs of the individual and his work potentials. It is equally important in the exclusion of emotional disturbance or physical handicap as a cause for apparent backwardness. Recognition of mental subnormality also makes it possible to avoid the placement of children in social or educational situations which they are intellectually incapable of surmounting, and which can give rise to severe psychic trauma to the individual concerned.

Finally, the lack of adequate provision for mentally subnormal persons may in part be due to past failures to ascertain the true extent of the problem of mental subnormality, and to plan suitably for the special educational, communal, and hospital care for all those in need of these facilities.—I am, etc.,

Rayleigh, Essex.
R. BEAVER

S.T.P. and Alcohol

SIR,—Your leading article (2 September, p. 570) ends with the admirable sentence, "Society has a responsibility to protect its members from drugs that can make them frankly insane or indeed kill them, as it has to stop the spread of communicable diseases." This certainly applies to marihuana.

However, the opposition of at least some psychiatrists to the prohibition of marihuana was intended to emphasize that the antics of a few hundred hippies was of trifling importance compared with the enormous damage to the health and happiness of the community caused by the current misuse of alcohol, which, after all, does in fact drive many people "insane or indeed kill them." In Scotland 20% of admissions to mental hospitals are now due to alcoholism, while W.H.O. lists alcoholism as the fourth most important cause of premature death. The number of chronic alcoholics in Great Britain is estimated at about 400,000.

Yet, so far from society feeling any responsibility for this, it allows the licensed trade to spend £23m. a year on advertisements designed to persuade families, especially teenagers and women, to drink not only more beer and wine but gin, whisky, and vodka; and the bizarre situation arises that the same newspaper might report a nine-month sentence on a purple-heart vendor and the elevation of a whisky vendor to the peerage. Yet it is known that the increase of alcohol consumed correlates with an increase of many social evils, including murders, suicides, divorces, road accidents, venereal diseases, and many other diseases such as tuberculosis, diabetes, and heart disease.

Reforms have been prevented to some extent because many believe that the only solution is prohibition, but that, as this is impossible, nothing more can be done. Recent studies, however, have indicated that social attitudes to drink are proportional to the degree of alcoholism in the community, and that much depends on the example of the medical profession.

Perhaps, therefore, we should reassess whether garish American bars are not out of place in medical premises, and whether young doctors, many of whom dislike drink, should not be offered soft drinks as well when offered alcohol. Also, are cocktails and liqueurs really necessary before and after medical dinners respectively? Or the announcement at 9.30 that the "bar is still open"? Is the argument that the sale of drinks is a gold mine for the society ethically sound, or should societies, like some Governments, refuse to benefit from such profits? Is there justification for the claim frequently made by the alcoholic that it is impossible to get on in England if you are a non-drinker? And is the propaganda image of the non-drinker as a dull, unsociable fellow really justified?—I am, etc.,

London W.1.
A. SPENCER PATERSON.

Sodium Uptake in Peritoneal Dialysis

SIR,—I wonder if Dr. J. D. Swales (5 August, p. 345) is doing himself an injustice in his apparent assumption that he failed to remove sodium from his patients by using hypertonic (6.36 g. dextrose/100 ml.) peritoneal dialysis fluid. The fall in sodium concentration which he observed when using this occurs always, even when the plasma sodium concentration equals or exceeds the initial level in the fluid, provided the observation is made during the first hour of the exchange. This is simply a reflection of the disparity of the osmotic and sodium gradients across the membrane. Dr. Swales did not mention the volume of fluid removed when the dialysate sodium concentration dropped to 123 and 122 mEq/l. (final Table), but if, as is likely, this corresponded to the volumes given in Fig. 4 (300–450 ml. for exchange) then the sodium balance referable to the patient would lie between +1.4 and −19.4 mEq per exchange. ([Vol. out × [Na] out]−[Vol. in × [Na] in].) That the postulated negative balance is the one that most likely obtains is apparent from the results shown in Fig. 4.

The significance of sodium balance during dehydrating peritoneal dialysis is of further importance when this form of treatment is applied to patients with fluid overload but relatively normal initial plasma sodium concentrations. We have observed[1] that the sodium concentration in the excess fluid removed (the above balance figure divided by the volume difference) ranges from 70 to 110 mEq/l. This means that even though the patients were in negative sodium balance they became hypernatraemic. Under these conditions we have observed plasma sodium concentrations as high as 168 mEq/l.

Like Dr. Swales, we have toyed with the idea of reducing the amount of sodium in the dialysate fluid, and Messrs. Allen & Hanbury have provided basic solutions for us with sodium concentrations as low as 115 mEq/l., with a corresponding adjustment of osmolality. This does make things complicated, and a satisfactory alternative is occasionally to substitute a litre of 5 g./100 ml. dextrose for one of the two units of peritoneal dialysis fluid. With a 45-minute equilibration period this will usually remove about 50 mEq of sodium, and is well tolerated by the patient. I cannot imagine, however, that even this would have benefited the patient who first drew the attention of Dr. Swales to the problem.—I am, etc.,

M. V. MORIARTY.

Department of Medicine,
University of British Columbia,
Vancouver, Canada.

REFERENCE

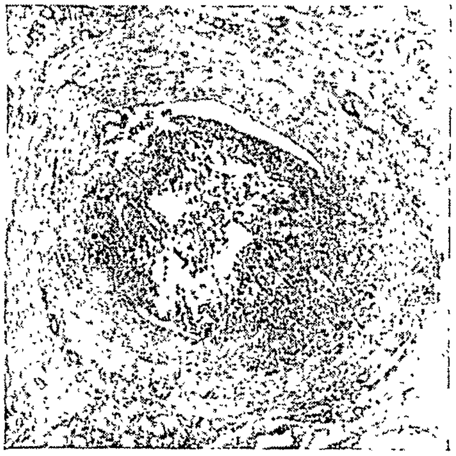
[1] Moriarty, M. V., and Parsons, F. M., in *Proc. Symposium European Dialysis and Transplant Association*, 1967, 3, p. 359. Amsterdam.

Peripheral Gangrene in Infancy and Childhood

SIR,—Referring to the correspondence "Peripheral Gangrene in Infancy and Childhood" (10 June, p. 700), I would like to add a few points to the discussion. Peripheral gangrene is also one of the intriguing problems in Kenya. Work on this condition has been done by J. R. M. Miller[1] and more recently by members of the Glasgow team of the Nairobi Medical School.

I had the opportunity to study the histopathological sections of tissues removed from a few of these patients. Invariably there was in these cases an infectious condition (pneumonia, gastroenteritis) antedating the onset of the usual symmetrical gangrene. The histopathological findings were controversial.

In a necropsy case no vascular lesions could be found in the arteries of the affected areas; vascular lesions were also excluded in another case. The histological sections of the other organs in the necropsy case revealed the presence of a "virus-infection." Unfortunately we could not identify the causative virus on the basis of the histopathological findings only (rickettsiosis? adenovirus infection?). Contrary to these findings a proliferative endovasculitis with secondary thrombosis was observed in two other cases (see Fig.). The histopathological lesions in those two cases resemble the morphology of a peripheral arteritis (vaguely resembling thromboangiitis obliterans) in young adult patients with an apparently identical condition. Identical observations of peripheral gangrene were also noticed in the course of an adenovirus infection.[2]



Proliferative endovasculitis. (H. and E. ×25.)

It appears to me that some of these cases with a peripheral gangrene of obscure origin may indeed be related to "infectious angiitis."[3] A. Th. Ariëns and B. E. Kingma[4] advocated the administration of prednisolone and antibiotics in such cases; these authors claimed to have obtained a dramatic improvement in one case after this form of treatment.—I am, etc.,

JAN WILLEM KOTEN.

Department of the
Royal Tropical Institute,
Amsterdam,
Nairobi, Kenya.

REFERENCES

[1] Miller, J. R. M., *East Afr. med. J.*, 1964, **41**, 419.
[2] Zaane, D. J. van, Sprangers, M., and Veen, J. van der, *Ned. T. Geneesk.*, 1961, **105**, 1281.
[3] Manion, W. C., in *The Peripheral Blood Vessels*, 1963, Chapt. 10, ed. J. L. Orbison and D. E. Smith. Baltimore.
[4] Kingma, B. E., and Ariëns, A. Th., ibid., 1961, **105**, 1290.

Activation Analysis

SIR,—Your leading article (26 August, p. 509) indicates that uniform irradiation of the thyroid gland is not possible with neutrons. In fact this is true only for irradiation by thermal neutrons as used in the technique being developed in France,[1] for which it is necessary to use an internal standard of radioactive iodine-129.

In reporting our measurements in man[2, 3] we have shown that by deliberately filtering out the thermal neutrons and using only neutrons of higher energies (epithermal and fast neutrons) not only is the irradiation adequately uniform but also the iodine in the gland is activated preferentially compared with sodium and chlorine, because of the behaviour of the neutron capture cross-sections of these elements as a function of neutron energy. Our own studies with thyroid phantoms of various sizes, and measurements by Fairchild,[4] confirm that uniformity of thyroid irradiation using epithermal and fast neutrons is to be expected. Good agreement has been obtained between in-vivo activation measurements, and subsequent in-vitro activation and chemical measurements of iodine in the same gland.[2 3]

Our reports have already shown that the in-vivo measurement of total intrathyroidal iodine in man can be made with radiation doses to the thyroid not exceeding those of an uptake test using 12 μCi of iodine-131.—We are, etc.,

W. D. ALEXANDER.
R. McG. HARDEN.

University Department of
Medicine,
Gardiner Institute,
Western Infirmary,
Glasgow W.1.

K. BODDY.

Scottish Universities
Research Reactor Centre,
East Kilbride,
Glasgow.

REFERENCES

[1] Lenihan, J. M. A., Comar, D., Riviere, R., and Kellersholn, C., *Nature (Lond.)*, 1967, **214**, 1221.
[2] Boddy, K., Alexander, W. D., 1967, Paper SM 91/13 I.A.E.A., *Sym. Nuclear Activation Techniques in the Life Sciences*. Amsterdam.
[3] —— Harden, R. McG., Alexander, W. D., *J. clin. Endo. and Met.*, in press.
[4] Fairchild, R. G., *Phys. in Med. Biol.*, 1965, **10**, 491.

Hypercalcaemia and Malignant Tumours

SIR,—The report of hypercalcaemia in yet another patient with a bronchial neoplasm (2 September, p. 590) was interesting because of the mental and neurological changes due to the hypercalcaemia. Removal of the tumour caused a fall of the plasma calcium to normal within hours. What was less interesting was the longish discussion on the mechanism of the rise in plasma calcium. The authors wrote that it was not possible to decide whether the tumour removed was producing a substance having the activity of parathyroid hormone or a "parathyrotropic" hormone.

In 1963 Liddle and his co-workers[1] demonstrated the presence of corticotrophin, or a closely related polypeptide, in the primary tumour and metastases from patients with greatly increased adrenal cortical activity in the presence of malignant disease. Other instances of ectopic hormone production by tumours have in recent years been reported fairly frequently, and in 1941 Albright[2] first suggested that tumours of nonparathyroid origin might produce a substance with biological activity similar to that of parathyroid hormone. Two recent studies,[3 4] the first using a bioassay and the second radioimmunoassay, have both shown the presence of parathyroid hormone-like material in nonparathyroid tumours from patients with hypercalcaemia but without bony metastases. Hyperplastic parathyroid glands have not been found in such patients, and in one patient (in whom primary hyperparathyroidism was excluded at post mortem) Sherwood and his colleagues[4] found an increased amount of parathyroid hormone in the blood which was in the hyperparathyroid range.

The correction of the hypercalcaemia within hours of the removal of the malignant tumour, the absence of skeletal metastases, the hypophosphataemia, the lack of hyperplastic parathyroid glands, and the results of assay of the tumours are evidence that some tumours in patients with malignant disease and hypercalcaemia produce a substance with activity like parathyroid hormone. There is no evidence for any "parathyrotropic" hormone in this syndrome, or for that matter in hyperparathyroidism (unless possibly sometimes growth hormone[5] and thyrocalcitonin might be included in this term).—I am, etc.,

Radcliffe Infirmary,
Oxford.

MILO KEYNES.

REFERENCES

[1] Liddle, G. W., Island, D. P., Ney, R. L., Nicholson, W. E., and Shimizu, N., *Arch. intern. Med.*, 1963, **111**, 471.
[2] Case Records of the Massachusetts General Hospital, 27461, *New Engl. J. Med.*, 1941, **225**, 789.
[3] Munson, P. L., Tashjian, A. H., Jr., and Levine, L., *Cancer Res.*, 1965, **25**, 1062.
[4] Sherwood, L. M., O'Riordan, J. L. H., Aurbach, G. D., and Potts, J. T., Jr., *J. clin. Endocr.*, 1967, **27**, 140.
[5] Harrison, M., and Fraser, R., *Brit. med. J.*, 1960, **2**, 535.

Dietary Calcium and Hypercalciuria

SIR,—The article by Dr. M. Peacock and others (19 August, p. 469) rightly stresses the difficulties associated with the definition of hypercalciuria. However, we are unable to agree with their conclusion that "hypercalciuria can *only* be defined in relation to calcium intake." We have recently observed[1] a highly significant relationship between the urinary excretion of calcium and sodium in stone-forming patients, confirming similar findings by other workers.[2–4] On recalculation of our original data on the basis of mg. calcium/kg./day we find that our comparatively young stone-forming males constantly excrete more than 6 mg. calcium/kg./day on a diet containing approximately 10 mg. calcium/kg./day. These cases are compared with a small group of normal young males who constantly excrete less than 4 mg. calcium/kg./day on the same diet.

The Table shows the comparative values for urinary calcium excretion when both groups of subjects were given a low calcium diet containing not more than 2.6 mg./kg./day. In period A this diet contained less than 80 mEq sodium/day. In period B the same diet was supplemented by 85 mEq sodium/day, administered as sodium chloride.

These results show that there is a significant difference between the two groups in period A when calculated as mg. calcium/kg./day, and also the difference is highly significant when mean total calcium excretion is expressed in mg./24 hours, as it was in our paper. The addition of sodium in period B also reveals a highly significant difference in the increase in calcium excretion between the two groups. The urinary calcium excre-

Diet	Group	No. of Patients Studied	Mean Urinary Calcium mg./kg./day (±SD)	t	P
Period A. Low calcium diet ≯2·6 mg./kg./day	Hypercalciuric	14	2·61 (±0·6)	4·2	<0·001
	Normal	10	1·58 (±0·38)		
Period B. Low calcium diet plus 85 mEq sodium/24 hours	Hypercalciuric	14	4·1 (±0·9)	6·9	<0·001
	Normal	6	2·3 (±0·37)		

tion of the stone-formers now significantly exceeds their dietary intake over a five-day period. The normal controls showed much less increase in calcium excretion. The levels of urinary sodium were in the same range in both groups. This observation appears to indicate that there is a renal factor involved in the production of hypercalciuria in our stone-forming subjects.

We feel, therefore, that hypercalciuria cannot be defined solely in relation to calcium intake, and that sodium intake is an equally important factor. While it is well established that patients with "idiopathic hypercalciuria" absorb more dietary calcium than normal subjects, this may be a compensatory mechanism for increased urinary calcium excretion rather than the basic cause.—We are, etc.,

M. J. PHILLIPS.
J. N. C. COOKE.

Royal Air Force Hospital,
Wroughton,
Swindon, Wilts.

REFERENCES

[1] Phillips, M. J., and Cooke, J. N. C., *Lancet*, 1967, **1**, 1354.
[2] King, J. S., Jackson, R., and Ashe, B., *Invest. Urol.*, 1964, **1**, 555.
[3] Kleeman, C. R., Bohannan, J., Bernstein, D., Ling, S., and Maxwell, M. H., *Proc. Soc. exp. Biol. (N.Y.)*, 1964, **115**, 29.
[4] Modlin, M., *Ann. roy. Coll. Surg. Engl.*, 1967, **40**, 155.

Oxygen Therapy

SIR,—Gratifying as it was to read Dr. I. D. Green's account (2 September, p. 593) of the performance of the modernized Tudor Edwards spectacles, it is essential to describe an important disadvantage.[1] Wearing the device does not preclude smoking. Small superficial burns round the nares after two or three quite exciting little conflagrations from this cause have been seen. Unfortunately, the consequences may not always be so limited.

Other experience[2] supports Dr. Green's finding that nasal catheters can be used successfully for "controlled oxygen therapy," but it also suggests that this illogical practice may be safely carried to its logical conclusion. Thus the most severely ill only get air to breathe with just as good a prognosis and a lot less trouble in management.—I am, etc.,

GEORGE ADDIS.

Department of Materia
Medica and Therapeutics,
Stobhill General Hospital,
Glasgow N.1.

REFERENCES

[1] Addis, G. J., *Lancet*, 1963, **1**, 1084.
[2] —— M.D. Thesis submitted to Glasgow University, 1967.

SIR,—We were interested to read the communication by Dr. I. D. Green (2 September, p. 593). However, we are not at all clear how the mean F_{IO_2} was obtained from the mass spectrometer trace. A true mean value is obtained only if the concentration trace is weighted in proportion to the instantaneous flow rate.[1] Even then it is necessary to distinguish between the mean concentration reaching the alveoli and the mean concentration reaching alveoli plus dead space.

These difficulties can be bypassed in normal subjects by using alveolar sampling, which provides a direct measure of the alveolar oxygen concentration produced by any device.[2] Arterial catheterization is avoided in this method. The dead space of each device can be determined quantitatively if the subject's ventilation is also measured.[3]

From the results of our own study[3] we do not consider a nasal catheter a reliable method of delivering oxygen unless it is inserted as far as the oropharynx, and our own preference for any hypoxic hypercarbic patient is the Ventimask. The Pneumask and the Polymask, especially the former, should be regarded as dangerous, in our opinion. If high oxygen concentrations are required the M.C. mask is nearly as effective and has a much lower dead space at all oxygen flows.

Dr. Green's comments on patient comfort are very pertinent; it is our experience that there is a marked inverse correlation between the effective dead space of a mask and the degree of patient comfort.—We are, etc.,

J. M. COLLIS.
D. W. BETHUNE.

St. Bartholomew's Hospital,
London E.C.1.

REFERENCES

[1] Nunn, J. F., and Newman, H. C., *Brit. J. Anaesth.*, 1964, **36**, 5.
[2] Kory, R. C., Bergmann, J. C., Sweet, R. D., and Smith, J. R., *J. Amer. med. Ass.*, 1962, **179**, 767.
[3] Bethune, D. W., and Collis, J. M., *Thorax*, 1967, **22**, 221.

Calcium Infusion Test

SIR,—We would agree with Dr. J. V. Lever, Dr. C. R. Paterson, and Dr. D. B. Morgan (29 July, p. 281) that a positive calcium infusion test does not always indicate histological osteomalacia, but would dispute their conclusion that for this reason the test is of no value.

Among 12 patients with chronic obstructive jaundice studied at the Royal Free Hospital six had a retention of calcium greater than that found in a control group of patients.[1] After one to three months of parenteral vitamin-D therapy the calcium infusion test remained abnormal in all except one patient, but after twelve months of treatment all these patients had a normal calcium infusion test. Although only one of the six patients had osteomalacia on biopsy, all of them clearly had some biochemical abnormality which was corrected by long-term vitamin-D treatment. On the other hand, in the four patients with subnormal calcium absorption this was restored to normal by a short course of vitamin D.

A normal calcium infusion test probably excludes osteomalacia, and may thereby spare many patients an unnecessary bone biopsy. Furthermore, an abnormal result may be the only biochemical indication that osteomalacia is present.[2] The test clearly merits further evaluation.—We are, etc.,

K. A. KEHAYOGLOU.

Royal Free Hospital,
London W.C.1.

C. D. HOLDSWORTH.

St. Bartholomew's Hospital,
London E.C.1.

REFERENCES

[1] Kehayoglou, K. A., Holdsworth, C. D., Agnew, J., Whelton, M., and Sherlock, S., 1967, in preparation.
[2] Anderson, I., Campbell, A. E. R., Dunn, A., and Runciman, J. B. M., *Scot. med. J.*, 1966, **11**, 429.

Haematomas of the Abdominal Wall

SIR,—I was interested in the correspondence (8 July, pp. 108 and 109) subsequent to your leading article (17 June, p. 716) on the above subject.

Two cases of this condition have been referred to me and there had been two other cases in the same hospital six months previously.

The patient was 24 weeks pregnant in her fifth pregnancy and had had a severe cold and cough for three weeks previous to admission, but this had greatly improved in the past few days. An acute pain had awoken her in the early morning. She was in shock, and the diagnosis of intra-abdominal haemorrhage was made with some misgivings, as the findings were atypical, and there was no shoulder pain such as should have been present with the amount of shock seen. At operation, the true state of affairs was evident. There was a rupture of the left rectus abdominis muscle below the umbilicus. Bleeding was continuing from small vessels in the muscle and there was a small haematoma beneath the muscle. Haemostasis was achieved and the abdominal wall closed by continuous suture without drainage. A sinus formed and there was a serous discharge for three weeks. Delivery of a live baby at term was normal.

The second patient was admitted as an emergency at 32 weeks' gestation in her fourth pregnancy, which had been eventless except for a mild cold and cough in the previous two weeks. She had severe left-sided lower abdominal pain with shock, and was diagnosed as a possible rupture of the gravid uterus. Lateral radiographs of the abdominal wall showed a definite area of dehiscence of the anterior musculature in the region of maximal tenderness on shallow palpation. Laparotomy was withheld and under muscle relaxants and analgesia the symptoms subsided. Delivery at term was uncomplicated and the infant alive.

All four patients were pregnant and multiparae, and all had recently had a head cold and associated cough, though none attributed the onset of the pain to any episode of coughing. All were grossly overweight with poor abdominal muscle tone. The two patients who had lateral abdominal *x*-rays taken showed a recognizable defect of the soft tissues, and this is a valuable diagnostic point in the differential between intra-abdominal haemorrhage and lesions of the abdominal wall.

The diagnosis is not simple, and, as pointed out,[1-3] under 30% are diagnosed before operation. The mortality rate is high in both mother and foetus, and this is felt to be an indication of preceding debility, which is also held to be predisposing. Where the deep epigastric arteries are torn and continue bleeding then operative therapy is mandatory.[4]—I am, etc.,

HENRY FITZGIBBON.

Penticton, B.C.,
Canada.

REFERENCES

[1] Thomas, R. C., *J. Obstet. Gynaec. Brit. Emp.*, 1945, **52**, 580.
[2] Torpin, R., *Amer. J. Obstet. Gynaec.*, 1943, **46**, 557.
[3] Schafer, C. S., *Amer. J. Surg.*, 1953, **86**, 157.
[4] Cullen, T. S., *Bull. Johns Hopk. Hosp.*, 1937, **61**, 295.

Diet and Diverticulitis

SIR,—I have read with great interest the comments on this subject made by Dr. C. D. Campbell in his letter (22 July, p. 243) and the one before (2 July 1966, p. 50) jointly with Dr. T. L. Cleave. They have strongly related colonic diverticular disease to the consumption of refined carbohydrate in any community irrespective of racial differences. Their view is rightly opposed by Dr. E. H. Goulston expressed in his letter (6 May, p. 378), at least as far as Ethiopians are concerned. Our experience in Kuwait conforms to the latter one.

Kuwait is inhabited mostly by Arabs and shared by large minorities of other nationalities, particularly Persians, Indians, and Pakistanis. We import nearly all our food items from all over the world, including refined wheat grain flour, rice, fruits, and vegetables. There is no doubt that this diet consists mainly of refined carbohydrates. Nevertheless, not a single case of diverticulitis has ever been seen in our department. Over the last three years 284 barium enemata were performed for various colonic disorders without showing any evidence of diverticulitis. Only in one case two small diverticula were detected in the sigmoid colon. On the other hand, diseases such as ischaemic heart disease, diabetes mellitus, in which diet is incriminated, and ulcerative colitis are found more or less in the same incidence as in Western countries. Therefore it is hard to accept that diverticulitis is the result of refined carbohydrate consumption.—I am, etc.,

Emirie Hospital,
Kuwait.
S. N. SALEM.

Dose of Metaraminol

SIR,—In the June 1967 addition to "Proplist," on page 7, the dosage for Aramine (metaraminol tartrate) given intravenously is shown as 15 mg.–100 mg. This, of course, is the dosage for intravenous infusion to be placed in 500 ml. isotonic saline or 5% dextrose, and the dosage for direct intravenous injection is 0.5 mg. to 5 mg.—I am, etc.,

A. B. REES,
Secretary,
Standing Joint Committee on the Classification of Proprietary Preparations.

London S.W.1.

Progestin Therapy of Breast Cancer

SIR,—The letter of Dr. B. Jolles on this subject (9 September, p. 682) is to be welcomed because of his important early work on the progestin therapy of cancer.[1] He stresses the possible advantage of combined oestrogen and progestin therapy in cancer of the breast as suggested by Landau *et al.*[2] It was on the basis of that very report that I carried out two clinical trials, which have both been reported.[3,4] In the first I *added* progestin therapy after stilboestrol 15 mg. daily had failed to induce regression of breast cancer. Response was noted in 3 out of 10 patients. In the second series I gave a progestin-oestrogen combination in the proportion used in the contraceptive pill. Response was noted in 9 out of 65 patients, and 5 out of the 9 had previously received and failed to respond to oestrogen or androgen therapy.

I therefore welcome a preliminary report by Dr. Jolles of a 32% response in 25 patients with breast cancer treated by a combination of 19-nor-17αhydroxyprogesterone with oestradiol. I look forward to examining the criteria of response used by him to account for this response rate. It will be interesting to know how many of the patients were treated by the combination after having failed to respond to the oestrogen alone. Only in this way, or by a controlled trial, can the value of the added progestin be assessed.

Dr. Jolles's final statement suggests that he read my paper[5] very carelessly. He states, "Effects on vaginal smears are not likely to be more reliable in this regard [in establishing potency ratios of progestins] in postmenopausal women, and caution should be exercised in drawing conclusions for the selection of patients suitable for this type of hormone therapy." I did not anywhere suggest that the *effect* of progestins on the vaginal smear could be used for selection of patients suitable for such therapy. I made it clear that the initial vaginal smear *before* therapy seemed to suggest a method of selecting patients more likely to respond to progestin therapy. My results suggested that the absence of oestrogen secretion in postmenopausal patients, as shown by an atrophic smear, militated against the likelihood of successful progestin therapy. This observation tends to confirm the suggestion made in the second sentence of this letter.—I am, etc.,

London N.W.11.
BASIL A. STOLL.

REFERENCES

[1] Jolles, B., *Brit. J. Cancer*, 1962, **16**, 209.
[2] Landau, R. L., Ehrlich, E. N., and Huggins, C., *J. Amer. med. Ass.*, 1962, **182**, 632.
[3] Stoll, B. A., *Med. J. Aust.*, 1966, **1**, 331.
[4] —— *Brit. med. J.*, 1967, **1**, 150.
[5] —— ibid., 1967, **3**, 338.

Sodium Chlorate Poisoning

SIR,—Renal failure due to sodium chlorate poisoning is, we believe, less rare than suggested by Dr. R. K. Knight and colleagues in their report of a case (2 September, p. 601). We reported three instances, with recovery, in 1963 among a large group of patients with severe acute renal failure treated with haemodialysis.[1]

One patient who attempted suicide on two separate occasions at a nine-month interval is of particular interest, since he demonstrates how complete recovery may ultimately be despite two severe episodes of acute renal failure with as powerful a nephrotoxin as sodium chlorate. The first admission was in May 1961, after swallowing five tablespoonfuls of sodium chlorate. He had the typical clinical and laboratory features of gross intravascular haemolysis and acute renal failure. Vitamin C was administered and haemodialysis was performed on admission in an attempt to remove sodium chlorate. The oliguric phase of the renal failure lasted for 14 days, and he required two further haemodialyses to control uraemia; the daily rise in blood urea averaged 80 mg./100 ml. At the time of discharge, to receive psychiatric treatment, creatinine clearance was 25 ml./min., and by August 1961 it had risen to 54 ml./min. In September 1961 he again attempted suicide, on this occasion swallowing a half-tumblerful of sodium chlorate. He was managed in a similar way with haemodialysis on admission, followed by a second haemodialysis four days later to control uraemia. The oliguric phase lasted seven days, and the daily rise in blood urea averaged 50 mg./100 ml. Renal biopsy in October 1961 showed considerable tubular atrophy, and it was felt likely that ultimate recovery of renal function would be incomplete.

He received inpatient psychiatric care for several weeks with marked improvement in his mental state, and returned to work. He was seen again in January 1966 as part of our recent study into the late prognosis of acute tubular necrosis,[2] and we were gratified to find him well, with a creatinine clearance of 90 ml./min. The only slight abnormality apparent was that the maximum urinary specific gravity after dehydration was 1.017.

The second patient[1] was a 65-year-old male gardener, who had taken a similar amount of sodium chlorate in a suicidal attempt. The oliguric phase of the renal failure was rather more prolonged, being 16 days, the average daily rise in blood urea was 80 mg./100 ml., and he required four haemodialyses in all.

He made a good immediate recovery from the acute renal failure and was discharged, but we were unable to determine the long-term prognosis because of his death from an unrelated cause.—We are, etc.,

A. C. KENNEDY.
R. G. LUKE.

University Department of Medicine,
Royal Infirmary,
Glasgow.

REFERENCES

[1] Kennedy, A. C., Luke, R. G., Linton, A. L., Eaton, J. C., and Gray, M. J. B., *Scot. med. J.*, 1963, **8**, 97.
[2] Briggs, J. D., Kennedy, A. C., Young, L. N., Luke, R. G., and Gray, M., *Brit. med. J.*, 1967, **2**, 513.

Disturbed Geriatric Patients

SIR,—In our letter (2 September, p. 614), which you were good enough to publish, you have omitted, doubtless for reasons of space, details about the positions held by each of us which were included in our version. We write to correct this, partly because only one of us (and not all three as implied in the published letter) is on the staff of the Department of Psychological Medicine. A more important reason is that our views were derived from experience of co-operation by four separate organizations concerned with the care of the elderly, that are often separated from one another by administrative barriers: the Health and Social Services Department of the City and County of Newcastle upon Tyne; departments of geriatrics in a general hospital and a local mental hospital under the aegis of the regional hospital board; and the University Department of Psychiatry. These facts appeared to us to deserve a note of correction.—We are, etc.,

M. R. P. HALL,
Consultant Physician,
Newcastle General Hospital.

R. C. M. PEARSON,
Medical Officer of Health,
City and County of Newcastle upon Tyne.

MARTIN ROTH,
Professor of Psychological Medicine,
Royal Victoria Infirmary, Newcastle upon Tyne.

Early Discharge of Maternity Patients

SIR,—The leading article "Early Discharge of Maternity Patients" (26 August, p. 508) makes the unqualified statement that "The doubts about the dangers to mother and baby from early discharge are largely dispelled by the Bradford reports" as though this were a new discovery. May I therefore bring to your attention a paper which appeared in the *Lancet* three years ago?[1]

In it you will observe that during a 12-month period in 1962/63, in the County Borough of Wolverhampton, a carefully designed *prospective* survey of *random* early discharge from hospital of 1,044 mothers and 1,044 babies, each of whom was followed up objectively for two months after confinement, made these important findings: that mortality was non-existent in mothers and small in babies; that morbidity was low for both; that neither could be attributed to early discharge; and that race, not duration of stay, was the most decisive and highly significant factor in establishment and maintenance of breast feeding.

It should be added that the final survey confirmed the results of a pilot survey—to test methodology and recording—of 969 simultaneous mother and baby discharges over the preceding twelve months and that it assisted substantially in presentation earlier this year of a case for the revision of the bed ratio on which planning of hospital maternity resources is based.[2]—I am, etc.,

E. D. McEWAN.

Birmingham Regional Hospital Board,
Birmingham.

REFERENCES

[1] McEwan, E. D., *Lancet*, 1964, 2, 744.
[2] —— ibid., 1967, 1, 489.

Future of General Practice

SIR,—Your gratuitous stricture of "successive Ministers of Health" (12 August, p. 383) might have been allowed to pass were it not coupled with that of "their administrations" as being responsible for the recent nadir of general practice, and the lack of "responsibilities towards their medical employees." The "administrations" include doctors, who, by their position, will hardly be able to reply and set the record straight. Not enough is known of their efforts, under what must have been well-nigh impossible conditions, to alleviate the results of B.M.A. policy; their known contributions deserve better.

The previous insistence on the myth of the general practitioner being an independent contractor has been the greatest obstacle to development, which is now hailed as a must. (A re-reading of the Cohen Report[1] will show this.) The recognition that most general practitioners are employees *de facto* if not *de jure* enables them now to claim rights. Their previous "independence" made them shoulder responsibilities that have worn them down. That it is still possible for general practice to develop is a credit (I would hazard) no less to the Ministry's medical advisers than to the political acumen of various Ministers in avoiding the cul-de-sac into which the Association's policy on general practice would have led. The continuous discussion about general practice outside the N.H.S. shows how much further thought is necessary among some influential leaders.

Apart from the political misappraisals, I would suggest that the future role assessment is also incorrect. Is the future development of general practice to be confined to "practice in groups and closer association with hospitals"?

Vickers[2] contrasts inpatient and community medicine; "about 1% of the population at any one time are not to be found in the world of the well." He continues, "The purpose of community medicine is far wider; it is responsible for managing, in the world of the well, the human estate of sickness and mortality. I include in this the management of the non-pathological crises of life, birth, growth, senescence—death also, unless we regard death as always pathological—and the management of all illnesses, whether curable or not." Words which many family doctors will readily warm to. The future of general practice with an ancillary role to the 1% in hospitals seems rather narrow compared with the needs of many of the 99% outside.

It might be that the Seebohm Committee in its deliberations on a family service will suggest a broader role for the general practitioners, but the profession itself must explore and transcend the old definitions in the face of new needs and possibilities. No less than the hospitals, the medical officers of health and community medicine must be seen as points of growth for general practice.—I am, etc.,

Birmingham. BERNARD BARNETT.

REFERENCES

[1] Central Health Services Council, *Report of the Committee on General Practice Within the National Health Service*, 1954. H.M.S.O., London.
[2] Vickers, G., *Lancet*, 1967, 1, 944.

Computer Control

SIR,—May I draw the attention of medical officers who are employed or paid by more than one authority to what can only be called bureaucratic dominance by computer. All employees have to contribute towards the National Graduated Pension Scheme. The maximum amount that can be deducted is 9s. 3d. per month. However, if a person is employed or paid by more than one authority, each authority deducts an amount—scaled down to the gross salary received by each—8s. 7d. being the next rate.

I challenged the Ministry of Social Security about this, and after a lengthy wait I was informed that my county authority was willing to accept the responsibility of paying my full salary, but agreement would have to be reached with my other authorities regarding reimbursement.

The Ministry in its letter to me stated: "In any scheme involving the majority of the working population the rules must be as simple as possible . . . when a person has two or more employments it is easier administratively for each employment to be treated separately and for graduated contributions to be deducted by each employer; excess payment being refunded on the completion of the person's insurance records at the end of the year." The Ministry do not reveal that no refund is made to the employers. The employers' contribution is double that of the employee. In the case of local authorities this means an unnecessary burden being placed on the ratepayers.

I would have thought that the authorities concerned would have been quite capable of making adjustments locally—either by paying the stamp in rotation or by making a cash adjustment. This is not permitted by the Ministry of Social Security—it would interfere with the computer programme.

The amount is small in a monetary sense, but it will not grow less, and the principle of employee and ratepayers being sacrificed to bureaucratic administrative expediency is wrong. I am sure that there must be a considerable number of medical officers in this situation. Is this a case for the Government Ombudsman?—I am, etc.,

ALEXANDER DONALDSON.

Bedlington,
Northumberland.

Night Visits

SIR,—Recently I have had to make four visits during the night to patients who were extremely ill. The first was a lady who I suspected had a pulmonary embolism and whose heart had stopped beating. Fortunately, by means of external cardiac massage and mouth-to-mouth respiration, she survived and is now well. Two of the other cases were old people with acute left ventricular failure, and the last was a patient who unfortunately died of bronchial asthma.

Probably to the delight of the Ministry of Health I am afraid I had neither the time, opportunity, nor inclination to ask them to sign the night-visit form. Could not we be trusted just to sign a list at the end of the quarter giving the names of patients and the nights on which they were visited?—I am, etc.,

King's Lynn,
Norfolk. J. D. WIGDAHL.

Points from Letters

Changed Character of Osteomyelitis

Mr. H. R. W. LUNT (Derby) writes: Two points made by Mr. N. H. Harris (9 September, p. 680) seem to require elucidation: (1) In the matter of operation I have been able to show, among 59 strictly comparable cases of long-bone osteomyelitis, that operation is only of significant value when the patient is received some four days after onset of the symptoms, speaking in general. After this stage pus is usually present, and it is important to let it out as soon as possible. (2) With regard to tetracycline, we find this is indeed a valuable drug.

Role of the Married Nurse

Dr. P. H. KIDNER (London E.9) writes: Nurses, even when wives and mothers, can be of considerable use to the hospital and society. The answer to the married nurse and work is not the crèche. The real answer is the part-time appointment with an adequate salary and proper and permanent status. Like it or not, some such answer will have to be found. The floating population of the "co-operative nurse" is creeping even into the teaching hospital. Many of my colleagues are married to nurses both willing and able to return to work if some attempt is made to meet them half-way. The nursing shortage is becoming acute. The day of the woman completely and utterly dedicated to full-time nursing has gone—and why not? Wives can be nurses and mothers too.

Obituary Notices

H. A. MAGNUS, M.D., F.R.C.P., F.C.PATH.

Professor H. A. Magnus, director of the pathology department at King's College Hospital, London, and professor of morbid anatomy, died suddenly on 12 September. He was 57.

Henry Adolphe Magnus was born on 11 November 1909, and was educated at Mill Hill School and St. Bartholomew's Hospital, London, qualifying with the Conjoint diploma in 1932, and graduating M.B., B.S. the following year. He held early house appointments at St. Bartholomew's Hospital, and in 1934 became resident medical officer at Papworth Village Settlement. In the same year he was appointed research assistant to the bacteriology department at St. Bartholomew's Hospital, and in 1935 became senior demonstrator in anatomy. In 1937 he was appointed lecturer in morbid anatomy and histology. At the outbreak of the second world war he joined the R.A.M.C. as specialist pathologist, serving overseas with the 9th Army and Eastern Command. After demobilization with the rank of lieutenant-colonel he returned to his post at St. Bartholomew's Hospital. In July 1946 he was appointed morbid anatomist at King's College Hospital, director of the pathology department in 1947, and professor of morbid anatomy at King's College Hospital Medical School, University of London, in 1948. In 1949 he became a member of the Royal College of Physicians, and in 1956 was elected F.R.C.P.

Magnus was, in addition, a member of the Board of Governors of King's College Hospital; he was an examiner for the Primary F.R.C.S. and F.F.A. R.C.S., as well as for the University of London and the Conjoint Board. He was a member of the Pathological Society of Great Britain and Ireland, and of the Association of Clinical Pathologists, and honorary secretary and vice-president of the section of pathology of the Royal Society of Medicine. He was honorary secretary of the section of pathology and bacteriology at the Annual Meeting of the British Medical Association in 1949. From 1960 to 1964 he was president of the Institute of Medical Laboratory Technicians, and in 1964 he became a Fellow of the College of Pathologists. Since 1956 he had been a valued member of the editorial board of the *Journal of Clinical Pathology*.

In 1935 he married Miss Kathleen Aiken, who survives him together with their two sons.

A colleague writes: When Magnus came to King's in 1946 the pathology department was just beginning to expand and to recover from the considerable disruption caused by the second world war and the evacuation of the main laboratory to Epsom. His flair for organization soon became apparent, and one of his major memorials at King's is the division of pathology, composed of four academic departments, each headed by a professor. In the early postwar days whole-time academic staff were a new and strange species at King's, and it was very largely due to the immensely human and vital personality of "the Prof." that they became accepted so rapidly. "Dick" Magnus was no dry academic; he had the happy knack of being interested in the patient as well as the disease, in the personality of his medical and technical staff as well as in their academic and professional abilities, and in the welfare of the medical students as much as in their transformation to doctors. Because of his intense interest in people, colleagues and students often sought his advice, and many will remember with gratitude his help in time of difficulty. As a teacher he was most stimulating, seasoning necessary facts with a wealth of apposite stories, and recalling with astonishing and vivid detail illustrative cases from his wide experience. He was popular with the students, and was often depicted with affection in the Christmas pantomime. Outside the hospital he had many interests, particularly gardening and deep-sea fishing. His enthusiasm for these hobbies was infectious; he would often give an entertaining and informative discourse on them, and on life in South Cornwall, where he spent his holidays. His sudden and early death comes as a sad loss to his friends and to King's. To his wife and two sons we offer our sincere sympathy.

EWEN CAMERON, M.D., F.R.C.P.(C.) D.P.M.

Professor Ewen Cameron, who had occupied the chair of psychiatry at McGill University and was the first president of the World Psychiatric Association, died suddenly at Lake Placid, New York, on 8 September. He was 65.

Donald Ewen Cameron was born at Bridge of Allan, Perthshire, on 24 December 1901, and received his medical education at the University of Glasgow, graduating M.B., Ch.B. with distinction in 1924. He took the D.P.M. in 1926, and proceeded M.D. with distinction in 1936. After early house appointments he was for a time assistant physician at Glasgow Royal Mental Hospital with Dr. D. K. (later Sir David) Henderson before going to train and work with Adolf Meyer at Phipps Clinic at Johns Hopkins Hospital from 1926 to 1928, and later with Bleuler at Zurich. At this point he was lost to British psychiatry, and returned to work in the U.S.A., soon becoming psychiatrist-in-chief at Albany Hospital, New York. In 1942 he became an American citizen, but very soon was appointed to the psychiatric department of McGill University, Montreal, Canada, of which he became a distinguished head. Here he became professor of psychiatry and director of the Allan Memorial Institute of Psychiatry. A little later he was chosen to be one of the experts gathered to decide the fate of Hess at Nuremberg, which resulted in his present detention in Spandau, rather than his being executed, because of mental illness. He became president of the American Psychiatric Association as early as 1952, among his many other honours. In 1961 he organized the 3rd World Congress of Psychiatry in Montreal, where the World Psychiatric Association was formed, and he became its first president.

Cameron had great organizing abilities, but he remained a clinician till the end. He always insisted on treating a number of his patients himself personally, rather than sitting too much in his professorial chair, which also carried so many administrative and teaching responsibilities. By this means he always remained aware of the individual patient's problems, and was able to discuss treatment matters from personal experience.

He did not always tolerate fools gladly, but supported with all his energies those he felt were doing all they could to improve the treatment of the mentally ill. He refused to follow the craze for psychoanalysis which swept American medical schools after the second world war. But, like Adolf Meyer and Henderson, he welcomed all types of approach being used at his clinics, provided patients were being helped rather than loose theories being propounded. He became interested in transcultural psychiatry, and encouraged the development of a special department for this. He had enormous numbers of psychiatrists in training, coming from all over the world, towards the end of his climb to world fame.

Cameron died as he would have wished—in full and very active harness, still planning his future research programme, and having specially moved to Albany to work which he could carry on beyond the normal age of retirement. It was also only a year ago that he had given up being the dynamic stimulator of the new World Psychiatric Association, of which he became the first president for a period of five years. He was one of the great clinical school of Scottish psychiatrists which have done so much in the last 50 years to spread good clinical psychiatry all over the world, their country's loss being others' gain. Getting up at 6 a.m. to do his writing, he worked very long hours to the end. He may well have died earlier than he needed to because of all his work for others. Last year, at the 4th World Congress of Psychiatry, he was still full of energy and planning for the future. It is difficult to think of his not being with us any more.

Ewen Cameron, by his work and example, helped not only many psychiatrists to become much better doctors but directly and indirectly helped hundreds and hundreds of patients, both personally and through those he had inspired and taught. He was always helped by a wonderful wife, Jean Rankine, a famous tennis player and a very human person. Her consolation will always be that he died continuing to help others to a better and fuller life, perhaps at the expense of his own health and life. But he would not have wished otherwise. I have lost a much admired and inspiring friend, and so have many other people.—W. S.

R. V. HUDSON, F.R.C.S.

Mr. R. V. Hudson, honorary consulting surgeon to the Middlesex Hospital, London, died in Monmouth on 10 September. He was 72.

Rupert Vaughan Hudson, son of Dr. J. W. Hudson, was born in January 1895, and was educated at Epsom College and the Middlesex Hospital Medical School. His studies were interrupted by the first world war, during which he served with the Hertfordshire Yeomanry and Cavalry Reserve, attaining commissioned rank. He returned to his medical studies on demobilization, and qualified with the Conjoint diploma in 1922. After holding early house appointments at the Middlesex Hospital he was appointed to the surgical staff, and took the F.R.C.S. in 1927. He became lecturer in operative surgery to the medical school and honorary consulting surgeon to the Middlesex Hospital; he was consulting surgeon to the Connaught Hospital at Walthamstow, to St. Saviour's Hospital, and to the Royal Infant Orphanage at Wanstead. Also he was examiner in surgery to the Universities of London and Cambridge, and a member of the committee for the therapeutic trials of penicillin and streptomycin. He married in 1929 Esme, daughter of Gladstone Wilson, and they had a son and two daughters.

D. H. P. writes: Vaughan Hudson left his mark at Middlesex, both as a student and as a member of the consultant surgical staff. Well built and handsome, he was a natural athlete. As a student he was a leading member of all the clubs, excelling particularly at cricket, which he had played for his county as a schoolboy. In spite of his prowess, however, he always regarded games as a secondary pursuit, a striking illustration of this being his turning down the chance to be a regular member of his county cricket team because this would interfere with what he regarded as the more important things of life. He was house surgeon, and subsequently surgical registrar, to Gordon Taylor, who made no secret of the fact that he regarded him as the most brilliant of his young men. On his appointment to the surgical staff of the Middlesex, Hudson was at first junior surgeon on Gordon Taylor's firm. He interested himself particularly in thyroid surgery. With the late Bernard Johnson as his anaesthetist, he developed more delicate and refined techniques for thyroidectomy than were then current in this country, inventing in the process instruments which are still a joy to handle. Just about this time Professor Charles Dodds established in the Courtauld Institute of Biochemistry, under the late Douglas Robertson, a basal metabolic unit to develop the therapeutic possibilities of this investigation in thyrotoxicosis. Until the establishment of the unit this country lagged behind the United States in the treatment of thyrotoxicosis, and many leading thyroid surgeons regarded the basal metabolic rate as unreliable, and as adding nothing to clinical assessment. Robertson and Hudson between them confirmed the American work on the necessity for an objective test to supplement clinical assessment if surgery for thyrotoxicosis was to be safe, and gradually converted the sceptics.

But Hudson's major contribution to medicine did not come till after the second world war and towards the end of his active career. This was the publication, with Dr. Deborah Doniach and Dr. I. M. Roitt, in October 1956, which demonstrated the importance of autoimmune factors in Hashimoto's thyroiditis —a paper which opened the gates for a flood of new investigations which are still profoundly influencing our understanding of disease processes. This work rapidly developed into a highly specialized complex, of which the surgeon perforce became merely an intensely interested onlooker. Hudson, however, deserves his full share of credit for first seeing that an obscure and uncommon condition of apparently minor importance was worthy of intensive investigation. This achievement was not fortuitous but the logical culmination of an attitude of a professional lifetime.

Hudson often found it difficult to express his ideas clearly, but his colleagues learnt that it was unwise on this account to dismiss them. I remember vividly a number of important occasions when Hudson resolved a complex situation of conflicting interests and opinions by reducing it to the two simple questions: what is the course most likely to lead to the advance of medicine? and, what is the course most likely to be for the good of the Middlesex and the medical school? Rupert Hudson managed to combine reserve and dignity with the capacity to be an easy and delightful companion, and he always respected the reserve and dignity of others. These characteristics made him popular with his colleagues, and, combined with his handsome appearance and obvious professional skill, won him the affection of his patients.

ISABEL M. S. REID, M.B., J.P.

Dr. I. M. S. Reid, a general practitioner in East Yorkshire, was killed in a railway accident on 31 July. She was 48.

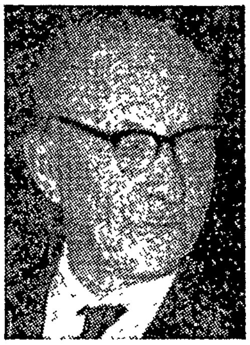
Isabel Mary Smart Reid (née Chalmers) was born in Keith in 1919, and received her medical education at Aberdeen University, where she graduated M.B., Ch.B. in 1942. She started with some general practice at Keith, and then took a post as house-surgeon in Aberdeen Royal Infirmary. After this she was house-officer in obstetrics in the Southern General Hospital, Glasgow. In 1944 she returned to general practice at Inverbervie, and remained there until she married David Reid in 1946. They went to live first at Winchester and then Maidstone, and during this time she maintained her interest in general practice. Twelve years ago the family moved to Hull, where she took a course in family planning and worked in both family planning clinics and public health centres, as well as continuing with general practice. Her major work was in the family planning clinics at Hull and in the East Riding, where she made a valuable contribution. She was appointed to the magistrates' bench a few years ago, where her work was much appreciated. Her humane personality, as well as her professional experience, enabled her to be a most excellent justice.

Isabel Reid was of a happy and kindly disposition which endeared her to all her fellow students in Aberdeen University. In practice and in her hospital work she was admired for her conscientiousness and great efficiency, and was full of unselfish consideration for others, which brought her love and respect from both patients and colleagues. She was devoted to her husband and her two sons, and managed to look after her family as well as maintain her keen interest in medicine. Those of us who had the privilege of enjoying her friendship and the hospitality of her gracious home will especially mourn her sudden passing. She will be sadly missed by all her friends, and our deepest sympathy goes out to her husband and sons in their irreparable loss.—I. M. S. and I. D. I.

F. R. BROWN, O.B.E., M.B., CH.B. F.R.C.S.ED.

Mr. F. R. Brown, surgeon emeritus, Dundee Royal Infirmary, died at his home in Dundee on 7 September after a long illness. He was 77.

Francis Robert Brown, son of a Roxburgh farmer, was born near Melrose on 20 September 1889, and was educated at Edinburgh University, graduating M.B., Ch.B. in 1913. After an early appointment as house-surgeon at Glasgow Royal Infirmary he returned to Edinburgh as house-surgeon at the Hospital for Sick Children. During the first world war he served with the R.A.M.C. in Salonika and the Caucasus. He was thrice mentioned in dispatches, and was awarded the O.B.E., and, in addition, the Order of St. Stanislaus. After demobilization with the rank of major he returned to Edinburgh, and in 1920 was elected a Fellow of the Royal College of Surgeons of Edinburgh, going at the end of the year to Dundee as assistant to the late Professor L. Turton Price. In 1931 he was appointed assistant in the department of surgery at University College, Dundee (now the University of Dundee), and an assistant surgeon at Dundee Royal Infirmary, becoming senior surgeon on the retirement of Professor R. C. Alexander in 1951.



Mr. Brown was an examiner at the Universities of Edinburgh, Glasgow, and Newcastle, and in 1938–9 was president of the Dundee Branch of the British Medical Association. He was a consultant surgeon to the Eastern Regional Hospital Board of Scotland until 1956, in which year he became a senior Fellow of the Association of Surgeons of Great Britain and Ireland. He retired in 1959, but continued in private practice. His wife died in 1952, and he is survived by a daughter and two sons.

D. M. D. writes: For almost 40 years Frank Brown was a notable figure in the medical school in Dundee. A pioneer in many fields of surgery, most notably in the surgery of the heart and great vessels, he remained a general surgeon. He had the gift of a neat, rapid operating technique, so that he never appeared to hurry, even in complex cases, and his results were excellent. After his retirement he had the unusual honour of being appointed reader in surgery at the University of St. Andrews. This by tradition is reserved for members of staff of special distinction.

Frank Brown's original and stimulating mind attracted outstanding young men to his side, and four of his house-surgeons occupy chairs in medical schools at home and abroad. He was an entertaining companion on any occasion, but particularly on his beloved South Esk, where his knowledge of the ways of trout and salmon made a day's fishing a memorable lesson in natural history. Although an outstanding athlete himself, he was a vigorous opponent of professional boxing, pointing out that this was the only form of athletics in which the infliction of head injuries was the primary aim.

His kindness to young men in surgery has left a host of devoted friends all over the world. They will be sad to hear of his passing, but grateful for the memory of a fine surgeon and a good companion.

S. F. S. writes: There are few branches of surgery in which Frank Brown was not actively interested. Although latterly he confined himself mainly to the field of gastroenterology, when first I had the good fortune to work with him he was also busily engaged in cardiac and orthopaedic surgery, and regularly performed leucotomies. He was a supreme technician, unhurried and unruffled, bringing to each operation the scrupulous skill and delicate touch which he had learned from his old teacher, Sir Harold Stiles. The expanding horizons of surgery attracted him; new methods were constantly introduced, and, once mastered, a search for new ventures began. His abiding interest was referred abdominal pain (although he disliked the term), and he contributed a number of papers on this subject. But he also held decided views on other matters—on the dangers of boxing and the use of a round ball in rugby football—and these he forcibly expressed from time to time in the local press. A former Border rugby player, he retained his interest in sport throughout his life. At one time a low handicap golfer, he latterly gave up the game, which he maintained was too easy—"like shooting a sitting bird"—to spend his leisure hours on river and moor. His hospitality to his junior colleagues on the South Esk was generous. He regularly attended meetings of the Moynihan Chirurgical Club, where his infectious good humour and gay spirit made him an ideal travelling companion. He was a man of great charm, modesty, and ease of manner who greatly valued the friendship of his numerous house-surgeons and registrars, in whose affairs he took the keenest interest and pride.

A. M. HENDRY, M.B., CH.B., F.R.C.S.ED.

Mr. A. M. Hendry, a leading Midland orthopaedic surgeon, died in the Queen Elizabeth Hospital, Birmingham, on 10 September. He was 70.

Anthony Morrice Hendry was born at Fraserburgh, Aberdeen, on 11 November 1896, and received his education at Fraserburgh Academy and the University of Aberdeen Medical School. His studies were interrupted by the first world war, during which he served in the Royal Navy aboard a minesweeper. After demobilization he resumed his studies, graduating M.B., Ch.B. with first-class honours in 1924. He became house-surgeon at the Royal Hospital for Sick Children in Aberdeen before moving south to Birmingham, where he was appointed resident surgical officer at the Ministry of Pensions Hospital, Highbury. This step was to determine his whole surgical career, since he worked directly under the late Mr. Naughton Dunn, and through him came under the influence of the late Sir Robert Jones. After some years at Highbury he went back to Aberdeen as assistant in the anatomy department, and took the F.R.C.S.Ed. in 1930. He then returned to Birmingham, and was appointed assistant surgeon to the Robert Jones and Agnes Hunt Orthopaedic Hospital, Oswestry; assistant orthopaedic surgeon to the Corbett Hospital, Stourbridge; and clinical assistant to the Royal Orthopaedic Hospital, Birmingham. He later became senior visiting surgeon to the Robert Jones and Agnes Hunt Hospital, surgeon to the Royal Orthopaedic Hospital, fracture and orthopaedic surgeon to the Corbett Hospital, Stourbridge, and honorary consulting orthopaedic surgeon to the Infirmary, Burton-on-Trent. He also served as orthopaedic specialist to the Ministry of Pensions, Midland Region, and was a member of the medical appeal tribunal of the Ministry of Pensions and National Insurance. During the second world war, in addition to his normal commitments, he became a member of the Emergency Medical Service, orthopaedic surgeon to the War Emergency Hospital at Barnsley Hall, Bromsgrove, and at the Derwen Rehabilitation Centre at Gobowen.

He was a fellow of the British Orthopaedic Association, and served on its executive committee, a member of the Société Internationale de Chirurgie Orthopédique et Traumatologique, and a member of the Naughton Dunn Club. For many years he was secretary to the Midlands Aberdeen Medical Graduates Association, and later became its president. He was vice-president of the section of orthopaedics at the Annual Meeting of the British Medical Association in 1953.

One of Hendry's great contributions to orthopaedic surgery was in the training of young surgeons. He was instrumental in persuading many young Scottish surgeons to come to the Royal Orthopaedic Hospital and to the Robert Jones and Agnes Hunt Hospital to work as residents under his guidance. His surgical judgement was of the highest order, and his operative technique confident and easy. He was never in a hurry, and always had time for every patient and to answer every question. He was a man of unbending principles, yet just and generous, especially towards his juniors. He had a ready wit, and was enthusiastically welcomed at all social functions.

His contributions to the literature were few but authoritative, and his article on the treatment of residual paralysis after brachial plexus injuries is regarded as a classic. He will be remembered for his courtesy, kindness, and consideration by all his patients and for his unfailing generosity by his countless friends.

He married Miss E. M. Lilley in November 1934, and is survived by his widow, by a daughter, and by his sons, to whom we extend our sympathy.—F. G. A.

J. G. STEVENS, M.R.C.S., L.R.C.P.

Dr. J. G. Stevens, formerly in general practice in Tooting, London, died suddenly on 8 August while on holiday in Ireland. He was 76.

John Greet Stevens was born in Portsmouth, on 20 March 1891, of a naval family, and was educated at Portsmouth Grammar School. He received his medical education at Guy's Hospital, qualifying with the Conjoint diploma in 1917. After an appointment as house-surgeon at Guy's Hospital, he served as surgeon lieutenant-commander in the Royal Navy until 1920. In 1919 he went to Archangel in the *London Belle*. After demobilization he became resident medical officer at the Weir Hospital, Balham, later joining the late Dr. M. M. Woods in general practice, and continued working in this district until 1958. For some years he was an anaesthetist at the Weir Hospital and the Fountain Hospital, London.

He is survived by his wife—their only son having been killed in 1943 while serving in the Royal Naval Reserve, Fleet Air Arm.

B. B. writes: I first met Dr. Stevens 40 years ago, when he was anaesthetist at the Weir Hospital, Balham. He was an able and conscientious practitioner with a remarkable clinical instinct. Kind, charming, and very busy, but never in a hurry, he always found time to chat over his cases. Even after his apparent retirement in 1958 he remained a keen clinician, and could be seen at all the local medical meetings. Held in high esteem by his colleagues, he spent his years of retirement doing locums, and was ever ready to give a helping hand. He enjoyed games, and excelled at tennis, which he played regularly, even after he had reached threescore years and ten. John Stevens was truly a family doctor of the old school, and his passing will be mourned by patients and fellow practitioners alike.

TERENCE EAST, M.A., D.M., F.R.C.P.

F. B. writes: The necessarily mainly factual account of Terence East's brilliant career leaves some scope, I feel, for an appreciation of other aspects of this many-sided and erudite cardiologist (obituary, 9 September, p. 68). A period of only three years between his graduation in 1921 and his election to the honorary staff in 1924 indicated not only the outstanding quality of Terence East but also a large measure of luck. But no one deserved this measure of luck more than Terence East, or justified to a greater degree the faith and good judgement of his senior colleagues who appointed him. It was my good fortune to be his first house-physician. I received from him much valuable tuition and encouragement, and many kindnesses. This was always especially gratifying from one who very definitely did not suffer fools gladly. We were especially happy to find him so serene in his retirement, with his many interests, not least in the cultivation of a garden exposed to the full force of Atlantic gales. We mourn the loss of a truly great scholar-physician.

News and Notes

EPIDEMIOLOGY

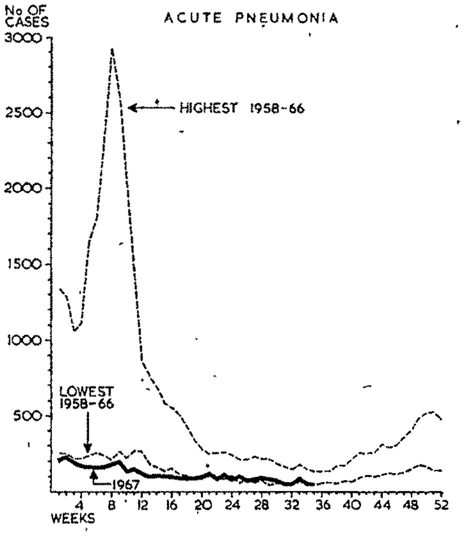
Infectious Diseases

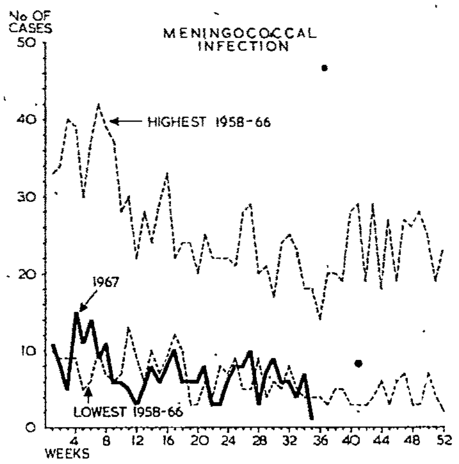
Areas where numbers of notifications were high in the latest two weeks for which figures are available.

	Week Ending 1 Sept.	Week Ending 8 Sept.
Dysentery		
Greater London ...	53	**34**
Redbridge	22	**15**
Lancashire	34	**50**
Yorkshire West Riding	41	**36**
Bradford C.B. ...	9	**10**
Leeds C.B.	16	**16**
Glasgow	58	**33**
Edinburgh	11	**18**
Food Poisoning		
Greater London ...	36	**41**
Havering	9	**15**
Lancashire	25	**25**
Surrey	6	**11**
Yorkshire West Riding ...	4	**14**
Glamorganshire ...	3	**12**
Typhoid Fever		
Warwickshire	0	**3**
Birmingham C.B. ...	0	**3**

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of acute pneumonia and meningococcal infection in England and Wales. Figures for 1967 are compared with the highest and lowest figures for each week in the previous years shown.





INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **2 September** (No. 35) and corresponding week 1966.

Figures of *cases* are for the countries shown and for Greater London. Figures of *deaths* and *births* are for the whole of England and Wales (London included), Greater London, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	1	0		0	0	1	0	
Dysentery ..	208	53	96	6	11	216	35	120	6	6
Encephalitis, acute ..	3	0		0		5	0		0	
Enteric fever: Typhoid ..	3	2	1	0		1	0	0	0	0
Paratyphoid	6	1	0	0		3	0	0	0	2B
Food-poisoning	183	36	15	2		151	26	17	2	
Infective enteritis or diarrhoea under 2 years				11	54				5	57
Measles* ..	1,192	78	4	5	24	3,378	403	33	41	83
Meningococcal infection ..	1	0	4	0		7	1	1	0	
Ophthalmia neonatorum	10	6	2	0		8	2	2	0	
Pneumonia† ..	53	8	77	2		46	6	76	1	
Poliomyelitis, acute: Paralytic ..	1	0	0	0		1	1	0	0	
Non-paralytic	0	0	0			1	0	0		
Puerperal fever§	87	21	3	0		68	22	21	1	
Scarlet fever ..	95	22	10	4	3	134	8	8	4	3
Tuberculosis: Respiratory	173	56	41	5		153	29	34	6	
Non-respiratory ..	34	3	11	0		29	5	11	5	
Whooping-cough	954	132	54	6	22	510	81	70	6	15

DEATHS	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0		0	0	0	0		0	0	0
Dysentery ..	0	0		0		2	1		0	
Encephalitis, acute ..					0					0
Enteric fever ..	0	0	0	0		0	0	0	0	
Infective enteritis or diarrhoea under 2 years	6	2	1	1	2	8	0	1	0	5
Influenza ..	2	0	0	0	1	3	0	0	0	0
Measles ..	0		0	0	0	0		0	0	0
Meningococcal infection ..			0					0		
Pneumonia ..	486	79	16	10	5	464	81	16	9	4
Poliomyelitis, acute ..	0	0		0	0	0	0		0	0
Scarlet fever ..	0		0	0	0	0		0	0	0
Tuberculosis: Respiratory ..	30	4	3	0	1	31	4	1	0	4
Non-respiratory ..				0	1				0	0
Whooping-cough	1	0	0	0	0	0	0	0	0	0
Deaths 0-1 year	213	45	21	8	12	272	54	13	6	11
Deaths (excluding stillbirths)	8,537	1379	465	109	157	8,596	1445	514	94	154
LIVE BIRTHS	13,941	2407	331	241	334	15,062	2570	924	246	293
STILLBIRTHS	182	16	19			254	36	18		

---

* Measles not notifiable in Scotland, whence returns are approximate. † Includes primary and influenzal pneumonia § Includes puerperal pyrexia.

MEDICAL NEWS

Professor of Physiology at Oxford

Professor David Whitteridge, F.R.S., has been appointed to the Waynflete Chair of Physiology in the University of Oxford in succession to Sir Lindor Brown, F.R.S., who has retired from the chair to become Principal of Hertford College. Professor Whitteridge was educated at Whitgift School, at Magdalen College, Oxford, where he took first-class honours in animal physiology in 1934, and at King's College Hospital, taking the B.M. in 1937. Returning to Oxford in 1938, he held a Beit Memorial Fellowship in 1940, the Schorstein Research Fellowship in 1944, and became a University Demonstrator in 1944. Having been a lecturer at Exeter and Balliol Colleges, he became a Fellow by special election at Magdalen College in 1945. In 1950 he succeeded Professor Ivan de Burgh Daly, F.R.S., as professor of physiology at Edinburgh. In 1953 he was elected to the Royal Society, in 1962 he received the Feldberg Prize, and in 1966 he was elected F.R.C.P. Among his other activities have been service as secretary of the Physiological Society between 1947 and 1951 and on its committee 1945–7 and 1951–5, and the presidency of the physiological section of the British Association in 1956. He has also been the editorial chairman of the *Quarterly Journal of Experimental Physiology.* His scientific work has been concerned chiefly with the physiology of vagal sensory fibres, the autonomic responses in patients with spinal injury (with Sir Ludwig Guttmann), the afferent responses from ocular muscles (with Dr. Sybil Cooper and Professor P. M. Daniel), and more recently the organization of the visual pathways and visual cortex.

[Walter Stoneman

Chair of Community Health

Professor Edward Maurice Backett has been appointed to the Foundation Chair of Community Health in the Medical School of the University of Nottingham. Professor Backett, who was educated at University College, London, and Westminster Hospital, qualified in 1944. Subsequently he served in the Royal Air Force, where he studied personnel selection and morale. In 1948 he became a Nuffield Fellow in Social Medicine, and in 1950 he took the M.R.C.P. Subsequently he taught social medicine and epidemiology at Queen's University, Belfast, at Guy's Hospital, and the London School of Hygiene and Tropical Medicine. In 1965 he was elected F.R.C.P.

Professor Backett became the first professor of social medicine in the University of Aberdeen in 1958. This department, which has two associated units (a medical records research unit and a general practice teaching and research unit), has been concerned with the evaluation of health services, the epidemiology of chronic disease, and geriatric care. Professor Backett's research interests have been mainly in the epidemiology of gastrointestinal cancers and duodenal ulcer, the organization of general practice, the problem of accidental death and injury, and in teaching methods. He has been particularly concerned with the development of his subject in Latin America and India, and with collaboration between different disciplines in teaching.

U.S. Professor at Glasgow

Professor Lewis L. Engel, the American Cancer Society professor of biological chemistry at Harvard Medical School, has been appointed to the Macfarlane Chair of Experimental Medicine at Glasgow University. He will work for a year from October in the department of pathology, Glasgow Royal Infirmary, on the biochemistry of endocrine neoplasms. Professor Engel, who is 58, graduated B.S. at Harvard College before beginning his career in research at Columbia University, where he obtained a Ph.D. in 1936. In the same year, after work at the Federal Polytechnic Institute, Zurich, he came to Britain as guest investigator at the Royal Cancer Hospital, London, under Professor J. W. Cook. He returned to the United States as John D. Archibald Fellow and Instructor in Medicine, Johns Hopkins University, and was then appointed instructor in biochemistry, Mayo Foundation for Medical Education and Research. After service in the Army during the second world war he returned to Harvard as tutor in biochemical sciences, and was later appointed assistant professor of biological chemistry at the Massachusetts General Hospital. He became associate professor of biological chemistry, Harvard University, in 1958, and in 1959 Permanent Faculty Fellow of the American Cancer Society. In 1960 he had a period of study at the Chester Beatty Research Institute and the radiotherapy department, Royal Marsden Hospital, London.

International Federation of Surgical Colleges

The International Federation of Surgical Colleges held its annual meeting in Vienna on 4 to 6 September in association with the International Society of Surgery. Professor J. F. Nuboer (Holland) acted as president in the absence of Professor J. Englebert Dunphy (U.S.A.), president, owing to illness. Professor J-L. Lortat-Jacob (France) was re-elected to the executive committee, and Professor Erik Husfeldt (Denmark) was elected chairman of the committee on surgical missions in succession to Professor Carl Semb (Norway). The council welcomed two new member-institutions to the International Federation, the Czechoslovak Medical Society J. E. Purkyne and the Association of Surgeons and Physicians of Malta. There are now 40 national colleges or associations within the Federation. During the year a meeting was held at Colorado Springs, at which particular interest was expressed in international collaboration on problems of traumatic shock. The next meeting of the Federation will be held in Jerusalem, where the hosts will be the Israel Surgical Society.

Order of St. John of Jerusalem

Those recently appointed to, or promoted in, the Most Venerable Order of the Hospital of St. John of Jerusalem include the following members of the medical profession :

As Commander (Brother) : Dr. W. Bain. *As Associate Commanders (Brothers)* : Drs. Kwong Lam Loh, D Paton, and G. B. Robson. *As Officers (Brothers)* : Professor A. J. Craig and Dr. J. Saliba. *As Associate Officer (Brother)* : Dr. W. S. Norton. *As Serving Brothers* : Drs. H. F. Cowper-Johnson, Z. Wisinger, D. Wyndham Evans, W. McIntosh, N. Shlosberg, P. Cassar, and J. F. Cremona.

Postgraduate Medical Education

Dr. J. O. F. Davies, senior administrative medical officer of the Oxford Regional Hospital Board, has been appointed medical secretary to the Central Committee on Postgraduate Medical Education (see *B.M.J.*, 24 June, p. 833). He will be taking up his appointment in October.

William Russ Pugh

In 1847 Dr. W. R. Pugh administered ether to two patients at St. John's Hospital, Launceston, Tasmania. He was the first man to administer an anaesthetic for a surgical operation in Australia. Dr. Pugh, who was a graduate of the Faculty of Physicians and Surgeons of Glasgow and of the Royal Colleges of Edinburgh, died in England in 1897 and was buried at Brighton. The grave and monument are now in poor repair. The Association of Anaesthetists of Great Britain and Ireland and the Australian Society of Anaesthetists have each contributed £25 to a restoration fund. Other contributions should be sent to the honorary treasurer of the Association of Anaesthetists, Royal College of Surgeons, Lincoln's Inn Fields, London W.C.2.

S.R.C. Support for Biological Research

Support of university research in biology by the Science Research Council has increased more rapidly than in any other sector except technology, the Council states in its annual report (H.M.S.O., 6s. 9d.). Research grants current at the end of March totalled over £2m. There were 645 research students, 52 advanced course students, and 46 research fellows. In 1966–7 about 200 new grants to a value of just over £1m. were approved. Awards are made on the advice of the Biology Committee, one of the 10 committees of the university science and technology board of the Council. Besides considering applications for grants the committee seeks out areas of special promise for examination and support. The first selected are industrial biology, regulation of cell activities, and neurobiology. In its report the Council says that the support it will be able to give to university research in the next few years will not match the rate at which requests have been growing. Support will have to be more selective.

Fellowships in Clinical Pharmacology

Applications are invited by Merck Sharp & Dohme Ltd. for international fellowships in clinical pharmacology for 1968. The fellowships are awarded for study in the United States for periods of up to two years. They are open to candidates who have completed the medical curriculum at an accredited school of medicine and are preparing for a career in teaching and research in clinical pharmacology. Further information can be obtained from the Medical Division, Merck Sharp & Dohme Ltd., Hoddesdon, Hertfordshire. The closing date for applications is 1 November.

Postgraduate Tropical Medical Centre

The International College of Tropical Medicine has published its first (September) newsletter. As already noted (see *B.M.J.*, 1966, 23 July, p. 248), it plans to establish in a tropical environment a major centre, including a teaching hospital, research institute, and a school of tropical preventive and social medicine. Professor T. A. LAMBO, dean of the medical faculty at the University of Ibadan, has been elected the first president. The inaugural meeting will be held from 5 to 7 March 1968 at Dakar, Senegal, West Africa.

British Society of the History of Medicine

At the congress held on 6 to 9 September at the University of Sussex, Brighton, Dr. W. S. C. COPEMAN was installed president of the British Society of the History of Medicine in succession to Dr. DOUGLAS GUTHRIE. LORD COHEN OF BIRKENHEAD was nominated president-elect.

T.V. Award for Medical Film

The programme on osteoporosis in the B.B.C. television series "Medicine Today" (see *B.M.J.*, 29 April, p. 295) was given an award at the international festival of medical television education held earlier this month at the University of Western Ontario, London, Canada. The festival was restricted to films designed to aid the continuing education of doctors.

Church Service for Doctors

A service for doctors will be held in All Souls Church, Langham Place, London W.1, on Sunday, 8 October, at 11 a.m. Sir ROBERT DREW and Mr. D. F. ELLISON NASH will read the lessons. Doctors who wish to reserve seats for themselves and members of their families should apply for tickets to the Church Secretary, 2 All Souls Place, London W.1. A buffet lunch will be available at the Royal Society of Medicine after the service at 15s. a head (7s. 6d. for children aged 14 and under). Applications for tickets should be accompanied by remittance.

People in the News

▶ Mr. T. A. CASEY, M.Ch., F.R.C.S., D.O., has been appointed to the corneo-plastic unit and regional eye bank at the Queen Victoria Hospital, East Grinstead, in succession to the late Sir Benjamin Rycroft. The scope and character of the specialized work at this unit will remain unchanged.

Grants and Awards

The British Empire Cancer Campaign for Research has made a grant of £3,100 to Dr. W. R. GREIG, of the University Department of Medicine, Royal Infirmary, Glasgow, for the purchase of equipment to study cell proliferation in the thyroid gland.

Coming Events

King Edward's Hospital Fund for London.—Exhibition, "The Patient in the Community," Hospital Centre, 24 Nutford Place, London W.1. From 25 September, 9.30 a.m. to 5.30 p.m., Monday to Friday.

Chartered Society of Physiotherapy.—Annual Congress, 30 September, Hotel New Ambassadors, London W.C.1.

British Medical Association.—Introductory course on use of computers in medicine, 12 October, Manchester. Details and forms of application from Assistant Secretary, British Medical Association, c/o North West Regional Office, Boyd House, Upper Park Road, Victoria Park, Manchester 14.

University College Hospital Old Students' Association.—Symposium, "The Investigation of Renal Disease," 19 October, 2 p.m., followed by annual general meeting and sherry party. Annual dinner, 20 October, Savoy Hotel, 7 p.m. for 8 p.m. Application for tickets, with remittance £2 5s. a head, to Honorary Secretary, Old Students' Association, University College Hospital Medical School, London W.C.1. Cheques should be made payable to "U.C.H. Dinner Fund."

Societies and Lectures

For attending lectures marked ● a fee is charged or a ticket is required. Applications should be made first to the institution concerned.

Monday, 25 September

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 5.30 p.m., clinical meeting.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—5.30 p.m., combined staff consultation clinical meeting.

KINGSTON-UPON-THAMES MEDICAL CENTRE.—5.15 p.m., slide seminar by Dr. M. E. A. Powell: Liver.●

Tuesday, 26 September

INSTITUTE OF CHILD HEALTH.—At Kennedy Lecture Theatre, 5.30 p.m., Dr. D. G. Freedman (Chicago): Longitudinal Studies of Twins.

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Chelsea Hospital for Women, 2 p.m., Dr. K. A. Newton: Chemotherapy.●

ROYAL STATISTICAL SOCIETY: MEDICAL SECTION.—At Manson Theatre, London School of Hygiene and Tropical Medicine, 5 p.m., Dr. P. M. Fraser: Use of the Computer in the Classification and Diagnosis of Liver Disease.

WHIPPS CROSS HOSPITAL.—At Medical Education Centre, 1 p.m., clinical meeting.

Wednesday, 27 September

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 12 noon, surgical meeting.

ROYAL COLLEGE OF SURGEONS OF ENGLAND—6 p.m., Robert Jones lecture by Mr. A. L. Eyre-Brook: Some Aspects of Congenital Dysplasia of the Hip.

ROYAL FREE HOSPITAL—5.15 p.m., Dr. J. B. L. Howell: The Breathless Patient.

STOKE MANDEVILLE HOSPITAL.—6 p.m., Dr. C. S. Pitcher: Haemorrhagic Disorders.

Thursday, 28 September

INSTITUTE OF OBSTETRICS AND GYNAECOLOGY.—At Queen Charlotte's Hospital, 11.15 a.m., discussion: Erythroblastosis. Speaker, Mr. A. C. H. Walker.●

KINGSTON-UPON-THAMES MEDICAL CENTRE.—2.30 p.m., (1) film: Marrow Puncture; (2) Dr. F. R. Ellis: Indications for Marrow Puncture and Some Typical Appearances.

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS.—4 p.m., William Meredith Fletcher Shaw memorial lecture by Dr. E. A. Gerrard: The Patient as an Individual.●

Friday, 29 September

BROOK GENERAL HOSPITAL.—At Postgraduate Medical Centre, 2 p.m., lecture demonstration by Dr. P. Forgacs: Respiratory Function Tests in Clinical Practice.

KENT POSTGRADUATE MEDICAL CENTRE AT CANTERBURY.—At Kent and Canterbury Hospital, 8.30 p.m., inaugural lecture by Mr. D. W. C. Northfield: Differential Diagnosis of Intracranial Tumours in the Adult.●

Deaths

Bentley.—On 10 September 1967, suddenly, Francis Joseph Bentley, M.D., F.R.C.P., D.P.H.

Corrections

The Newcastle Regional Hospital Board have corrected a recent appointment issued by them and published (29 July, p. 318). E. T. Young, M.B., M.R.C.P. (consultant in geriatrics, Wansbeck), should read (consultant physician, Wansbeck).

The University of Glasgow wish to point out that in anouncing the award of M.D. to Dr. Jean R. Nairn (22 July, p. 253) they omitted to say that it was "with commendation."

In our issue of 2 September 1967, page 606, the publisher of *The Medical Annual*, 1966, was inadvertently given as Longmans, Green, of London. This book was published by John Wright & Sons, of Bristol.

New Issues of Specialist Journals

Obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London W.C.1.

BRITISH JOURNAL OF MEDICAL EDUCATION

Contents of the September issue are as follows:

Editorial.
Association for the Study of Medical Education.
The General Medical Council's Recommendations as to Basic Medical Education 1967:
  1. The Views of a General Practitioner. Ronald Gibson.
  2. The Views of a Teacher of Physiology. K. B. Roberts.
  3. The Views of a Teacher of Medicine. G. A. Smart.
The Role of the University in the Future. Bror Rexed.
Factors Influencing the Development of a Curriculum. V. Ramalingaswami.
The Objective Examination in the Evaluation of Medical Students. H. J. Walton and J. Drewery.
Evaluative Study of a Preceptorship Programme in General Practice for Senior Medical Students. Moshe Prywes, Moshe Sarrell, and Yair Yodfat.
Role of the Peripheral Hospital in Postgraduate Anaesthetic Training. J. D. Hill.
Teaching of Diagnostic Radiology in Britain and the United States. J. H. Middlemiss.
A British View of the American Surgical Residency. Adolf Singer.
Teaching Medical Ethics—Empirical or Rational? I. B. Pless.
Teaching Public Health in the Faculty of Medicine, University of Khartoum, Sudan. Mamoun Yousif.
On Evaluating the Success of Teaching. An Inquiry in London University Medical and Dental Schools. Ruth M. Beard.
Glasgow Conference on Specialist Training. James H. Hutchison.
Book Reviews. News and Notices.

Volume 1, No. 4. Yearly subscription (4 numbers) £3 3s., abroad £3 10s.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON W.C.1. TELEPHONE: 01-387 4499 TELEGRAMS: *Aitiology, London W.C.1.* ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.
Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs.
ADVERTISEMENT AND SUBSCRIPTION ORDERS should be addressed to The Manager at B.M.A. House, London, or at 415 Bourke Street, Melbourne, Victoria, Australia.
MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the British Medical Association, B.M.A. House, London, or to the Scottish Secretary, B.M.A. Scottish Office, Drumsheugh Gardens, Edinburgh.

BRITISH MEDICAL JOURNAL

LONDON SATURDAY 30 SEPTEMBER 1967

Pointers

Facial Palsy: Discussion of the aetiology and the case against surgical treatment (p. 815).

Alcohol and Motoring: Leading article on this page. Report on discrepancies between different methods of testing blood and urine (p. 819). Letter at p. 861. Police tests in hospital (*Supplement*, p. 142).

Tropical Splenomegaly: Patients with idiopathic "big spleen disease" in Uganda treated by splenectomy were symptomatically and haematologically much improved (p. 823).

Plasma Therapy in Haemophilia: Prompt infusion of plasma can reduce duration of incapacity and incidence of new deformities of joints, but there is widespread ignorance about this method of treatment (p. 828). Plasma prophylaxis in Christmas disease (p. 864).

Management of Haematemesis: Gastric cooling as an adjunct to usual conservative treatment in severe cases conferred no extra benefit (p. 831).

Effects of Folate Deficiency: There is a positive correlation between C.S.F. and serum folate activity, but mean C.S.F. folate levels in patients with various neurological diseases were the same as in a control group, except drug-treated epileptic patients who had a high proportion of subnormal folate levels (p. 834).

Amputation in Atherosclerosis: Results using Gritti–Stokes amputation compare very favourably with other techniques and immediate fitting of prostheses has been successful (p. 837).

Brief Case Reports: Myasthenia gravis in two generations of one family (p. 839). Oleogranuloma following self-injection of petroleum jelly (p. 840). Pituitary dwarf attaining age of 77 years before requiring treatment (p. 842). Pyloric obstruction produced by adenomyoma of stomach (p. 843). Spontaneous rupture of uterus at 22 weeks' gestation (p. 844). Compression of spinal cord complicating diaphysial aclasia (p. 844).

Immunization: Schedules (p. 846).

Polycythaemia with Aortic Stenosis: Clinicopathological Conference at the Royal Postgraduate Medical School (p. 848).

"Swabs Correct?": Use of a fixed number of polyurethane sponges in place of conventional gauze swabs could make the swab count an anachronism (p. 852).

Appointment System: Effect of demands for urgent treatment (p. 856).

Whom to Resuscitate: Neasden memorandum and official comment (p. 858). Letter (p. 861) and leader (p. 814).

Hospital Junior Staffs Group Council: Report of meeting, *Supplement*, p. 139.

Organization Committee: *Supplement*, p. 141.

Alcohol and the Law

On 9 October the Road Safety Act[1] comes into operation, making it an offence for a motorist to drive, attempt to drive, or be in charge of a vehicle if his blood alcohol level is over 80 mg./100 ml. or his urine alcohol is over 107 mg./100 ml. This brings Britain into line with the many other countries which have a statutory level for blood alcohol, and reflects the widespread acceptance of the need for measures to reduce the numbers of deaths and injuries caused by road accidents. At p. 819 of this week's *B.M.J.* Professor J. P. Payne and his colleagues comment on the interpretation of tests for alcohol in blood and urine and on the different techniques that may be used.

Payne and his colleagues have confirmed that gas chromatography with an internal integrator—the technique that will be used in police laboratories throughout Britain—is a reliable method of estimating the alcohol content of small volumes of fluid, but they report disturbing discrepancies in the values obtained when different methods of sampling blood were used. When capillary tubes were used the alcohol content of the blood was found to be considerably lower than that of corresponding venous blood. Capillary blood samples from volunteers were analysed in a number of centres (with the co-operation of the Home Office) and wide discrepancies were found in the values obtained from samples in capillary tubes. When the blood was collected in plastic pots more consistent results were obtained, and the levels were closer to those found in venous blood, but there was still disagreement. It seems that the source of these errors is the method used to obtain the sample rather than the technique of analysis. If the operation of the Act is to be fair the Home Office should draw up a protocol for the taking of samples of blood and its subsequent handling which reduces the risk of error to a minimum.

Estimates of the level of alcohol in the urine were the first scientific tests to be used widely in Britain in prosecutions of motorists alleged to have been drinking. Police and police doctors have become familiar with the tests, which have the advantage that it is usually easy to obtain large volumes of urine from the suspect. However, it has long been recognized[2] that the relation of the level of alcohol in the urine to that in the blood is not constant and is influenced by several factors, some known and some unknown. In its report *The Drinking Driver*[3] in 1965 the B.M.A. special committee recommended that blood and breath tests should be used in preference to urine under the law prevailing at that time, and in commenting on the Road Safety Bill during its passage through Parliament the B.M.A. Council stated[4] that it "would prefer samples of blood to be taken in every case."

No doubt recognizing that there could be arguments in court about the conversion factor, the Government has specified 107 mg./100 ml. as the critical level for alcohol in the urine (a second specimen taken one hour after the first). Defence counsel will not be able to challenge the relationship of this level to the blood level of 80 mg./100 ml. Payne

© British Medical Journal, 1967. All reproduction rights reserved.

and his co-workers report the results of estimations of the level of alcohol in the blood and urine of motorists suspected of offences under the present law. When the ratio of blood to urine levels was calculated the range of the factor was from about 1 to about 2.5—much wider than the range found in laboratory experiments on volunteers. So a motorist with alcohol in his body close to the levels laid down in the Act might have a blood level below the limit and a urine level above it or vice versa. Analysis of these results by a professional gambler would lead him to advise suspects to opt for the blood test—but should such advice need to be given? If the Act is to be seen to be fair in its application urine samples should be used as little as possible and if possible not used at all.

Legislation to discourage driving under the influence of alcohol is welcome, and most drivers will want to co-operate. Press comment suggesting that the level of 80 mg./100 ml. is the upper limit for safe driving is dangerous. The ability of most drivers to drive properly is impaired when the blood alcohol is well below this level. Doctors asked for advice by their patients should tell them that they should not drive after drinking. Patients who find this impossible should be told to stick to the "rule of three"—three half pints of ordinary beer or three single-measure whiskies—but those not used to alcohol should take no alcohol before driving. No alcohol should be taken before driving if the stomach is empty; and it is never safe for a person to drive if he feels he has been affected by alcohol. Doctors should also warn their patients against taking alcohol if they are taking drugs such as barbiturates or tranquillizers.

The publicity campaign by the Ministry of Transport is designed to produce better attitudes to drinking and driving. A change in social habits of drivers is more likely if the public is convinced that the element of luck in the application of the new law has been eliminated. This will be the case only if all prosecutions are based on blood samples taken by a uniform procedure which eliminates chance errors.

[1] Road Safety Bill (179), 1967. H.M.S.O.
[2] Haggard, H. W., Greenberg, L. A., Carroll, R. P., and Miller, D. P., *J. Amer. med. Ass.*, 1940, **115**, 1680.
[3] *The Drinking Driver*, 1965. B.M.A.
[4] *Brit. med. J. Suppl.*, 1967, **2**, 67.

Aspirin and Gastric Bleeding

Aspirin was first shown to damage the gastric mucosa 30 years ago,[1] and histological[2] and physiological studies[3] have confirmed that this is a direct toxic effect. Until recently gastric erosions caused by aspirin were thought to result from particles of the drug "burning" holes in the mucosa. However, biochemical and cytological investigations[4] have now shown that soluble aspirin dispersed in saline causes exfoliation of the surface epithelial cells of the stomach within five minutes of ingestion, and D. N. Croft[5] has suggested that this may initiate the formation of haemorrhagic erosions.

The clinical importance of the toxicity of aspirin must be assessed in the light of the huge consumption of the drug in Britain and the two ways in which it is used. Firstly, aspirin is prescribed for the treatment of chronic rheumatic disorders in doses of 1 g. four times a day for weeks or months; and, secondly, a large proportion of the population take it, with or without medical supervision, as an occasional analgesic or antipyretic.

Repeated ingestion of soluble aspirin in the dosage used to treat rheumatoid arthritis has been shown by P. H. N. Wood and others[6–8] to cause chronic gastrointestinal bleeding which can lead occasionally to iron deficiency anaemia.[9] Patients taking three aspirin tablets four times a day were studied by Croft and Wood,[10] who found that of 218 investigated 67% lost 3 ml. to 10 ml. of blood each day. A minority of patients (22%) were insusceptible, losing less than 3 ml. a day, but 11% lost more than 10 ml. daily. These workers also found gastric erosions in specimens removed at partial gastrectomy from subjects who had taken repeated doses of aspirin for a few days before elective surgery. This suggests that chronic bleeding due to aspirin can occur from erosions.

The role of aspirin in the pathogenesis of haematemesis and melaena remains controversial, but there is good evidence for an association between acute bleeding from erosions and the use of aspirin as an occasional analgesic.[11–13] This relationship does not appear to be influenced by the age of the patient or by the frequency of ingestion of aspirin. As aspirin is such a commonly used drug acute bleeding is clearly a rare complication, and carefully controlled studies are required to demonstrate the association. In populations where other factors such as alcohol are more important any role that aspirin has in initiating the bleeding may be obscured. D. J. Parry and Wood have recently[14] described their findings in a careful study of 637 patients admitted consecutively during fifteen months to two medical wards of a hospital in south-east England. The patients were questioned carefully about their ingestion of aspirin during the week before admission. Of 542 patients admitted for complaints other than gastro-intestinal haemorrhage one-third had consumed aspirin—a surprisingly high proportion. The 95 patients admitted with haematemesis and melaena were examined by gastroscopy and if no lesion was found a barium meal was performed. Of those who had a chronic gastric or duodenal ulcer 51% had taken aspirin, which was little higher than the control group. The remarkable finding in this study was that of the 35 patients admitted with acute bleeding who had either an acute gastric erosion or in whom no lesion was found (implying a small acute lesion) no fewer than 33 (94%) had taken aspirin

[1] Douthwaite, A. H., and Lintott, G. A. M., *Lancet*, 1938, **2**, 1222.
[2] Muir, A., and Cossar, I. A., *Brit. med. J.*, 1955, **2**, 7.
[3] Davenport, H. W., *New Engl. J. Med.*, 1967, **276**, 1307.
[4] Croft, D. N., *Brit. med. J.*, 1963, **2**, 897.
[5] —— *J. Pharm. pharmacol.*, 1966, **18**, 354.
[6] Wood, P. H. N., Harvey-Smith, E. A., and Dixon, A. St. J., *Brit. med. J.*, 1962, **1**, 669.
[7] Pierson, R. N., Holt, P. R., Watson, R. M., and Keating, R. P., *Amer. J. Med.*, 1961, **31**, 259.
[8] Stubbé, L. Th. F. L., *Brit. med. J.*, 1958, **2**, 1062.
[9] Summerskill, W. H. J., and Alvarez, A. S., *Lancet*, 1958, **2**, 925.
[10] Croft, D. N., and Wood, P. H. N., *Brit. med. J.*, 1967, **1**, 137.
[11] Waterson, A. P., ibid., 1955, **2**, 1531.
[12] Alvarez, A. S., and Summerskill, W. H. J., *Lancet*, 1958, **2**, 920.
[13] Allibone, A., and Flint, F. J., ibid., 1958, **2**, 1121.
[14] Parry, D. J., and Wood, P. H. N., *Gut*, 1967, **8**, 301.
[15] Langman, M. J. S., Hansky, J. H., Drury, R. A. B., and Avery Jones, F., ibid., 1964, **5**, 550.
[16] Croft, D. N., Pollock, D. J., and Coghill, N. F., ibid., 1966, **7**, 333.
[17] Goulston, K., and Skyring, A., ibid., 1964, **5**, 463.

during the previous week. The likelihood of this finding being due to chance alone was less than one in a thousand. These observations support other evidence[13 15] that aspirin causes acute bleeding from gastric erosions. In this series at least one-third of the acute bleeds appeared to have been initiated by aspirin.

Is it possible to define a population at risk ? Croft[6 10 16] has suggested that resistance to the effect of aspirin in inducing occult bleeding may be due to a higher than normal rate of turnover or replacement of the surface epithelial cells of the stomach. There is no clear answer, however, for acute episodes of bleeding. Parry and Wood investigated the problem by studying 39 of their patients in whom there was strong circumstantial evidence that aspirin had precipitated the haemorrhage. Once the patients had recovered they were given aspirin continuously for a few days and occult blood loss was measured. The subjects were found to be no more susceptible to aspirin, as measured by this test, than was a control group. This suggests that aspirin initiates acute bleeding only at times and under circumstances when the gastric mucosa is temporarily susceptible. It "takes the mucosa by surprise." The factors responsible for enhanced susceptibility require investigation, and may include alterations in the turnover or healing power of atrophic areas of gastric mucosa.

What should the clinician's attitude be to aspirin ? When given continuously it is an invaluable treatment for rheumatoid arthritis and other chronic rheumatic conditions. Under these circumstances iron deficiency anaemia occurs occasionally and patients may need treatment with iron. But there is at present no method of predicting the circumstances in which a patient may be susceptible to the risk of acute bleeding. Those who have had an episode of bleeding should be warned to avoid aspirin. Paracetamol, which does not cause bleeding,[17] is a satisfactory analgesic for occasional use and in intermittent doses it is unlikely to have any other deleterious effects. Surely the time has come to advise patients to keep this drug, rather than aspirin, in the medicine cupboard.

Operations on the Gall Bladder

Modern biliary surgery started 100 years ago when J. S. Bobbs[1] performed the first cholecystotomy, though it was a completely unplanned procedure—the preoperative diagnosis was an ovarian cyst. Despite this century of experience there is still controversy about some aspects of surgery in this region, particularly at the two ends of the spectrum of disease of the gall bladder—symptomless gall stones and acute cholecystitis. Recent careful studies have provided factual information[2-4] to add to the mass of clinical impressions on these topics.

Gall stones are extremely common and their frequency has been well shown by several necropsy studies. Thus G. Horn[2] reviewed some 5,000 necropsies on adults in Birmingham. The overall incidence of biliary stones was found to be 5.8% in males and 13.2% in females. The incidence increased as age advanced so that about 20% of subjects over the age of 70 had calculi. The sex difference was much less definite in the older age groups. M. W. Comfort and his colleagues[3] studied 112 patients in whom stones were discovered incidentally in the course of *x*-ray investigations and found that over a 20-year period half the patients had developed symptoms due to the stones. Recently A. Wenckert and B. Robertson[4] described a similar study in Malmo, Sweden. There were 781 patients with gall stones demonstrated cholecystographically who had neither operation nor complications within the first year of the *x*-ray examination. They were then followed up for a period of 11 years. Half the patients remained symptom-free or had had only mild symptoms. One-third suffered attacks of biliary colic, and many of these were submitted to elective operation. In the remaining one-sixth serious complications occurred, including acute cholecystitis, obstructive jaundice, pancreatitis, and, in three cases, malignant change in the gall bladder. The incidence of complications was higher in patients who were 60 years of age or more, but there was no sex difference. These complications of gall stones are serious, painful conditions, and the conclusion to be drawn is that when gall stones are discovered incidentally in otherwise healthy patients elective surgery should be advised.

Acute cholecystitis is usually treated conservatively in Britain, emergency operation being reserved for patients in whom the diagnosis is in doubt or where the signs indicate progression of the inflammatory process. Elective cholecystectomy is usually advised some three months after the acute episode. The risk of perforation of the inflamed gall bladder is small. H. Ellis and K. Cronin,[5] for example, reviewed 795 patients admitted to the Radcliffe Infirmary, Oxford, with acute cholecystitis. Eleven (1.4%) had bile peritonitis, but only one of these had developed the condition while in hospital, on the seventh day of an undiagnosed illness. The mortality and morbidity rates for operations performed in the acute phase of cholecystitis are usually higher than those in elective surgery. K. A. Meyer and his colleagues,[7] surveying a large series of cases in the department of surgery of the North Western University Medical School, Chicago, found the overall death rate in their series with acute cholecystitis to be 4.5% as compared with 1.1% in those who underwent surgery for chronic cholecystitis. Indeed the mortality rate for cholecystectomy alone when carried out for acute cholecystitis was higher than that for those patients operated upon for chronic cholecystitis even when the latter group had a common duct exploration performed at the same time. Similar results have been obtained by other workers. C. G. McEachern and R. E. Sullivan[7] reported a mortality rate of 5.8% in 155 patients who had emergency cholecystectomy performed for acute cholecystitis, though it should be noted that five of their nine patients who died had perforated gall bladders, and A. W. Hargreaves[8] has recently reported 55 cases treated by emergency surgery at the Salford Royal Hospital; there were three deaths and nine cases of wound infection.

The advocates of early surgery in the acute phase of cholecystitis argue that the operation is easily performed (owing to the presence of inflammatory oedema), the risk of bile duct or vascular damage is small in experienced hands, and readmission to hospital is avoided. Moreover, the later elective operation is often made difficult by the development of dense adhesions around the gall bladder and its ducts.

---

[1] Bobbs, J. S., *Trans. Indiana St. med. Soc.*, 1868, 18, 68.
[2] Horn, G., *Brit. med. J.*, 1956, 2, 732.
[3] Comfort, M. W., Gray, H. K., and Wilson, J. M., *Ann. Surg.*, 1948, 128, 931.
[4] Wenckert, A., and Robertson, B., *Gastroenterology*, 1966, 50, 376.
[5] Ellis, H., and Cronin, K., *Brit. J. Surg.*, 1960, 48, 166.
[6] Meyer, K. A., Capos, N. J., and Mittelpunkt, A. I., *Surgery*, 1967, 61, 661.
[7] McEachern, C. G., and Sullivan, R. E., *Arch. Surg.*, 1959, 78, 300.
[8] Hargreaves, A. W., *Postgrad. med. J.*, 1967, 43, 406.

Like most controversial topics in medicine, the truth probably lies between the two schools of thought. In the early acute case—roughly within the first 48 hours—operation is indeed quite simple and there is no contraindication to its performance in an otherwise fit patient provided a skilled surgeon is available and that there are full facilities for operative cholangiography. Surgery is also indicated if the gall bladder has perforated before admission or if the disease does not settle with conservative treatment, when a cholecystotomy is usually necessary. However, in the patient whose acute attack has been in progress for some days, or who is grossly fat or a poor risk or who is in a hospital where adequate operative facilities are not available, a conservative regimen is the wiser course—better a living problem than a dead certainty.

Nonbacterial Vegetations on the Heart Valves

Nonbacterial vegetations are seen on the heart valves in rheumatic carditis and the Libman–Sacks endocarditis of systemic lupus erythematosus.[1] They consist of platelet aggregates covered with fibrin, and they arise on areas of inflammation and necrosis in the valve substance. Vegetations may also occur on valves that are apparently normal in the condition of nonbacterial thrombotic endocarditis—sometimes called terminal endocarditis because it is usually considered a terminal phenomenon of little clinical significance.[2] [3] In one series it was noted in 78 of 18,486 consecutive necropsies, and in 11 cases there was systemic embolism with infarction, which was in some instances the immediate cause of death,[4] an indication that the condition is not always terminal. It is specially prone to complicate widespread cancer,[5] [6] but it may occur in many other conditions and may be the first indication of a systemic disease.[4]

The valves affected are usually the mitral and the aortic, which show slight degenerative changes in the collagen framework without a cellular reaction. It has been suggested that altered collagen forms the bulk of the vegetations,[7] but they are in fact thrombi developing on slightly abnormal valves.[5] It is likely that in some cases the clotting time of the blood is decreased.[6] The vegetations may become organized, and it is possible that the common Lambl's excrescences, small filiform processes found on the valves of elderly people, have their origin in minute thrombi of this nature.[8] [9]

Nonbacterial valvular vegetations can be produced experimentally in animals by creating an arteriovenous fistula between the femoral or iliac arteries and veins or between the aorta and the inferior vena cava.[10] These vegetations are apt to become infected spontaneously, and if bacteria are injected intravenously a bacterial endocarditis invariably results.[11] It is possible that the cardiovascular stress produced as a result of the shunt leads to minor valve damage which predisposes to thrombosis and bacterial infection. Recently K. Nakao and A. A. Angrist have studied the pathogenesis of these valvular lesions in rats in which arteriovenous fistulae had been produced between the aorta and the inferior vena cava below the renal vessels.[12] They found that the first changes occurred in the loose connective tissue underneath the endothelial basement membrane. There was an oedematous dissociation of the collagen fibres, due probably to a biochemical change in the ground substance. At the site of these lesions there was a patchy denudation of endothelial cells, and platelet aggregation tended to occur on the fibrinoid material consisting of collagen fibres, fibrin, and acid mucopolysaccharide. A constant feature of this type of experiment is hyperplasia of the adrenals. Its cause is unknown, but it has been suggested that excessive production of glucocorticoids plays a part in the connective tissue changes in the valves.[13] [14]

While this experimental work seems to have no immediate application to man, it serves to throw light on the pathogenesis of both nonbacterial thrombotic endocarditis and the bacterial variety, which is a serious complication of pre-existing valvular disease and congenital heart disease. It is interesting that subacute bacterial endocarditis is not uncommon in the elderly, and that in the majority of cases there is no gross valvular disease to account for its localization.[15] [16] It is likely that these "virgin valves"[15] are the seat of nonbacterial thrombotic endocarditis which subsequently becomes infected. It is evident that this variety of vegetation is not necessarily a terminal event or of little clinical importance. In a study of its pathogenesis may lie a greater understanding of the mechanism of bacterial localization in the infective type of endocarditis.

---

[1] Libman, E., and Sacks, B., *Arch. intern. Med.*, 1924, **33**, 701.

[2] —— *J. Amer. med. Ass.*, 1923, **80**, 813.

[3] Gross, L., and Friedberg, C. K., *Arch. intern. Med.*, 1936, **58**, 620.

[4] MacDonald, R. A., and Robbins, S. L., ibid., 1957, **46**, 255.

[5] Barry, W. E., and Scarpelli, D., *Circulation*, 1961, **24**, 882.

[6] Smith, J. P., and Yates, P. O., *J. Path. Bact.*, 1955, **70**, 111.

[7] Allen, A. C., and Sirota, J. H., *Amer. J. Path.*, 1944, **20**, 1025.

[8] Margarey, F. R., *J. Path. Bact.*, 1949, **61**, 203.

[9] Pomerance, A., ibid., 1961, **81**, 135.

[10] Lillehei, C. W., Bobb, J. R. R., and Visscher, M. B., *Ann. Surg.*, 1950, **132**, 577.

[11] —— Shaffer, J. M., Spink, W. W., Bobb, J. R. R., Wargo, J. D., and Visscher, M. B., ibid., 1951, **63**, 421.

[12] Nakao, K., and Angrist, A. A., *Brit. J. exp. Path.*, 1967, **48**, 294.

[13] Angrist, A. A., Oka, M., Nakao, K., and Marquiss, J., *Amer. J. Path.*, 1960, **36**, 181.

[14] Asboe-Hansen, G., in *International Review of Connective Tissue Research*, ed. Hall, D. A., New York, 1963, p. 29.

[15] Anderson, H. J., and Staffurth, J. S., *Lancet*, 1955, **2**, 1055.

[16] Wallach, J. B., Glass, M., Lukash, L., and Angrist, A. A., *Ann. intern. Med.*, 1955, **42**, 1206

Acute Necrotizing Encephalitis

"Encephalitis" is one of the most unsatisfactory clinical diagnoses in neurology. If the illness is mild the patient recovers and the diagnosis is rarely firmly established, while in those seriously ill the diagnosis is often incorrect and if too readily made may mask until too late some lesion such as a tumour or an abscess which may have required urgent surgical treatment. Several devastating affections of the brain which are apparently encephalitic have been classified pathologically, but clinical diagnosis is very difficult and in few of these conditions is either the aetiology or the treatment clear. However, one condition—acute necrotizing encephalitis—is being clinically recognized more frequently by neurologists and neurosurgeons, and evidence is growing that many of these cases are due to the herpes simplex virus. J. Hume Adams and W. Bryan Jennett[1] have recently described eight typical cases and list most of the published accounts. The earlier literature is reviewed by W. Haymaker and his colleagues[2] and by L. van Bogaert and his colleagues.[3]

The disease occurs at all ages and the sexes are equally affected. There may be a prodromal illness with general malaise, pyrexia, and possibly upper respiratory infection, and then over two or three days the patient becomes confused and develops headache of moderate severity, high pyrexia, and slight neck stiffness. Convulsions, which may be focal, often occur and a moderate hemiparesis may develop at the same time or later. The picture is that of a rapidly expanding cerebral lesion, though clinical localization is sometimes difficult and the systemic signs are unusual. The cerebrospinal fluid has a raised cell count (60 to 300 leucocytes/cu. mm.), perhaps a number of red cells, and a high protein but normal sugar content. If the centrifuged deposit is stained and examined the cells may be found to be atypical mononuclears belonging to the plasmacyte series, some showing mitotic figures, the picture suggesting an acute inflammatory process. Electroencephalography shows diffuse slow wave abnormalities often with multiple sharp foci, though the tracing is not diagnostic in any way. A normal E.E.G. virtually excludes the condition. Echo-encephalography may show a non-specific shift of mid-line structures, and arteriography or ventriculography may also suggest a unilateral expanding lesion in one or other temporal lobe. If an exploratory biopsy is carried out, however, necrotic brain only will be found, but specimens of brain taken at this time can be examined for the presence of the herpes simplex virus, and the diagnosis can be confirmed by the demonstration of a rising titre of herpes antibody in the blood.

The mortality rate has so far been very high, but measures aimed at reducing intracranial pressure combined with the use of corticosteroids and antibiotics have apparently saved several patients' lives though leaving some with serious neurological deficits.

The condition can often be recognized macroscopically at necropsy by the markedly asymmetrical oedema and softening of the brain, affecting principally the temporal lobes and posterior orbital gyri, scattered through which are multiple haemorrhagic foci, the lesions often extending across the corpus callosum. Histology shows general changes of encephalitis, but most striking is the selective necrosis in the grey matter and subjacent white matter of the temporal lobes, the orbital and cingulate gyri, and the insula. Occasionally intranuclear inclusions of herpes type may be shown, and when these have been studied by electron microscopy they have been considered confirmatory of the presence of herpes simplex virus.

Whether this condition is due to direct virus invasion or represents yet another antigen-antibody reaction, and whether herpes virus is the only cause or the only one so far demonstrated are all points as yet uncertain. Nevertheless it is important to recognize the existence of the disease not just as a pathological curiosity but as a serious and not too uncommon condition capable of being diagnosed by full neurological and neurosurgical investigation and offering a chance of successful treatment if the effects of the high intracranial pressure can be combated. Herpes simplex encephalitis was at one time too readily diagnosed and fell somewhat out of favour when it was realized that there are several diseases characterized by an encephalopathy with inclusions. Now perhaps it is coming back into prominence in its correct role.

---

[1] Adams, J. H., and Jennett, W. B., *J. Neurol. Neurosurg. Psychiat.*, 1967, **30**, 248.

[2] Haymaker, W., Smith, M. G., van Bogaert, L., and de Chenar, C., in *Viral Encephalitis*, 1958, pp. 95–204, ed. W. S. Fields and R. J. Blattner. Springfield, Ill.

[3] Gruner, J. E., in *Encephalitides*, 1961, pp. 203–282, ed. L. van Bogaert, J. Radermecker, J. Hozay, and A. Lowenthal. Amsterdam.

Increase in Stabbing

Stab wounds differ from other penetrating injuries by being in most cases inflicted deliberately and with malice, but they share with them the possibility of causing deep and serious damage that may go unrecognized until complications develop. For doctors working in accident and emergency departments it is wise to regard all puncture wounds with deep suspicion until the amount of damage done has been established beyond doubt. Deliberate stabbing, accidental stabbing, and falling or being thrown against sharp and sometimes blunt projections[1] have it in common that penetration is forcible, and what the victim feels at the time rarely gives any indication of the depth of penetration or the damage caused. Far from feeling " a stabbing pain," many stabbed persons are aware of no more than a blow, and some do not know that they have suffered injury until they are found to be bleeding.

As much detail as possible should be sought about the direction and force of the blow, about the victim's posture, and about any feelings such as numbness, tingling, and loss of power at the moment of injury. It is particularly important that unconscious persons and victims of assault be examined thoroughly after being stripped because stab wounds may be widespread as well as multiple, and those overlying important organs are not necessarily the most important ones. Useful information may come from any discharge from a wound and from *x*-ray examination.

When exploration is necessary it should be undertaken as a formal surgical procedure, with whatever facilities may be needed to deal with the complications of the wound concerned. Bleeding is the most dangerous.[2 3] Even when there is no evidence of deeper damage, it is generally wise to explore wounds near large blood vessels and wounds of the face and eyelids[4] and of the buttocks and perineum. Nevertheless, it can take a good deal of experience to know not only when to explore but also how to explore a wound that may be small and apparently superficial and harmless. Probing can be a dangerously inadequate test of the depth and importance of a penetrating wound. Senior surgeons should do all they can to pass on their experience to their juniors, which may mean holding themselves in readiness to advise, supervise, or operate in such cases, which are likely to occur during the evenings of the weekend.

Stab wounds of the trunk penetrate the various sections of body cavity less often than might be supposed ; N. R. Batey and G. C. MacBain[5] found that only half did. In the chest emergency thoracotomy is necessary to deal with severe bleeding, a torn bronchus or trachea, and perforation of the gullet. Stab wounds of the lower part of the chest may penetrate the diaphragm and abdominal viscera. Otherwise the active treatment required is usually no more than to drain a pneumothorax, which may be valvular, a haemothorax, and, occasionally, a haemopericardium.

---

[1] Wood, S., *Ann. roy. Coll. Surg. Engl.*, 1961, **28**, 122.

[2] Pridgen, J. E., *et al.*, *Ann. Surg.*, 1967, **165**, 901.

[3] Roberts, G., and Lavelle, E., *Brit. J. Surg.*, 1966, **53**, 88.

[4] Guthleich, A. N., *Brit. med. J.*, 1960, **2**, 842.

[5] Batey, N. R., and MacBain, G. C., *Scot. med. J.*, 1967, **12**, 251.

[6] Mason, J. H., *J. Trauma*, 1964, **4**, 210.

[7] Wilder, J. R., Habermann, E. T., and Schachner, S. J., *Surgery*, 1967, **61**, 231.

[8] Cornell, W. P., Ebert, P. A., Greenfield, L. J., and Zuidema, G. D., *J. Trauma*, 1967, **7**, 307.

[9] Steichen, F. M., Pearlman, D. M., Dargan, E. L., Prommas, D. C., and Weil, P. H., *Ann. Surg.*, 1967, **165**, 77.

[10] Lipschitz, R., and Block, J., *Lancet*, 1962, **2**, 169.

The general rule that stab wounds of the abdomen should be explored needs revision in view of the fact that about half the victims have been found to have suffered no damage to viscera.[5-7] Even when exploration is carried out only in those patients with general or local evidence of serious damage a few bellies have been opened unnecessarily, as it turned out.[6 7] Coeliotomy is unnecessary when a radio-opaque liquid injected through a catheter fitting snugly into the wound does not enter the peritoneal cavity,[8 9] but the further refinement of peritoneal lavage[2] is of value if the liquid is contaminated by bile or intestinal content or if it comes out clear. If it is blood-stained, only exploration will show whether the blood has come from the abdominal wall or from inside it. To sum up, the surgeon who opens the belly to be on the safe side is less likely to make a serious mistake than the one who practises selective exploration, with whatever tests.

It seems likely that violent and malicious fashion has played a part in the recurrent increase in stabbing,[3 5] which has fortunately carried a mortality rate of no more than 10–15%. The heavy sentences that subdued razor slashing in Glasgow[5] and deliberate stabbing of the spinal cord in South Africa[10] might act as a deterrent again.

Senescence

Is there a single cause of ageing, or are there a number of independent ageing processes? The question, asked once more in the latest annual report of the Medical Research Council,[1] is important because it bears on prevention. If the causes of senescence are different in every person control seems unlikely—unless behind the multiplicity of changes there is a further overall process accessible to treatment.

One of the most interesting biological explanations of ageing is the evolutionary and selectionist theory formulated first by J. B. S. Haldane and developed by Sir Peter Medawar. It runs roughly as follows. Once the contribution of an individual to the pool of offspring ceases, so, indirect selection apart, does the power of evolution to select against adverse changes in the individual due to age alone. Indeed, a gene array producing high fertility and vigour in youth but cancer in middle age would be positively selected. In this view ageing is the random accumulation of failures which evolution has failed to suppress.

D. C. Wallace has recently developed this argument further by mathematical studies. The evolution of lifespan is by no means a straightforward business. It is hard to see, for instance, why small birds with a normal wild life of about nine months, a very high random mortality, and early loss of reproductive power should have potential lifespans of nearly 20 years, or why large fish, with 99% of their mortality concentrated in the first few days of life, should have potential lifespans greater still. The general plausibility of the Haldane–Medawar theory remains, however.

Wallace[2] draws from his equations the pessimistic conclusion that, since ageing is a random accumulation of delayed genetic effects, it is unlikely that anything can be done about it: there can be no unitary cause, though there may be consistencies as to which system fails first. This view may be correct, but it is by no means self-evident, particularly in view of the growing body of evidence locating senile deterioration in the store of information in the cell nucleus. In fact if, as Wallace himself agrees, we are dealing with a variety of harmful and accumulating mutations this is in itself an accessible unitary cause, and biochemical geneticists will not share his pessimism. If the stability of the gene can be improved then changes in the individual's genetic composition can be postponed. If this is correct the problem of slowing the process of ageing becomes analogous to that of conservative dentistry, with the conservation of genes substituted for that of teeth. Recent work on antioxidants, antiradiation drugs, lysosomal stability, and other related topics makes it clear that, while it might be difficult to deal with multiple late-acting genetic defects present from birth, loss of information through instability of D.N.A. might well be controllable. There are also rodent experiments which indicate that the "clock" of the lifespan can be considerably slowed by simple calorie restriction. All in all, pessimism over the controllability of ageing derived from mathematical considerations is unlikely to daunt gerontologists in search of a means of tampering with the rate of human decline.

---

[1] *Medical Research Council Annual Report,* 1967. H.M.S.O.

[2] Wallace, D. C., *J. chron. Dis.,* 1967, **20,** 475.

Vital Decision

Not all patients who die should be subjected to attempts at resuscitation. No doctor who himself has had to use modern techniques of resuscitation would suggest otherwise—nor would he be unaware of the distress caused to relatives and other patients in the ward by the failure of a lengthy attempt which should never have been made. Earlier this year we stated[1] that "the close of a long life or an incurable illness should be allowed to occur peacefully." This is in the best tradition of medicine.

To be successful resuscitative measures must be started within a minute or two of cardiac arrest. In hospital the first person on the scene is usually a nurse, who is trained to initiate cardiac massage while medical support is summoned. The doctors who arrive often will not have seen the patient before, and their time will be fully occupied in maintaining oxygenation and the circulation, taking an electrocardiogram, and setting up an infusion to combat the acidosis. This is not a time when anyone can consider the patient's history and diagnosis to decide whether or not resuscitation should be attempted.

So if patients with terminal irreversible disease are not to be resuscitated the individual doctor looking after them must decide this in advance. Nursing and medical staff who may be summoned in an emergency must be in no doubt as to the decision that has been made. The method used at Neasden Hospital (see p. 858) has been the subject of some hysterical and ill-informed comment in the last week. Those unfamiliar with the practical problems find it hard to appreciate that the decision to resuscitate or not must be made before the emergency occurs. Moreover, it must be made known to all concerned. Patients and their relatives need not be alarmed by the recent outcry. The decision is not a difficult one for doctors. Every patient, whatever his age or his disease, should be resuscitated unless the doctor looking after him has no doubt at all that he should be allowed to rest in peace.

---

[1] *Brit. med. J.,* 1967, **2,** 65.

Papers and Originals

Facial Paralysis*

HENRY MILLER,† M.D., F.R.C.P.

Brit. med. J., 1967, 3, 815–819

At first sight facial paralysis seems a banal and even uninteresting subject. After all it is a common condition, often of no great clinical importance, and we deal with most of our cases by rule of thumb. In fact, it poses a number of intriguing and unanswered questions in the fields of anatomy, neurophysiology, and pathology. Its systematic consideration covers a wide range of general medicine, and it affords a promising field for research by the subtle techniques of the applied neurophysiologist, as well as by the simpler methods of the clinician.

If there is one particular lesson to be learnt from a review of this subject it concerns the extent to which therapeutic practice depends on personal impression and uncontrolled observation, rather than on any scientific or rational basis. Nowhere is this more evident than in the case of Bell's palsy, which is bound to occupy a good deal of any discussion devoted to the problem of facial paralysis.

An extensive review of the world literature has yielded no single shred of scientifically valid evidence that surgical treatment exerts a favourable influence on the course of this disorder, yet there are surgeons all over the world who profess an almost religious conviction of its efficacy, and who apparently perform an operation of one kind or another on practically every case referred to them. Some such enthusiasm may of course be a spontaneous manifestation of that innate physical energy and *joie de vivre* that so often distinguishes the surgeon from his more debilitated medical colleagues. On the other hand, I do not find it easy to dissociate the repeated and urgent pleas that reverberate through the American literature describing Bell's palsy as a surgical emergency and begging the physician to refer it at once to the nearest otolaryngologist from the special economic conditions of practice in the United States.

I am reminded of a revealing comment of that great medical historian Henry Sigerist, of Johns Hopkins University, 30 years ago. He observed that the treatment of chronic rheumatism in the United States comprised a prolonged series of expensive injections carried out in the physician's office; in the Soviet Union it consisted of a protracted and expensive course of physiotherapy carried out in a trade union nursing-home on the shores of the Black Sea. We have no evidence to show which of these was the more effective routine, or indeed whether either procedure influenced the course of the patient's disease for better or for worse. What this contrast certainly did reveal was the potent influence of social and economic considerations on medical practice in general and our therapeutic habits in particular. Perhaps the slight hint of therapeutic nihilism that our Continental visitors detect in the British approach to the treatment of facial palsy may not be entirely unconnected with the fact that we work in a professional environment where it is necessary neither to ensure the patient's gratitude nor to impress him with the dynamism of our therapeutic approach.

Clinico-anatomical Considerations

The diagrammatic anatomy of the medical neurologist is of course a far cry from the flesh-and-blood anatomy of the surgeon. It is true also that there are many aspects of the finer structure and function of the facial nerve about which we remain woefully ignorant. However, we know enough to allow us to localize anatomical lesions of this particular nerve on the basis of simple clinical examination, an exercise always pleasurable to the neurologist. Here we will first discuss some of the commoner types of facial palsy as they arise from lesions at various sites on the motor pathway.

Supranuclear Lesions

In the first place it must always be remembered that facial paralysis or weakness may be due to a lesion above the nucleus of the nerve, affecting the corticopontine tract at any part of its course. It may present as an isolated facial paralysis due to a cortical or subcortical lesion, or alternatively as part of a hemiparesis in which infarction or tumour has involved the corticopontine and corticospinal fibres where they are more closely packed together in the neighbourhood of the internal capsule, or lower still in the brain stem. The facial paralysis of a corticopontine tract lesion is characterized by sparing of the upper face. It is not infrequent for a neurologist to be called out to see a patient who is believed to have had a stroke and to observe at once the paralysis of the whole face on the one side that enables him to dispense reassurance that there has been no serious cerebral accident and that the patient is suffering from nothing more serious than a simple attack of Bell's palsy. The upper face escapes in corticospinal tract lesions, because the neurones of the facial nucleus that control movement of the upper face receive impulses from both cerebral hemispheres, while the neurones of the facial nucleus that control the movements of the lower face are activated only by impulses reaching them from the opposite hemisphere.

There is another intriguing feature of facial weakness caused by lesions of the upper motor neurone. Sometimes the involuntary movement of the face that occurs on smiling is retained and may be more than usually conspicuous, even though the patient cannot contract the same muscles at the side of the mouth at all on voluntary movement. This may be very striking, and it is of course never encountered in lesions of the lower motor neurone, where the final common pathway is interrupted and the whole face is paralysed for movement of any kind. There is also a less frequent condition in which the converse is observed: voluntary movement of the face is normal, but emotional and involuntary movement paralysed or weak. This also arises from lesions above the nucleus, but not from damage to the corticopontine fibres of the pyramidal tract. The sites of the lesion or lesions that produce this so-called mimetic facial paralysis are uncertain. They are usually at or below the thalamic level. Sometimes at least they are in the corpus striatum and may be regarded as a localized variant of the remarkable mask-like bilateral facial weakness that is seen in advanced parkinsonism.

---

* Based on a paper delivered at the Second British Academic Conference in Otolaryngology, 4 August 1967.

† Professor of Neurology, University of Newcastle upon Tyne.

There is one other feature of supranuclear palsy that deserves mention. For reasons that are obscure, disease in the temporal lobe sometimes produces facial paralysis closely simulating that caused by a lesion of the opposite facial nerve.

Nuclear and Infranuclear Lesions in the Pons

In the pons, facial weakness may be caused by damage to the nucleus of the nerve, or to its fibres as they pass through the pons in close relation to the sixth nerve nucleus to emerge from its lateral aspect. So there are really two anatomical varieties of intrapontine facial paralysis—nuclear and infranuclear. The widespread employment of vaccination against poliomyelitis may shortly render this disease obsolete, but there can be no doubt that typical lower motor neurone facial paralysis may be a sign, and indeed the only neurological sign, of an acute attack of paralytic poliomyelitis. We are not very likely to make a correct diagnosis of poliomyelitic facial paralysis except under epidemic conditions. On the other hand, such cases have occurred in every major outbreak. There is one clinical feature that might lead the observer to suspect a poliomyelitic aetiology. Poliomyelitic paralysis does not develop out of the blue in a perfectly fit patient. No matter how limited the paralytic phenomena there is likely to be a recent history of fever, headache, and neck stiffness that is lacking in the ordinary case of Bell's palsy. A clue in this connexion may also be furnished by the presence of fasciculation in the facial muscles. This may occur in any severe acute lower motor neurone lesion, but it tends to be more prominent and more constant where the nucleus itself is involved, and should lead one to suspect a nuclear rather than an infranuclear lesion.

If we seek an example of facial palsy of peripheral type arising within the pons from the emerging fibres rather than the nucleus of the seventh nerve, we need look no further than multiple sclerosis. It has often been remarked that facial paralysis is the only lower motor neurone lesion encountered in this puzzling disorder. It is not uncommon, and may either herald the onset of the disease or occur at any time during its course. Like most of the lesions of multiple sclerosis, facial palsy tends to recover. It can sometimes be distinguished from Bell's palsy by the absence of initial pain and by the fact that taste is not involved. This is, of course, because the lesion is due to a patch of inflammatory oedema or demyelination within the white matter of the brain stem, where the afferent fibres conveying taste in the accompanying *nervus intermedius* of Wrisberg have already left the entering facial nerve trunk on their way to the medullary *nucleus solitarius*. Unexpectedly, the facial paralysis that develops in the course of multiple sclerosis is infrequently associated with the concurrent involvement of the sixth nerve that might well be expected in view of the site of the lesion, or with the severe and prolonged vertigo that characterizes a more diffuse acute pontine lesion in multiple sclerosis.

The fact that flaccid palsy of the face may originate in the brain stem and not merely from the banal lesion of the facial nerve associated with the name of Sir Charles Bell emphasizes the need for neurological examination in facial paralysis to ensure that more generalized or serious disease of the nervous system is not overlooked.

Facial Nerve in the Cerebellopontine Angle

When the seventh nerve leaves the lateral surface of the pons it has a short intracranial course in the cerebellopontine angle before it enters the internal auditory canal, and in this situation it is susceptible to a number of pathological processes that often involve paralysis of other cranial nerves. The commonest cause of unilateral facial palsy originating in this part of the nerve is a space-occupying lesion, characteristically acoustic neurofibroma. Meningioma, chordoma, and aneurysm of the basilar artery are less frequent. Curiously, taste is often spared in lesions here. Paralysis arising at this site is often bilateral and may occur in any variety of chronic meningitis. The successes of chemotherapy have reduced the number of such cases, and today even syphilitic basal meningitis is a rarity. At the present time the commonest form of chronic meningitis is carcinomatosis, which often affects the facial among other cranial nerves.

Involvement of the nerve in its intracranial course before it enters the auditory canal is also the source of the bilateral facial weakness often encountered in the Guillain–Barré syndrome, a widespread lesion, certainly inflammatory and probably allergic, characterized by demyelination of proximal nerve roots with relative preservation of the axonal fibres themselves.

Lesions in the Internal Auditory and Facial Canals

Most cases of facial palsy originate in the bony canal that the nerve traverses between the internal auditory meatus and its emergence at the stylomastoid foramen. The most important cause within the internal auditory canal is acoustic neuroma, but whatever the lesion anatomical considerations predicate the frequent involvement of the eighth nerve. In severe cases paralysis of the greater superficial petrosal nerve, which leaves the geniculate ganglion, causes loss of both affective and reflex tear formation, and interruption of conduction in the chorda tympani leads to loss of taste in the anterior two-thirds of the tongue with diminished salivation. Where the patient escapes deafness, paralysis of the nerve to the stapedius occasionally leads to hyperacusis. Rarely a neurofibroma originates from the sheath of the facial nerve itself with similar results, and in exceptional cases changes seen on an *x*-ray film may indicate the origin of a similar syndrome in an intratemporal dermoid cyst.

The geniculate ganglion owes its picturesque reputation in clinical neurology to the historic contribution of Ramsay Hunt in 1907, who described the condition known as geniculate herpes—a syndrome consisting of acute facial paralysis and a rash in or behind the ear, with or without deafness and vertigo. That such a syndrome is occasionally encountered cannot be denied, but that it arises from changes in the geniculate ganglion itself is open to question. The frequent relation of the syndrome to herpes zoster is indubitable, and has been confirmed by serological tests. However, the situation of the rash is inconstant, and it may be present on the tongue, in the trigeminal distribution, or even in the upper cervical region. Zoster is a general infection by a neurotropic virus, and the fact that every level of the sensory system is pathologically affected probably accounts for the extreme intractability of post-herpetic neuralgia. Facial palsy is one of the uncommon motor complications of zoster which are probably due to a spread of virus from sensory to motor neurones, producing a lesion comparable with that of poliomyelitis, rather than to the inflammatory swelling of the nerve trunk in the facial canal so often suggested as its basis. If the paralysis is indeed due to invasion of the motor nerve cell by virus, peripheral decompression of the nerve is unlikely to help.

There are some conditions other than Bell's palsy, chronic otitis, cholesteatoma, and mastoidectomy that may affect the facial nerve in its bony canal. Among the most important is head injury, and this presents some points of special interest. The first is that post-traumatic facial paralysis nearly always recovers spontaneously. I know that some surgeons operate on these cases as a routine; their example is not followed by English neurosurgeons. Indeed, my own experience and that of the Newcastle School of Neurosurgery, as well as that of such authors as Ritchie Russell (1960) and Brodie Hughes (1964), indicate such a good outlook as to permit the argument that leaving the condition alone produces results that are actually better than, and not merely as good as, those of operation. The small proportion of cases where there is no recovery arise where the facial nerve has been actually torn across in a severe fracture of the middle fossa. With this exception post-traumatic facial palsy nearly always shows good recovery, whether it is sustained at the time of injury, develops within two or three days, or—as occasionally happens—begins two or three weeks after the accident.

Facial paralysis complicating head injury is, of course, commonest where there has been bleeding or a discharge of spinal fluid from the ear, and there is often coincident deafness from middle-ear damage. Taste is frequently involved.

There are some rarer but interesting causes of paralysis of the facial nerve arising in this part of its course. It may be compressed by leukaemic deposits. It is a well-known occasional manifestation of severe hypertension, occurring acutely, for example, in the child with acute glomerulonephritis or in the pregnant woman with toxaemia, probably due to haemorrhage into the canal. Sarcoidosis is another occasional cause in a young patient, with a negative Mantoux reaction and often with uveoparotid fever or systemic evidence of sarcoidosis. In most such instances the paralysis is bilateral and is due to granulomatous involvement of the nerve either within or just outside the auditory canal. Again, although decompression has been advised, spontaneous recovery is usual.

Before we consider Bell's palsy, some lesions of the facial nerve after it has left the stylomastoid foramen deserve brief mention. The trauma of a stab wound or of parotid gland surgery are occasional causes. Prolonged excessive opening of the mouth during dental procedures is occasionally responsible. However, probably the commonest mechanical cause is forceps delivery or difficult labour, and in these instances the complete or partial flaccid weakness of the face that ensues usually recovers within a week of the baby's birth. Parotid tumours themselves often cause facial paralysis, and this tends to be subacute and to involve the branches of the nerve unevenly and progressively. Leprosy produces a rather similar neurological lesion, but it is worth noting that this is the only cause of bilateral facial paralysis in which the upper face is more often affected than the lower.

Bell's Palsy

Bell's palsy can often be distinguished from other forms of facial paralysis by the local pain that precedes it, usually with tenderness on pressure over the stylomastoid foramen in front of the ear, and also by the acuteness with which the paralysis develops. Often this is already virtually complete when the patient becomes aware of its existence, and it is exceptional for its development to occupy more than a few hours. Food sticks uncomfortably in the cheek because of buccinator paralysis, inadequate closure causes the eye to water, and in the elderly all the muscles of the affected side of the face sag. Slight deafness and tinnitus may occur but are always transient. The ear-drum may be pink and congested. Loss of taste occurs in about 10% of cases: for the most part these are more than averagely severe, and the symptom is of unfavourable prognostic significance. Though the sensory fibres of the facial nerve are probably involved in severe cases, the loss of sensation behind the ear that might be anticipated is never encountered, almost certainly because of overlap.

The history of an acute and non-progressive lesion is characteristic, and though this may also be a feature of facial paralysis in multiple sclerosis (unilaterally) and the Guillain–Barré syndrome (bilaterally) pain is absent in both these instances.

Differential diagnosis is implicit in the accounts that have already been given of other kinds of facial paralysis. Under outpatient conditions middle-ear disease, significant deafness, hypertension, involvement of other cranial nerves, and evidence of organic disease of the nervous system must all be carefully excluded. If these precautions are taken in cases where the history is typical, the chances of serious diagnostic error are probably less than in most neurological disorders. The serological exclusion of syphilis is traditional, but I have never found it contributory, nor have I ever found facial paralysis to be a harbinger of diabetes. It is more important to bear in mind that *progressive* paralysis virtually excludes the banal diagnosis.

Recurrent Bell's palsy rightly arouses suspicion, but the condition is not very uncommon, especially in younger patients, in whom the nerve may be affected on both sides at different times. The occasional familial incidence of this syndrome suggests the incrimination of some minor anatomical anomaly.

Prognosis and Sequelae

Arguments about prognosis are confused by a frequent failure to distinguish complete from functionally adequate recovery. It is certainly true that nine out of 10 patients with Bell's palsy do well enough from the functional and cosmetic points of view to make routine surgery unjustifiable. This is not to say that they recover completely. In some, either inappropriate associated movement or a shadow of residual weakness is detectable on careful examination, but amounts to nothing in the way of actual disablement. If any voluntary movement whatever is present five days after the onset, functional recovery will be nearly perfect, even where some evidence of denervation and reinnervation remains.

The fact remains that in about 10% of all cases there is persisting paralysis, often with troublesome permanent sequelae. Nearly all these patients have shown a complete loss of nerve conduction within a few days of onset, and in most of them taste has been noticeably impaired. The sequelae include ectropion, facial contracture on the affected side, inappropriate contraction of the affected side of the face on contraction of the normal side, and occasionally clonic facial spasm or crocodile tears, both of which usually begin some months after onset. Numerous explanations have been offered to account for crocodile tears, but the likeliest is misdirection to the lacrimal of regenerating fibres intended for the salivary glands. The failure of co-ordinated facial expression evident in closure of the eyelid on opening the mouth after recovery from Bell's palsy is also probably due to misdirection of regenerating axones.

Early Recognition of Unfavourable Cases

The real issues concern, firstly, the early recognition of this small proportion of unfavourable cases, and, secondly, a critical examination of the evidence that any of the surgical measures advised have been convincingly shown to improve the outcome.

In about 50% of all cases conduction time in the peripheral part of the facial nerve is never impaired, electromyographic fibrillation never appears, and recovery will be complete. In rather more than 30% a transient slowing of conduction indicating partial denervation occurs, but functional recovery is complete. In a minority, however, the nerve becomes unresponsive to stimulation within a few days of the onset and denervation is complete. It is this group that furnishes the residue of cases with persisting paralysis and the complications already described. Electromyographic evidence of fibrillation may be delayed for two to three weeks, and is therefore of little value in any early decision about surgical decompression. Since perfect or at any rate adequate recovery is almost certain unless complete denervation is present at the end of the first week, conduction velocity should be measured at this stage in patients who show no sign of recovery. The high correlation of denervation with loss of taste confirms the prognostic value of this symptom.

Dr. Taverner has been a pioneer in this field (Taverner, 1959 ; Langworth and Taverner, 1963). It is clear that the combination of simple clinical and electrophysiological data facilitates prognosis and the formulation of criteria on which to base controlled therapeutic trials.

Unfortunately the proponents of surgical decompression can quote no such controlled observations, and base their practice on the uncertain grounds of theoretical justification and clinical impression. To the best of my knowledge the nearest published approach to a controlled trial of this form of treatment is found in some fragmentary but suggestive observations made at the Royal Free Hospital in London (Groves, 1965). Groves selected 10 cases of Bell's palsy in which nerve conduction had been lost, thereby fulfilling Dr. Taverner's criteria for complete denervation, and decompressed the nerve in five of these patients shortly after onset. These five did worse than a similar group who declined operation (Groves, 1967). The figures are small, but the value of decompression would need to be firmly established on the basis of similarly strict criteria.

Where is the Lesion ?

The site of the lesion in Bell's palsy has been sought by neurophysiological methods and by surgical exploration. Jepsen (1965) and Zilstorff-Pedersen (1965) used similar techniques, comprising quantitative studies of taste, elicitation of the stapedius reflex, and measurement of lacrimation. Their results were identical. Except in a very small minority of cases the lesion was localized below the geniculate ganglion, and in about half below the origin of the chorda tympani. Of those above the chorda tympani about half are above the nerve to the stapedius and half below. In other words, the findings of applied neurophysiology support those of the many surgeons who have decompressed the nerve, and confirm Sir William Gowers's clinical pronouncement that the lesion involves especially the part of the nerve trunk that lies within the lower part of the facial canal.

Recalling similarly graphic descriptions of the operative appearances of the sciatic nerve in syndromes which we now know to have had their origin at a much higher level from disc prolapse, the physician may be pardoned an unworthy suspicion that the surgeon who describes the swollen and congested facial nerve observed at operation for decompression is less likely to be familiar with the appearance of the entirely normal nerve under similar circumstances. He may even have some reservations about statements that the histopathological findings encountered in the very rare cases that have come to necropsy favour an ischaemic rather than an inflammatory pathogenesis, or that swelling of the nerve within its sheath is more significant than compression by the bony canal. However, he will be more impressed by experimental observations that transient facial paralysis can be produced in the experimental animal by injection of saline into the nerve within but not outside the facial canal (Jain and Sharma, 1964). This experiment may well be relevant to both the pathogenesis and the prognosis of Bell's palsy. It would fit well with the varying severity of the lesion and with the concept of an initial simple conduction block, below which the nerve will remain healthy, with a normal conduction velocity, unless compression is sufficiently severe and prolonged to cause death of the axone below. Such a view of the lesion is compatible with everything we know about the pathogenesis of Bell's palsy, but contributes nothing to aetiological knowledge, a situation with which we are all too familiar in neurology.

Aetiology

Both sides of the face are equally affected, the disease is somewhat more frequent in older age groups, it manifests no convincing seasonal incidence, and it does not occur in epidemic form. On the other hand, we know that acute facial palsy occurs as an occasional complication of certain virus infections, as well as quite often in the course of the Guillain–Barré syndrome. We remain uncertain whether the pathology in these cases is similar to that of Bell's palsy, and in the case of the Guillain–Barré syndrome the initial lesion is in fact likely to be both demyelinative and more proximal, in keeping with the general pathology of the condition.

It is truly remarkable that we really have no idea regarding the cause of this simple and ubiquitous condition, and are uncertain whether it is a result of ischaemia produced by exposure to cold, due to virus infection, or a variant of the allergic neuritis that can be produced by antigen-antibody reactions both in man and in the experimental animal. Bell's palsy takes its place among such mysterious conditions as neuralgic amyotrophy, retrobulbar neuritis, and paralysis of the long as well as the short nerve of the distinguished anatomist who gave it his name (Bell, 1829).

Treatment

Only 10% of all patients with Bell's palsy are ultimately dissatisfied with the outcome. Recovery may not be electrophysiologically or even clinically complete, but it is functionally and cosmetically adequate. The value of radical treatment can be assessed only by its effect on this critical 10% of patients.

With regard to general management, the elderly patient may need to be reassured that the condition is not a stroke. Neither massage nor galvanism has any proved value in the treatment of this condition, and merely fill the physiotherapy department with people who should be at work. There is no earthly reason why cervical sympathetic blockade should be of value in Bell's palsy and no evidence that it is. Few of my patients have found the wearing of a wire splint or a piece of strapping on the face worth the trouble involved, but some with persistent paralysis have been helped by plastic surgery.

I have never referred a patient for surgical decompression, and in view of recent therapeutic developments I am unlikely to do so in the future. What is really important, where the paralysis is severe enough to prevent reflex blinking, is to protect the eye. If complete disappearance of reflex blinking leaves a good deal of cornea permanently exposed a patch should be worn over the eye and bland drops used several times daily. The reflex usually recovers fairly quickly, but if not the help of an ophthalmologist should be sought in management.

The validation of treatment with A.C.T.H. represents the most important therapeutic advance in the history of Bell's palsy. Dr. Taverner's careful observations (Taverner *et al.*, 1966) confirm my own less organized experience that really early treatment is highly successful. Recent controlled observations in Manchester have confirmed a similar though rather less dramatic efficacy of the same form of treatment in retrobulbar neuritis (Rawson *et al.*, 1966). With regard to Bell's palsy, a form of treatment that produces satisfactory results in 76 out of 77 cases leaves little room for improvement. The earlier treatment begins the better, and even on present evidence both efficiency and economy might best be served by side-stepping special investigations and regarding the condition as one to be treated at once by the general practitioner with a short course of A.C.T.H. Direct evidence of the effectiveness of prednisone in the treatment of this condition is lacking, but it is possible that in really adequate dosage it would prove as effective as the less convenient pituitary hormone: a careful trial of early treatment with the oral preparation would be a very suitable project for the Research Committee of the College of General Practitioners.

REFERENCES

Bell, C. (1829). *Phil. Trans.*, **119**, 317.
Groves, J. (1965). *Arch. Otolaryng.*, **81**, 486.
—— (1967). Personal communication.
Hughes, B. (1964). *Acute Injuries of the Head*, 4th ed., edited by G. F. Rowbotham, p. 428. Edinburgh.
Hunt, J. R. (1907). *J. nerv. ment. Dis.*, **34**, 73.
Jain, S. N., and Sharma, A. P. (1964). *J. Laryng.*, **78**, 266.
Jepsen, O. (1965). *Arch. Otolaryng.*, **81**, 446.
Langworth, E. P., and Taverner, D. (1963). *Brain*, **86**, 465.
Rawson, M. D., Liversedge, L. A., and Goldfarb, G. (1966). *Lancet*, **2**, 1044.
Russell, W. R. (1960). *Injuries of the Brain and Spinal Cord, and Their Coverings*, 4th ed., edited by S. Brock, p. 124. London.
Taverner, D. (1959). *Proc. roy. Soc. Med.*, **52**, 1077.
—— Fearnley, M. E., Kemble, F., Miles, D. W., and Peiris, O. A. (1966). *Brit. med. J.*, **1**, 391.
Zilstorff-Pedersen, K. (1965). *Arch. Otolaryng.*, **81**, 457.

Observations on Interpretation of Blood Alcohol Levels Derived from Analysis of Urine

J. P. PAYNE,* M.B., F.F.A. R.C.S., D.A.; D. V. FOSTER,* T.D., M.R.C.S., L.R.C.P.
D. W. HILL,* M.SC., PH.D., F.INST.P., C.ENG., F.I.E.E.; D. G. L. WOOD*

Brit. med. J., 1967, **3**, 819–823

For many years it has been customary to derive blood alcohol concentrations from the analysis of urine, and despite the fact that the accuracy of such derivations has often been questioned British courts have been content to accept them as evidence in prosecutions for drunken driving, presumably on the grounds that such evidence was merely confirmatory and not vital. However, with the impending change in the law which will make it an offence to drive with more than a stated amount of alcohol in the blood, the reliability of the method of determining blood alcohol concentrations assumes much greater significance, particularly as the use of urine analysis has not been excluded (Ministry of Transport, 1965).

In the interpretation of blood levels derived from urine analysis two problems arise. The first concerns the accuracy of the analytical method used to measure the alcohol concentration in urine, and the second is related to the choice of the conversion factor for the derivation of blood level. In the case of urine analysis the accuracy of the Nickolls modification of the Cavett technique is well established, but the method is tedious, time-consuming, and critically dependent on the technical skill of the operator. Gas chromatography is free from these disadvantages (Chandela and Janák, 1960), and it is claimed that when used in combination with an internal standard and an integrator the alcohol content of a minute sample of either blood or urine can be measured accurately within five minutes (Curry, Walker, and Simpson, 1966). One purpose of the investigation to be described was to determine the accuracy of the gas chromatographic method.

In the case of the conversion factor no unanimity of opinion exists about the correct choice, and it was the second purpose of the investigation to examine the validity of the conversion factor of 1.33 recommended in the Report of a Special Committee of the British Medical Association (1965).

Material and Methods

During the Christmas period of 1966 and the succeeding weeks one of us (D. V. F.) in his capacity as police surgeon obtained two specimens of urine at known time intervals and one of venous blood and sometimes one of capillary blood from 35 motorists suspected of driving under the influence of drink. The times at which the samples were obtained were noted and the samples themselves were divided into three equal parts for distribution to the suspect, the police laboratory, and this department. Anonymity was preserved by the designation of a reference number. Initially the samples were analysed both by the Nickolls (1960) modification of the Cavett technique and by the gas chromatographic technique described in detail by Curry *et al.* (1966) but modified to use a Poropak Q porous polymer bead column instead of a polyethylene glycol 400 column. The Poropak column offers the advantage of a much lower column bleed and elutes the water peak first after 30 seconds followed by ethanol at 1.5 minutes and n-propanol at 3.5 minutes. With polyethylene glycol, unless the column is carefully conditioned with water before use, a tailing water peak is produced which prolongs the analysis. Latterly the samples were analysed by the gas chromatographic method alone.

For chromatographic analysis the blood or urine sample was diluted with ten times its volume of an aqueous solution containing 24 mg. of propranol per 100 ml. to act as an internal standard. One microlitre (μl.) of this diluted sample was injected into the Poropak Q chromatographic column maintained at 170° C. The resultant peaks were detected by a flame ionization detector and the output signals fed into a digital integrator. Whenever possible the analyses were carried out in triplicate.

The accuracies of both the Nickolls and the gas chromatographic methods were tested by analysing samples of pure water and normal blood to which known quantities of alcohol had been added to achieve a range between 52 and 242 mg./100 ml. The purity of the absolute alcohol used in the preparation of standards was certified by the Laboratory of the Government Chemist using a refractive index method, as were the dilute solutions of standards. The solutions themselves were prepared by weight by means of an accurate analytical balance to achieve an alcohol content in distilled water which was between 30 and 32 mg./ml. In the preparation of the blood samples the alcohol solution was added by weight to a flask containing a known weight of blood equivalent to not less than 50 ml. The blood itself was magnetically stirred during and after the transfer for five minutes.

When the values for urine and the corresponding venous blood had been obtained it became obvious that additional information on urine: blood ratios would be an advantage. The co-operation of the forensic laboratories was sought and Dr Morgan, of the Department of Industrial and Forensic Sciences in Belfast, supplied values additional to those already published (Morgan, 1965), which allowed a more extensive statistical analysis based on a computer programme specifically designed for the purpose. The programme was used to obtain mean urine and blood values together with their standard deviations, to calculate individual and mean urine:blood ratios, and to determine their distribution. In the case of our own observations a corrected urine:blood ratio was also derived which took into account the time difference between the collection of the venous blood specimens and the corresponding second urine specimens.

---

* Research Department of Anaesthetics, Royal College of Surgeons of England, London W.C.2.

Because of the suggestion that capillary blood could provide a satisfactory answer to the problem of blood sampling, both venous blood and capillary blood samples were collected whenever possible. The venous samples were obtained in 20-ml. Steriseal syringes from a superficial vein on the forearm after preparing the skin with cetrimide *B.P.* solution. After collection the samples were decanted into the standard 5-ml. fluoride-oxalate bottles available in the police station. The capillary samples were obtained from a stab puncture on the ball of the thumb and collected in capillary tubes or in plastic pots.

Four types of glass capillary tubes were used. The first was the standard straight capillary tube (type D.551) supplied for blood-gas estimations by Radiometer Limited, Copenhagen. These tubes are heparinized, have a capacity of 60–80 µl., and are fitted with plastic caps and a magnetic armature to facilitate mixing. The second type was also straight but was larger, with a capacity of 150 µl., and was coated with fluoride-oxalate. These tubes were manufactured by Harshaw Chemicals Limited, of Daventry, for the East Midland Forensic Science Laboratory. The third type was U-shaped, had a capacity of 140 µl., and was supplied to the Northern Forensic Science Laboratory by MacFarlane Robson Limited, Blaydon, Newcastle upon Tyne. Fluoride-oxalate was used to prevent clotting in the U tube and also in the fourth type, which was S-shaped with a capacity of 150 µl. The S-shaped tubes were made by Morbank Limited, of Pontypridd, for the Home Office Central Research Establishment. Both the U-shaped and the S-shaped tubes were originally designed to facilitate weighing on a torsion balance in relation to the estimation of blood alcohol content by another technique. The polypropylene plastic pots, which were heparinized, had a capacity of 300 µl., and were supplied to the North-Western Forensic Science Laboratory by Tinker Grayson Limited, Huddersfield.

Early in the study certain discrepancies were noticed in the determinations of the alcohol content of capillary blood. Because of these discrepancies the co-operation of the Home Office laboratories was again sought, and blood samples collected in capillary tubes and plastic pots from volunteers in this department were distributed to a number of centres for analysis.

On five occasions, in addition to measuring the alcohol concentration in whole blood, that in plasma and in red blood cells was also determined. For this purpose 10–15 ml. of the blood sample was placed in a glass test-tube sealed with a ground-glass stopper and centrifuged at 2,300 r.p.m. for 20 minutes at room temperature in a Griffin-Christ centrifuge (type UJ 3). At the end of this period the separated plasma was pipetted into a second tube, which was then sealed until analysed by gas chromatography. Because the packed cells tended to block the needle of the microsyringe when inserted into the heated inlet tube of the gas chromatograph the alcohol content of the red blood cells was measured by the Nickolls method. Two-millilitre aliquots of undiluted packed cells were used for this analysis; this had the added advantage of eliminating the possible difficulties of handling minute quantities of red blood cells. The haematocrit value for each blood sample was determined and this together with a correction factor for trapped plasma (Chaplin and Mollison, 1952) was used to calculate the alcohol concentration in whole blood.

Results

Accuracy of Gas Chromatography

In preliminary studies known amounts of ethanol were added to 15 blood samples to achieve concentrations in the range from 52 to 242 mg./100 ml. On analysis 98% recovery was achieved on average with the Nickolls method, with a correlation coefficient of 0.99 between duplicate samples. The gas chromatograph gave equally satisfactory results; 99% of the added ethanol was recovered and the correlation coefficient for duplicate samples was again 0.99.

Known amounts of ethanol were added to water to achieve concentrations between 76 and 197 mg./100 ml. and 13 separate samples were analysed in duplicate by the two methods. With the Nickolls method 100% of the added alcohol was recovered and the correlation coefficient between duplicate samples was 0.99. Gas chromatography was slightly less efficient; the percentage recovery was 97 and the correlation coefficient 0.97.

Despite the apparently satisfactory recovery achieved with gas chromatography from blood, the Nickolls method continued to be used during the initial stages of the study of blood and urine obtained from suspects. The first 12 samples were analysed in duplicate by the Nickolls method and in triplicate by gas chromatography. Comparison of the results obtained by the two methods gave a correlation coefficient of 0.99, and this provided the justification for continuing the study by gas chromatography alone.

Urine : blood Ratios

The analyses of one blood and two urine samples from 35 suspects gave 70 paired results, and the details are set out in Table I. The mean alcohol concentration of 35 first urine samples was 262±54 mg./100 ml. The corresponding mean

TABLE I.—*Measured Alcohol Concentrations in One Blood and Two Urine Samples Collected from 35 Motorists, Together With Derived Values, Ratios, Means, and Standard Deviations*

Subject No.	First Urine U_1 (mg./100 ml.)	Venous Blood VB (mg./100 ml.)	Second Urine U_2 (mg/100 ml.)	Time Interval T_1 (mins.)	Time Interval T_2 (mins.)	Corrected Blood (mg./100 ml.)	U_1/VB	U_2/VB	U_1/U_2
1	365	241	365	60	−13	236	1·51	1·51	1·00
2	270	178	253	55	35	164	1·52	1·42	1·07
3	313	224	296	44	5	222	1·40	1·32	1·06
*4	331	246	339	65	15	240	1·35	1·38	0·98
5	150	109	132	45	37	94	1·35	1·21	1·14
*6	402	302	405	67	37	287	1·33	1·34	0·99
*7	305	207	310	40	30	195	1·47	1·50	0·98
8	207	127	187	50	20	119	1·63	1·47	1·11
*9	216	138	230	30	−11	134	1·57	1·67	0·94
10	213	103	190	39	16	97	2·07	1·84	1·12
11	293	190	265	31	16	184	1·54	1·39	1·11
12	253	161	224	36	29	149	1·57	1·39	1·13
13	170	124	161	45	22	115	1·37	1·30	1·06
14	356	239	336	34	21	231	1·49	1·41	1·06
15	216	109	172	30	−25	99	1·98	1·58	1·26
16	89	40	54	35	−15	34	2·22	1·35	1·65
17	331	210	328	46	56	196	1·52	1·50	1·01
*18	250	195	267	40	−8	192	1·28	1·37	0·94
19	302	239	287	45	33	226	1·26	1·20	1·05
20	175	103	170	25	−16	97	1·70	1·65	1·03
*21	285	184	293	46	19	176	1·55	1·59	0·98
22	313	213	279	50	16	207	1·47	1·31	1·12
*23	150	184	230	50	28	173	0·82	1·25	0 65
24	256	178	253	41	20	170	1·44	1·42	1·01
25	316	127	310	26	−12	122	2·59	2·44	1·02
26	305	201	305	25	−22	192	1·52	1·52	1·00
27	359	270	359	61	23	261	1·33	1·33	1·00
*28	204	164	213	49	52	143	1·24	1·30	0·96
29	305	262	287	50	18	255	1·16	1·10	1·06
30	207	150	207	32	22	141	1·38	1·38	1·00
*31	190	230	296	35	10	226	0·83	1·29	0·64
32	256	193	253	30	8	190	1·33	1·31	1 01
33	239	167	230	55	15	161	1·43	1·38	1·04
34	274	207	264	35	12	202	1·32	1·28	1·04
*35	289	194	294	40	−10	190	1·49	1·52	0·98
Mean	262	183	258				1·43	1·41	
S.D.	54	55	71						

* Indicates second urine samples collected without evidence that the peak concentration had been reached.

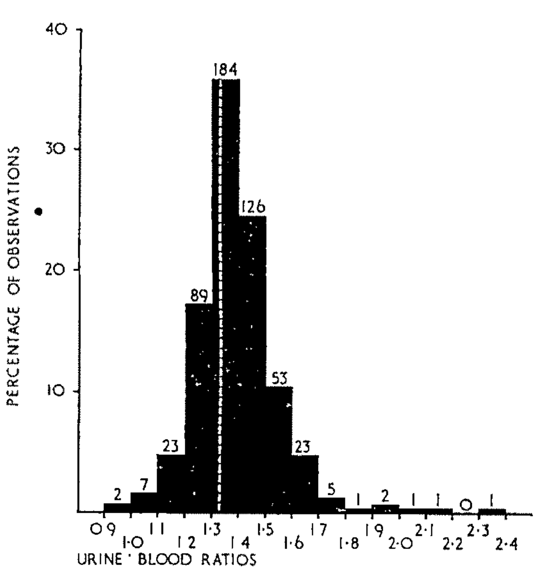
T_1 Time interval between collection of first and second urine samples.

T_2 Time interval between collection of blood sample and second urine sample. A negative value signifies that the urine sample was collected before the blood sample.

for the second urine samples was 258±71 mg./100 ml., and the mean venous blood value was 183±55 mg./100 ml. When both first and second urine values are used these figures give an overall urine:blood ratio of 1.42:1. Of the 35 second urine samples analysed 25 were collected after the peak alcohol concentration in urine had been reached. When these were related to the corresponding blood values a mean urine:blood ratio of 1.44:1 was obtained. However, individual ratios in this second group varied from 1.10 to 2.44:1, and the range was even greater in the first group, from 0.82 to 2.59.

An attempt at back-calculation was made. For this purpose the alcohol clearance from the blood was derived from values obtained in a previous study (Payne, Hill, and King, 1966). Results from 16 volunteers were analysed, and it was found that the rate of clearance varied between 10 and 38 mg./100 ml./hour, with a mean value of 24 mg. No correlation with the weight of the subject could be obtained. The mean value was used to derive a corrected urine:blood ratio of 1.48.

From the 518 paired urine and blood results made available from Belfast the mean urine:blood ratio was 1.38. The distribution of these ratios is set out in the Chart. Just over 35% of these results fall into the ratio range of 1.30–1.39:1. The range of urine values was from 43 to 481 mg./100 ml., and the urine:blood ratios extended from 0.92:1 to 2.32:1.



Percentage distribution of the urine:blood ratios derived from Belfast data. The figures at each step denote the actual number of ratios determined. The dotted line indicates the urine to blood ratio of 1.33.

Capillary Blood Analysis

In most instances the alcohol content of the capillary blood was substantially below that of the corresponding venous blood. In the case of the straight tubes 10 separate samples contained, on average, 61% of the alcohol content found in the corresponding venous blood. When the U tubes were used 10 tubes contained an average of 79% of the alcohol content of the corresponding venous blood. Of 10 samples collected in S-shaped tubes six contained, on average, only 53% of the alcohol content of the corresponding venous sample; the remaining four tubes had an alcohol content 7% higher than the venous blood. The capillary blood collected in the 11 plastic pots had a higher average alcohol concentration than that of the tubes but still contained only 90% of that found in the corresponding venous blood.

Of the limited number of capillary tubes and polypropylene pots distributed to other departments, only the samples stored in the pots gave good agreement on analyses. There were wide discrepancies in the results obtained from the capillary tubes.

Plasma : Red Blood Cell Ratios

The distribution of alcohol in the plasma and packed cells of whole blood was studied in five venous samples, and the relevant data are set out in Table II. The calculated alcohol content of whole blood in column 5, derived by measuring the packed cell volume and the alcohol content of both plasma and red blood cells, largely confirmed the accuracy of the methods used. A mean plasma:red blood cell ratio of 1.43:1 was obtained and a somewhat lower ratio of 1.15:1 expressed the relation between plasma and whole blood.

Table II.—*Difference in Alcohol Content Between Whole Blood, Plasma, and Red Blood Cells. The Calculated Whole Blood Content was Derived From That of the Plasma and Red Blood Cells by Means of the Haematocrit*

Haematocrit (1)	Alcohol Content (mg./100 ml.)				Ratios	
	Whole Blood (2)	Plasma (3)	R.B.C.s (4)	Calculated Whole Blood (5)	Plasma: R.B.C.s (6)	Plasma: Whole Blood (7)
45	117	132	93	115	1·41/1	1·13/1
43	151	173	124	151	1·40/1	1·15/1
42	181	217	146	187	1·49/1	1·20/1
44	125	144	102	126	1·41/1	1·15/1
42	194	217	152	190	1·43/1	1·12/1

Discussion

The conclusion by Curry *et al.* (1966) that when gas chromatography is combined with an internal standard and an integrator the alcohol content of small samples of body fluid can be measured accurately within five minutes has been substantiated.

The fact that the alcohol content of urine can be measured accurately does not necessarily mean that an exact determination of the amount of alcohol present in blood can be derived from urine analysis. The considerable difference of opinion on the correct conversion factor to be used implies a degree of uncertainty that is amply justified by experiment. On the basis of more than 7,000 analyses of urine and the corresponding blood samples Froentjes (1963) calculated the ratio of urine alcohol to blood alcohol as 1.52:1. He emphasized, however, that if this conversion factor was applied a 50% chance existed that the actual blood alcohol concentration would be lower than the calculated value, and for this reason in practice he advocated the use of a conversion factor of 2:1. Notwithstanding Froentjes's views the special committee of the British Medical Association set up to consider the problem of the drinking driver came to the conclusion that once the peak concentration in the urine had been passed a urine to blood ratio of 1.32:1 could be adopted. Using this ratio, Payne *et al.* (1966) demonstrated good agreement between urine and blood analyses when studying the uptake, distribution, and elimination of alcohol in a group of healthy volunteers. But these results were obtained under well-controlled conditions in the laboratory, and the present work, confirming that of Stevens, Mason, and Bowden (1966), shows that it would be invalid to use this factor in the less rigidly controlled environment of a busy police station.

That this is so is apparent from the data presented. Of the 518 paired urine and blood samples analysed in Belfast an overall urine:blood ratio of 1.38:1 was obtained, but only 35% fell into the range from 1.30 to 1.39:1, and the remainder extended from 0.92 to 2.32:1.

Further evidence of the variation in urine:blood ratios was obtained from the analyses of the blood and urine samples presented in Table I. Of the 35 second urine samples obtained from detained motorists, 25 had an alcohol concentration equal to or lower than the first, and were therefore to be regarded as having been collected after the peak concentration in urine had been passed. The significance of this has been discussed by Payne *et al.* (1966). These values gave a mean ratio of

1.44:1, somewhat higher than the 1.32 recommended by the special committee of the B.M.A. In only one of these 25 suspects was a precise urine: blood ratio of 1.32:1 obtained, and the range was from 1.10 to 2.44, substantially greater than that of 1.2:1 to 1.4:1 quoted in the B.M.A. report. The overall mean ratio for the second urine samples was 1.41. Furthermore, as has been shown previously (Payne *et al.*, 1966), it is apparent from the data in Table I that the urine: blood ratio is not even constant for one individual but varies with time.

The argument is of considerable practical importance; for example, if the urine analysis of Subject No. 10 in Table I had given a value of between 110 and 150 mg./100 ml. the use of the conversion factor of 1.32 would yield a blood alcohol concentration of between 82 and 112 mg./100 ml., a level which almost certainly would lead to his conviction under the new Act. But in this particular individual the urine: blood ratio was measured and found to be 1.84:1, which under the circumstances described yields an actual blood concentration between 60 and 80 mg./100 ml., a level below the maximum envisaged as compatible with safe driving in the White Paper on Road Safety Legislation (Ministry of Transport, 1965). In the case of Subject No. 25, whose urine: blood ratio was 2.44:1, the discrepancies would have been greater. Thus the suggestion by the Special Committee of the B.M.A. that any injustice to individuals was extremely unlikely when a urine to blood ratio of 1.33:1 has been used will certainly cease to be true if present proposals become law. (The B.M.A. report used the factors 1.32 and 1.33 at various times.) Indeed there is every likelihood that the uncritical acceptance of a urine to blood ratio of 1.33:1 will lead to miscarriages of justice when it becomes an offence to drive or to be in charge of a motor vehicle with more than a stipulated amount of alcohol in the blood.

As might have been expected from the variation in the rate of removal of alcohol from blood the attempt at back calculation not only failed to bring the urine to blood ratio closer to 1.33:1, it also confirmed the difficulty of interpolating accurately a blood alcohol level to an earlier point in time.

The failure to obtain definitive results from urine analysis focused attention once again on blood. The lack of enthusiasm among doctors for venepuncture combined with the convenience and accuracy of gas chromatography suggested that capillary blood analysis might prove an acceptable compromise. Unfortunately, most capillary blood samples were found on analysis to contain substantially lower alcohol concentrations than the corresponding venous samples. Two possibilities existed: either the alcohol concentration in capillary blood was in fact lower than in the corresponding venous blood, or some of the alcohol content was lost after the blood was shed. Since Harger (1963) and his colleagues have shown that the alcohol content of capillary blood is not lower than that of venous blood, it must be accepted that loss has occurred.

The most likely time for such loss is during collection, especially if the flow of blood is too slow to allow rapid filling of the capillary tube; ethyl alcohol is sufficiently volatile to be lost fairly rapidly from exposed blood at body temperature. Another possible source of loss is from the capillary tube, either by a leak past the plastic seal or by adsorption by the seal itself; plastic materials have recently been shown to interfere with several blood constituents (Whitehead, 1967, personal communication). The capillary tubes themselves were glass, so that loss through the walls was unlikely. When polypropylene pots were used to collect capillary blood the alcohol content of the samples was closer to the venous level than was that in the capillary tubes, but some loss was apparent and it is possible that adsorption on the walls or even diffusion through them had taken place. However, the fact that good agreement was obtained when separate aliquots of the same samples were analysed by different laboratories suggests that the loss probably occurs during sampling rather than during storage in the pot.

During the investigation of this loss it was observed that the blood in some S-shaped and U-shaped capillary tubes had a substantially higher alcohol content than the corresponding venous blood. These high contents were associated with separation of plasma from red cells within the tube, with problems of mixing and with subsequent difficulties in obtaining good agreement on duplicate analyses; therefore the possibility that alcohol was distributed unevenly between plasma and red blood cells was considered. Definitive information on this aspect is limited; however, Grüner (1957) has shown that alcohol is distributed in human plasma and in whole blood in a ratio of 1.15:1, and is dependent on the distribution of water as suggested by the work of Polonovski, Lindenberg, and Rabussier (1951) on dogs. The evidence reported here confirms and amplifies these observations.

The fact that human plasma contains about 40% more alcohol than an equal volume of red blood cells would explain the high alcohol content in some capillary tubes, but it also raises new problems. In particular, it implies that certain accepted standards such as the urine to blood ratio and the blood to breath ratio cannot be constant, but must be related to the haematocrit. It also implies that the plasma alcohol concentration might be a more useful determination for future experimental work if it is assumed that tissue levels are in equilibrium with the plasma. It would certainly help to explain the difficulties that have been encountered in seeking an answer to the apparent discrepancies in the blood: breath ratio.

Conclusions

From the data presented certain conclusions can be drawn.

Firstly, the fact that the urine to blood ratio is not constant at 1.33:1 means that an accurate estimation of a blood alcohol level cannot be derived from the analysis of urine with any degree of certainty when a urine to blood ratio of 1.33:1 is used.

Secondly, the difficulties encountered in the analysis of capillary blood suggest that the determination of blood alcohol levels should be carried out on venous blood until these difficulties have been overcome. The possibility that unsatisfactory handling techniques are involved emphasizes the need to establish a standard protocol for the withdrawal and handling of blood for the determination of alcohol levels.

Thirdly, the demonstration that human plasma contains about 40% more alcohol than an equal volume of red blood cells strengthens the argument for such a protocol. It also implies that the alcohol concentration might be better measured in plasma rather than in blood in experimental studies.

Summary

The fact that gas chromatography when combined with an internal standard and an integrator will measure the alcohol content in minute samples of body fluids rapidly and accurately has been confirmed.

The analysis of blood and urine samples from 35 motorists suspected of driving while under the influence of drink gave a mean urine to blood ratio of 1.44:1, substantially higher than the recommended conversion factor of 1.33:1. Moreover the range of values found—from 1.10 to 2.44:1—suggests that the uncritical acceptance of this urine to blood ratio of 1.33:1 will lead to miscarriages of justice when it becomes an offence to drive or to be in charge of a motor vehicle with more than a stipulated amount of alcohol in the blood.

The failure to obtain good agreement between capillary blood samples and the corresponding venous samples when analysed for alcohol indicates that it would be unwise to depend on capillary blood analysis for accurate results at the present moment. Probably the discrepancies are due to sample-

handling difficulties, which may be overcome with more experience.

The analysis of five samples of human blood showed that when alcohol is present the plasma contains over 40% more than whole blood (plasma to R.B.C. ratio, 1.43 : 1 ; plasma to whole blood ratio, 1.15 : 1). Thus the alcohol content of a given blood sample will be critically dependent on the separation or otherwise of plasma from red blood cells during handling.

We are indebted to the directors of the Metropolitan Police Laboratory ; the Home Office Central Research Establishment ; the North-Western (Preston), the Northern (Newcastle), and the East Midland (Nottingham) Forensic Science Laboratories ; and the Department of Industrial and Forensic Science (Belfast) for their cooperation. We are also grateful to Professor F. E. Camps and Dr. E. G. Davies for advice and criticism.

Addendum

Since this paper was written the Road Safety Act 1967 has been published. In section 7 subsection (4) it is stated that "For the purposes of this Part of this Act 107 milligrammes of alcohol in 100 millilitres of urine shall be treated as equivalent to 80 milligrammes of alcohol in 100 millilitres of blood."

What in effect this means is that it becomes an offence to drive or to be in charge of a motor vehicle when the alcohol content of the urine is 108 mg./100 ml. or more. But of the 35 suspects studied in our series no fewer than 19 would have had less than 80 mg. of alcohol per 100 ml. in blood when the equivalent urine sample contained 108 mg./100 ml.; indeed subject No. 25, whose urine to blood ratio was 2.44 : 1, would have a blood level of only 44.3 mg. of alcohol per 100 ml. at this urine level.

Thus the warning given in our paper that the uncritical acceptance of a urine to blood ratio of 1.33 : 1 will lead to miscarriages of justice when it becomes an offence to drive or to be in charge of a motor vehicle with more than a stipulated amount of alcohol in the blood is entirely justified. In the interests of justice therefore suspected drivers would be well advised to insist on a blood specimen being taken if asked to provide a sample of urine for examination.

REFERENCES

B.M.A. Special Report (1965). *The Drinking Driver.* London.
Chaplin, H., jun., and Mollison, P. L. (1952). *Blood*, **7**, 1227.
Chundela, B., and Janák, J. (1960). *J. forens. Med.*, **7**, 153.
Curry, A. S., Walker, G. W., and Simpson, G. S. (1966). *Analyst*, **91**, 742.
Froentjes, W. (1963). In *Alcohol and Road Traffic*, p. 179. London.
Grüner, O. (1957). *Dtsch. Z. ges. gerichtl. Med.*, **46**, 10.
Harger, R. N. (1963). In *Alcohol and Road Traffic*, p. 212. London.
Ministry of Transport (1965). *Road Safety Legislation, 1965–6*, p. 12. London.
Morgan, W. H. D. (1965). *J. forens. Sci. Soc.*, **5**, 15.
Nickolls, L. C. (1960). *Analyst*, **85**, 840.
Payne, J. P., Hill, D. W., and King, N. W. (1966). *Brit. med. J.*, **1**, 196.
Polonovski, M., Lindenberg, B. A., and Rabussier, H. (1951). *C.R. Acad. Sci. (Paris)*, **232**, 1595.
Stevens, P. J., Mason, J. K., and Bowden, C. H. (1966). *Med. Sci. Law*, **6**, 96.

Splenectomy in "Big Spleen Disease"

P. J. S. HAMILTON,* M.B., D.P.H., D.T.M.&H. ; JOHN RICHMOND,† M.D., F.R.C.P.ED., M.R.C.P.
G. W. K. DONALDSON,‡ M.B., B.SC., M.R.C.P., M.R.C.P.ED. ; ROGER WILLIAMS,§ M.D., M.R.C.P.
M. S. R. HUTT,|| M.D., F.R.C.P., F.C.PATH. ; V. LUGUMBA¶

Brit. med. J., 1967, **3**, 823–825

Idiopathic or cryptogenic tropical splenomegaly is sometimes treated empirically by splenectomy. Moreover, in areas where this condition is commonly encountered medical facilities are usually not available for the full investigation of such cases before or after splenectomy. Recently, a group of patients suffering from idiopathic tropical splenomegaly were studied in detail in the Mulago Hospital, Kampala, Uganda. All known causes of tropical splenomegaly were excluded in these patients, who on liver biopsy showed varying degrees of lymphocytic infiltration of the liver sinusoids and Kupffer-cell hyperplasia. In addition they all had high fluorescent antibody titres for malaria. This association is known locally as "big spleen disease" (Hamilton *et al.*, 1966) and is referred to by that title in this paper. Williams *et al.* (1966) showed in haemodynamic studies that these patients suffered from considerable portal hypertension, apparently due to increased spleen blood flow. Richmond *et al.* (1967), reporting the haematological findings on the same group of patients, found that they all had anaemia, sometimes of severe degree, and this appeared to be due to sequestration of a large proportion of the red cell mass in the spleen, expansion of the plasma volume, and reduction of the red cell life-span. Seven of the 15 patients were treated by splenectomy in June–July 1965, the indications for splenectomy being either incapacitating abdominal pain or discomfort or the finding of pronounced hypervolaemia with anaemia. Follow-up studies on these seven patients two months after splenectomy showed satisfactory improvement in the haemoglobin level in six of them and correction of the red cell survival time in the four in whom this was measured.

This paper describes follow-up studies on five of the splenectomized patients 15 months after the operation.

Patients and Methods

Six of the seven patients splenectomized in June–July 1965 were traced to their homes in October 1966 by one of us (V. L.) ; one patient, who was in good health, could not be traced. Five patients were studied in detail.

All were males aged 20–55 years. Full clinical examination, routine haematological tests (Dacie and Lewis, 1963), standard liver-function tests, and brucella and salmonella serum agglu-

---

[*] Late Lecturer in Medicine, Makerere University College Medical School, Kampala, Uganda. On secondment from London School of Hygiene and Tropical Medicine. Present address: London School of Hygiene and Tropical Medicine, Keppel Street, London W.C.1.

[†] Senior Lecturer in Medicine, Department of Medicine, University of Edinburgh.

[‡] Lecturer in Medicine, Department of Medicine, University of Edinburgh.

[§] Physician and Medical Tutor, King's College Hospital, London S.E.5.

[||] Professor of Pathology, Makerere University College Medical School, Kampala, Uganda.

[¶] Social Worker, Makerere University College Medical School, Kampala, Uganda.

tination reactions were carried out. Each patient had a liver biopsy by the Menghini technique. The serum fluorescent antibody titre for malaria was measured, ***Plasmodium falciparum*** being used as antigen (Voller, 1964). Plasma volumes were estimated by ^{131}I-labelled human albumin ; the test sample being taken 20 minutes after the injection of albumin.

Results

Subjectively all the patients felt much better after the operation and were particularly relieved of their constant abdominal discomfort. Four patients had put on weight and all had been able to work again. No patient had had a haematemesis or melaena. Immediately after the operation all had been started on antimalarial drugs prophylactically, these being continued for six to eight months ; after this interval they all defaulted from further attendance. None of them had taken antimalarial drugs for at least six months previous to this study. They all complained of occasional attacks of fever, but none of them described having had a classical attack of malaria.

On examination they looked well, liver size was not significantly different from that before operation, and there were no other abnormalities.

Haematological Changes.—The haematological findings are given in the Table. There was a marked rise in haemoglobin level and haematocrit values in all cases. Except for one patient (Case 1) who had a reticulocytosis of 6%, the postoperative reticulocyte counts were not significantly different from those before the operation. In all cases the plasma volume dropped —in Cases 3 and 5 by 2 and 4 litres respectively. The volumes in Cases 1, 3, and 4 were within normal limits, while that in Case 5 was just outside the upper limit for Africans in Kampala as reported by Leonard *et al.* (1965). The plasma volume in Case 2 remained rather high, though the haemoglobin rose from 9.5 to 14.6 g./100 ml. and the P.C.V. from 30.5 to 40.0%.

Liver Changes.—The repeat liver biopsy in Case 1 showed immature myeloid cells and occasional megakaryocytes in the hepatic sinusoids consistent with myeloid metaplasia. Difficulty was experienced in withdrawing marrow, which suggested the patient had myelofibrosis. A review of earlier liver biopsies on that patient from 1965 and 1964 showed some immature cells within the hepatic sinusoids which differed from the usual findings in big spleen disease. Re-examination of the splenectomy histology also showed the presence of immature myeloid cells, confirming the diagnosis of myeloid metaplasia. Despite this, both preoperative and postoperative studies showed a very high malarial antibody titre, and it seems possible that there were two factors accounting for the splenomegaly. Whether or not this was so, the haematological and haemodynamic results were exactly comparable to the other four cases, and so the patient has been included in this series. Liver biopsies from the other four cases showed varying degrees of lymphocytic infiltration of the liver sinusoids with some Kupffer cell hyperplasia ; these changes were not significantly different from those found in 1965. Standard liver-function tests were normal before and after splenectomy except for two slightly raised alkaline phosphatase levels in 1966. Total serum proteins have risen in all cases (see Table). In two out of the four cases for which results are available the rise is accounted for by a marked increase in the serum albumin, while in three out of four cases the serum globulin levels are almost unchanged.

Malaria and Other Studies.—No malaria parasites were found in six successive films on three patients and three successive films on two patients. In all cases the malaria antibody titre was equal to or above that found before splenectomy (see Table). Three patients had developed very light hookworm infections and two had high antibody titres to brucella, but no patient had a raised antibody titre for salmonella.

Discussion

The symptomatic and haematological improvements in these patients 15 months after splenectomy are most striking. Richmond *et al.* (1967) concluded that the improvement in the haematocrit two months postoperatively is largely due to the fall in the plasma volume. Our results confirm this and show that there has been a further improvement in the 15 months since the operation. These findings are in keeping with those of McFadzean *et al.* (1958), Cook *et al.* (1963), Weinstein (1964), and Bowdler (1967).

The immediate effect of splenectomy is to remove from the body a certain mass of red cells and plasma, but the mass of plasma contained in the spleen is quantitatively quite insufficient to account for the marked changes in the plasma volume. Neither the mechanics of the preoperative hypervolaemia nor that of the postoperative fall in plasma volume is understood. Weinstein (1964) suggested that changes in the plasma proteins and other macromolecules might be an explanation. This series is too small from which to draw any conclusions about the protein pattern ; however, there has been a rise in the total serum proteins in all cases, and in two there was a marked rise in the serum albumin level after surgery. Studies of the macroglobulin pattern in these cases are being undertaken in greater detail and will be reported later.

A number of cases of big spleen disease respond well to treatment with antimalarial drugs and show a marked symptomatic improvement and a reduction in spleen size (Hamilton, unpublished observations). It is not yet clear exactly which cases will respond in this way, but one patient with big spleen disease in the 1965 study has been on continuous antimalarial therapy for 14 months. In this time his spleen has regressed from 17.8 to 8 cm. below the costal margin. He feels better, his plasma volume has fallen from 73.1 to 46.4 ml./kg. (total from 3,380 to 1,940 ml.), and his P.C.V. has risen from 30 to

Clinical, Haematological, and Immunological Data in 5 Patients with Splenomegaly Before Splenectomy and 15 Months after Splenectomy

	Case 1		Case 2		Case 3		Case 4		Case 5	
	Before	After	Before	After	Before	After	Before	After	Before	After
Age (yr.)	52	—	27	—	20	—	55	—	40	—
Wt. (kg.)	50·7	54·5	50	50	45·5	58	57	64·5	63·5	63·6
Hb (g./100 ml.)	10·0	11·8	9·5	14·6	8·2	16·6	12·0	15·3	5·6	13·3
P.C.V. (%)	30	41	30·5	40·0	27	56	38	48	18	41
Retics (%)	3	6	4	1	3	0·5	1·0	1·0	2	1·0
Platelets (× 10³/cu. mm.)	151	291	145	207	177	172	163	203	111	260
W.B.C. (/cu. mm.)	6,400	17,000	3,300	5,800	3,300	6,000	8,100	15,000	9,000	9,000
M.C.H.C. (%)	33	25	32	30	33	30	31	32	32	32
Spleen wt. (g.)	1,438	—	4,200	—	1,930	—	1,032	—	5,050	—
Plasma vol. total (ml.)	3,240	2,560	3,810	3,310	4,690	2,760	3,310	2,540	7,780	3,970
,, ,, ,, (ml./kg.)	63·9	46·9	76·2	66·2	95·0	47·5	54·6	39·3	122·5	62·4
Serum albumin (g./100 ml.)	2·5	2·7	2·2	3·1	1·3	3·2	2·7	2·4	Not avail.	2·5
,, globulin ,,	3·8	4·2	4 4	4·6	5·4	5·3	4·2	5·2		5·0
Total protein ,,	6·3	6·9	6·6	7·7	6·7	8·5	6·9	7·6	4·9	7·5
Malaria antibody titre	3,200	3,200	3,200	12.800	3,200	6,400	1,600	12,800	3,200	12,800
Brucella ,, ,,	<1 : 50	1 : 1,600	<1 : 50	1 : 1,600	<1 : 50	<1 : 50	<1 : 50	<1 : 50	<1 : 50	<1 : 50
Salmonella ,, ,,	1 : 50	<1 : 50	1 : 50	<1 : 50	1 : 50	<1 : 50	1 : 50	<1 : 50	1 : 50	<1 : 50

44%. His only treatment has been a 15-day course of primaquine followed by 100 mg. of proguanil daily. This is further evidence for a malarial cause of this syndrome and also for implicating the spleen in the plasma volume changes. The role of the spleen is also shown by a case of Felty's syndrome (Pengelly, 1966), in which a marked reduction in spleen size and plasma volume after corticosteroid therapy was found.

Not all patients with big spleen disease or idiopathic tropical splenomegaly respond to antimalarial therapy, and even for those cases which do respond long-term supervision may be impossible. In those patients with chronic abdominal pain, an enormous spleen, and gross dilution anaemia, splenectomy may be the treatment of choice. M. Paliwoda (personal communication, 1967) carried out 70 splenectomies for cases such as these in Uganda with an operative mortality of only 4.3%, and though the follow-up data are incomplete the patients in general seem to have done well. However, the spleens are large, and good surgical technique with wide exposure is necessary. There is a danger of overtransfusing a hypervolaemic patient and also the added risk in the tropics of patients being particularly prone to infection after splenectomy. Fatalities from *P. falciparum* after splenectomy have occurred in West Africa (Watson-Williams, personal communication). In this series, postoperatively, the patients all registered high antibody levels to malaria and two developed a high brucella antibody titre; however, none seem to have suffered from significant clinical malaria. Against these dangers must be set the marked improvement in the well-being of these patients, who were able to return to doing a normal day's work after splenectomy.

Summary

The clinical and haematological effects of splenectomy on five Ugandan patients with "big spleen disease" were studied 15 months after operation and the results compared with those obtained preoperatively.

All patients were symptomatically much improved and they all showed a marked improvement in their haemoglobin and P.C.V. levels. Before operation the patients had marked hypervolaemia and dilution anaemia, but after splenectomy the plasma volumes had returned to normal in three patients and in two were still slightly raised. One patient had developed evidence of myelofibrosis, but the others showed no marked change in liver biopsy appearances.

There were no untoward effects of splenectomy and no acute attack of malaria was described, though the malaria antibody titre had been maintained or raised.

We are grateful to Professors A. W. Woodruff, J. A. Tulloch, and W. A. Parson for their encouragement and criticism, and to Dr. G. Cook and Dr. D. Wykoff for their help in this study. Financial support was provided by the Leverhulme Trust, the World Health Organization, and the U.S. Army Medical Research and Development Command, Department of the Army, under Research Grant Number DA-MD-49-193-63-6101.

REFERENCES

Bowdler, A. J. (1967). *Proc. roy. Soc. Med.*, **60**, 44.
Cook, J., McFadzean, A. J. S., and Todd, D. (1963). *Brit. med. J.*, **2**, 337.
Dacie, J. V., and Lewis, S. M. (1963). *Practical Haematology*, 3rd ed. London.
Hamilton, P. J. S., Gebbie, D. A. M., Hutt, M. S. R., Lothe, F., and Wilks, N. E. (1966). *Brit. med. J.*, **2**, 548.
Leonard, P. J., Blackman, V., and Jones, K. W. (1965). *Clin. Sci.*, **29**, 427.
McFadzean, A. J. S., Todd, D., and Tsang, K. C. (1958). *Blood*, **13**, 524.
Pengelly, C. D. R. (1966). *Brit. med. J.*, **2**, 986.
Richmond, J., Donaldson, G. W. K., Williams, R., Hamilton, P. J. S., and Hutt, M. S. R. (1967). *Brit. J. Haemat.* In press.
Voller, A. (1964). *Bull. Wld Hlth Org.*, **30**, 343.
Weinstein, V. F. (1964). *Lancet*, **2**, 218.
Williams, R., Parsonson, A., Somers, K., and Hamilton, P. J. S. (1966). Ibid., **1**, 329.

Splenectomy in Tropical Splenomegaly

D. S. PRYOR,* M.B., B.S.

Brit. med. J., 1967, **3**, 825–828

Massive splenomegaly of uncertain cause is frequent in New Guinea and is particularly prevalent in the Upper Watut Valley, 50 miles (80 km.) south-west of Lae, where over 80% of the inhabitants of some villages have enlarged spleens (Pryor, 1967a). Though idiopathic tropical splenomegaly occurs in areas where malaria is endemic (Hamilton *et al.*, 1965), a causal relationship has not been established. The villages of the Upper Watut are situated at 3,000 to 5,000 ft. (914 to 1,524 m.) above sea level, malaria is endemic, and the incidence of splenomegaly decreases at the highest altitudes. Other causes of tropical splenomegaly such as leishmaniasis, schistosomiasis, haemoglobinopathies, and hepatic cirrhosis can be excluded in these patients. The natural history of the disorder in this area is not known, but though enlargement of the spleen is often very great it appears to be a relatively benign condition causing little disability in the majority of individuals.

Anaemia, leucopenia, and thrombocytopenia are commonly associated findings, but haemoglobin values as low as 5 g./100 ml. may occur without apparent disability. A raised reticulocyte count is usual, and studies with radiochromium-labelled cells demonstrate a shortened red cell life-span with evidence of excessive red cell destruction in the enlarged spleen (Pryor, 1967b). However, the main cause of the low haemoglobin value is a greatly expanded plasma volume, which may be more than twice the normal value.

A few individuals complain of symptoms of anaemia or pain and discomfort due to the size and weight of the spleen. Splenectomy has been performed in 15 patients who had disabling symptoms, and the results form the basis of this report.

Methods

Selection of Patients.—Twelve of the 15 patients requested splenectomy and the other three were similar patients with disabling symptoms. Twelve patients were from the Watut Valley and the remainder from villages in the Lae medical region. Eleven were males and four were females aged from 10 to 45 years (Table I). In each case the spleen was enlarged to below the umbilicus and in nine cases it extended into the right iliac fossa. All had an enlarged liver with a smooth firm edge. Ten patients had precordial systolic murmurs and 10 had raised jugular venous pressures. Less frequent signs were dependent oedema, leg ulceration, and mild jaundice. In all cases chest *x*-ray examination showed moderate enlargement of the heart with prominent pulmonary vascular markings.

---

* Haematology Research Unit, Angau Memorial Hospital, Lae, New Guinea. Present address: the Prince Henry Hospital, Little Bay, New South Wales, Australia.

Laboratory Techniques.—Standard haematological techniques were used (Dacie and Lewis, 1963). Radiochromium-labelled red cell studies were carried out by a modification of the method of Crawford and de Gruchy (1958). Plasma volume was measured with radioiodine (^{131}I)-labelled human serum albumin (Veall and Vetter, 1958).

Results

Haematological Findings

The preoperative haematological findings are recorded in Table I. All patients were anaemic, with haemoglobin values ranging from 4.8 to 11.1 (mean 7.3) g./100 ml. Reticulocyte counts ranged from 6.6 to 23.3 (mean 11.3)% and white cell counts from 1,400 to 5,500 (mean 3,700)/cu. mm. All had thrombocytopenia, platelet counts ranging from 21,000 to 117,000 (mean 54,000)/cu. mm.

Various measurements with radioactive isotopes were performed preoperatively on 12 individuals (Table II). Red cell survival was measured in six subjects, ^{51}Cr-labelled autologous red cells being used. The half-life ranged from 9 to 19 (mean 13) days, the normal range in New Guinea natives without splenomegaly being from 25 to 30 days (Pryor, 1967b). Despite the low haemoglobin values, the red cell volume measured with ^{51}Cr-labelled red cells was normal or raised, the volumes in 12 subjects ranging from 24.0 to 51.2 (mean 35.5) ml./kg. The normal range in New Guinea natives is similar to that in Caucasians—that is, 23 to 35 ml./kg. (Pryor, 1967b). Plasma volume measurements with ^{131}I-labelled albumin in nine subjects gave high values ranging from 76.5 to 115.0 (mean 93.3) ml./kg., the normal range being 40 to 50 ml./kg. (Dacie and Lewis, 1963).

Preoperative Management

During investigations in hospital the patients received a course of chloroquine (600 mg. of chloroquine base followed by 300 mg. on the first day, 300 mg. daily for two further days, and 300 mg. weekly), ferrous sulphate 300 mg. three times daily, and a course of 5 g. of bephenium hydroxynaphthoate (Alcopar) daily for three days. Patients were also given individual treatment such as diuretics for oedema and antibiotics for urinary or chest infections. In view of the increased blood volume, transfusions of packed red cells were given to achieve a haemoglobin level of about 9 g./100 ml. only. Eleven patients received an average of 4 units of packed cells (1 unit being equivalent to 400 to 500 ml. of whole blood) and four received none. The packed cells were given within two days of operation, since transfused cells have a short survival time in these patients and the haemoglobin level falls quickly after transfusion (Pryor, 1967a).

Operation

The peritoneal cavity was opened through an abdominal incision and at least 200 ml. of clear fluid was found in each case. The liver was enlarged in all, with prominent left lobe enlargement in two cases. The splenic blood vessels were large and not tortuous, curving down over the tail of the pancreas to reach the large splenic hilum. A systolic thrill was palpable over the vessels in two cases, one of which had had an audible bruit over the spleen before operation. Adhesions between the spleen and adjacent parts proved a major difficulty only once (Case 11). Splenic vein pressures were measured at operation in five cases with a simple glass manometer filled with sterile isotonic sodium citrate solution. The results ranged from 12 to 20 (mean 18) cm., normal values being from 4 to 19 cm. (Atkinson and Sherlock, 1954).

Considerable shrinking of the spleen followed ligation of the splenic artery, and this facilitated the subsequent dissection and delivery of the organ, also producing an autotransfusion of

TABLE I.—*Results of Routine Haematological Tests Before and After Splenectomy in 16 Cases of Tropical Splenomegaly*

Case No.	Sex and Age	Before Splenectomy				After Splenectomy			
		Haemoglobin (g./100 ml.)	Reticulocytes (%)	White Blood Cells ($\times 10^3$/cu. mm.)	Platelets ($\times 10^3$/cu. mm.)	Haemoglobin (g./100 ml.)	Reticulocytes (%)	White Blood Cells ($\times 10^3$/cu. mm.)	Platelets ($\times 10^3$/cu. mm.)
1	M 14	9·0	8·3	2·7	34	14·0	1·8	9·0	350
2	M 28	6·4	15·7	4·8	21	15·1	1·4	19·7	293
3	F 29	7·5	8·6	4·1	42	14·2	0·6	13·5	190
4	M 26	7·8	7·6	1·4	67	11·4	2·6	7·6	360
5	F 45	6·5	11·5	4·3	54	12·7	1·4	9·5	627
6	M 30	7·0	7·5	5·5	78	11·3	1·2	9·2	294
7	F 30	5·7	6·9	3·2	54	12·4	0·4	11·2	109
8	M 16	7·9	9·3	3·7	45	9·7	2·6	11·9	197
9	M 15	11·1	12·6	4·8	117	11·6	0·4	6·2	370
10	M 18	7·0	13·6	3·7	28	12·7	2·6	12·6	860
11	F 22	4·8	10·4	2·0	51	—	—	—	—
12	M 30	9·5	8·4	2·9	84	11·4	—	17·8	520
13	M 35	6·3	6·6	3·3	39	11·4	2·6	9·5	425
14	M 28	6·6	18·4	5·5	56	10·1	2·8	8·9	500
15	M 10	6·6	23·3	2·9	45	13·3	2·4	6·0	750

TABLE II.—*Results of Red Cell Survival and Blood Volume Measurements Before and After Splenectomy for Tropical Splenomegaly*

Case No.	Before Splenectomy				After Splenectomy				
	Red Cell Survival (T½ Cr. days)	Red Cell Volume (ml./kg.)	Plasma Volume (ml./kg.)	Total Blood Volume (ml./kg.)	Time After Operation (weeks)	Red Cell Survival (T½ Cr. days)	Red Cell Volume (ml./kg.)	Plasma* Volume (ml./kg.)	Total Blood Volume (ml./kg.)
1	14	41·0	—	—	—	—	—	—	—
2	9	26·4	—	—	2–8	25	25·9	64·0	89·9
3	13	40·4	—	—	33–37	26	29·5	59·3	88·8
4	—	34·8	98·0	132·8	47	—	—	66·7	—
5	—	24·0	76·5	100·5	5	—	—	63·0	—
6	—	37·1	104·0	141·1	3	—	—	75·4	—
7	—	34·9	105·4	140 3	16–22	30	29·2	58·3	87·5
8	8	39·3	115·0	154·3	4	—	—	97·0	—
9	—	51·2	80·5	131·7	3	—	—	63·0	—
10	19	32·5	86·0	118·5	9	—	—	68·8	—
11	—	29·3	87·6	116·9	—	—	—	—	—
12	15	35·4	87·0	122·4	2	—	30·9	70·2	101·1

* Where plasma volume was measured more than once after splenectomy, the last result is given. The other results may be seen in the Chart.

blood at this stage of the operation. Operative blood loss was replaced by transfusion of whole blood so that the haemoglobin level immediately after operation was higher than before.

Postoperative Complications

Four patients required transfusion for postoperative bleeding, in two of whom re-exploration of the abdomen was carried out. In one (Case 2) further ligation of the splenic artery stopped the bleeding, and the other (Case 11) died after continuous bleeding from the diaphragm and liver, which had been densely adherent to the spleen. Wound infections occurred in five cases but did not cause serious morbidity. Three patients had chest infections in the postoperative period and one had malaria due to *Plasmodium vivax* six weeks after operation. Two patients had marked dependent oedema and ascites after operation, which gradually subsided over about eight weeks.

Pathology of Spleens and Livers

The spleens weighed 2,090 to 4,380 (mean 3,270) g. Even after removal as described, almost 1 litre of blood ran from the spleen in two cases when the clamps were removed from the vessels. The spleens were firm in consistency, with rounded edges and one or two distinct notches on the medial border. The capsules were normal except for some patchy thickening in three cases. The cut surface of the spleens was a uniform dark red ; no infarcts were seen though one specimen showed a subcapsular scar. The Malpighian bodies were not visible.

Microscopical examination of the splenic tissue revealed greatly dilated sinuses with reticuloendothelial hyperplasia and marked erythrophagocytosis. There was atrophy of the Malpighian bodies, a paucity of fibre, and no malarial pigment.

In 11 patients microscopical examination of a wedge biopsy of the liver showed sinusoidal dilatation, Kupffer cell hyperplasia, and lymphocytic infiltration of sinusoids and portal tracts, but no cirrhosis. The morphology of these livers and spleens has been reported in detail by Pitney *et al.* (1967).

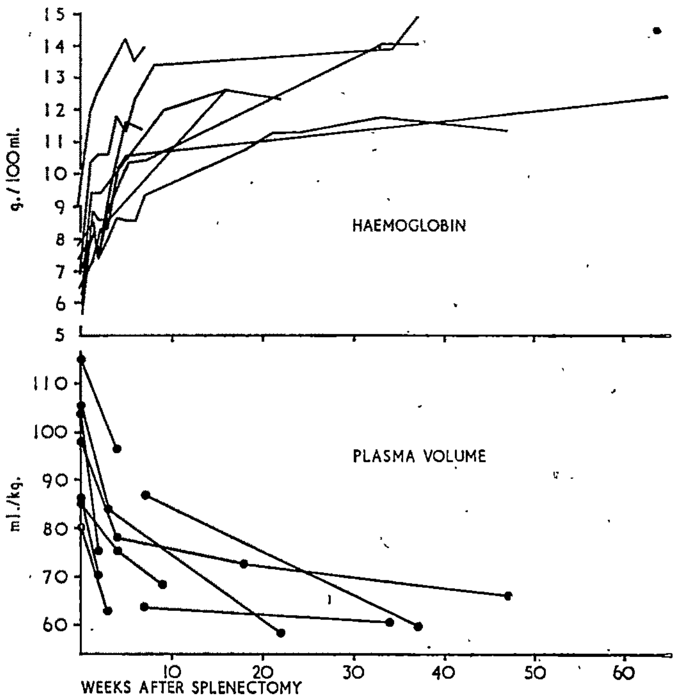
Results of Splenectomy

Four patients were well 14 to 18 months and four at two to nine months after operation. Only a short time had elapsed since splenectomy in two cases. One Watut patient died the day after operation from uncontrolled haemorrhage, as described above, and two males (Cases 8 and 13) died of acute illnesses in the village five and three months after operation, respectively. Two patients had malaria due to *P. vivax* four and six months after operation, and two others had pneumonia while under observation, four and eight months after operation. One man had acute gouty arthritis three weeks after operation, and after four months was admitted to hospital with cervical tuberculous lymphadenitis, which responded well to chemotherapy. Two of the three patients not belonging to the Watut area have been lost to follow-up. Thus of 11 patients followed for more than two months, eight were well and three had died—one as a direct result of operation and two from unknown causes.

Effect of Splenectomy on the Haematological Findings

In each case splenectomy was followed by a rise in haemoglobin (Table I). An initial temporary rise was related to blood transfusion and was followed by a gradual rise over several months (see Chart). Reticulocyte counts fell after one to two weeks to a mean of 1.4% (range 0.4 to 2.6%). Howell–Jolly bodies and target cells were seen in the peripheral blood as early as 24 hours after operation. White cell counts rose promptly and a temporary leucocytosis often developed, final counts ranging from 6,000 to 19,700 (mean 10,600) cu. mm. Platelet counts rose in the first two weeks, in three cases to over 1,000,000/cu. mm. and in one case to over 2,000,000/cu. mm., finally reaching a mean of 335,000/cu. mm.

Red cell volume and red cell survival studies were repeated in three cases and normal values were obtained (Table II) except in Case 2, and this man was studied only 16 days after splenectomy, before equilibrium had been reached after massive blood loss and transfusion. Plasma volume studies were made in 10 cases at various times after splenectomy. There was a steep fall from the high preoperative level and a subsequent slow fall continuing over several months (see Chart). In the first four to eight weeks weight loss was marked (mean 5.9 kg. for seven cases), but this was subsequently recovered, to result in a final gain in weight (mean 3.2 kg. for five cases). Therefore the absolute plasma volume fell even more than is shown with the volume expressed in ml./kg. of body weight.



Effect of splenectomy on haematocrit and plasma volume in cases of tropical splenomegaly.

Discussion

In this group of patients with tropical splenomegaly, splenectomy produced correction of the anaemia and relief of symptoms. The main cause of the sustained rise in haemoglobin value was the progressive fall in plasma volume. Though increased red cell destruction occurred preoperatively and was corrected by splenectomy, haemolysis was not an important cause of anaemia, since the red cell volume was often raised and usually fell after splenectomy. The reason for the high plasma volume and its correction by splenectomy is not known. Similar results were recorded by McFadzean *et al.* (1958) in cryptogenic splenomegaly in Hong Kong and by Prankerd (1963) and Bowdler (1963) in patients with splenomegaly associated with blood disorders. In the present cases hypervolaemia was possibly related to hyperimmunity to malaria or other antigens causing increased rates of globulin synthesis. Splenectomy may have caused a decrease in globulin synthesis, giving rise to the fall in plasma volume. The lower red cell volume after splenectomy probably occurs because red cell production no longer has to maintain a large volume of cells in the splenic red cell pool (Prankerd, 1963 ; Weinstein, 1964 ; Pryor, 1967b).

It is generally recognized that splenectomy, at least temporarily, increases susceptibility to bacterial infections (Lowdon *et al.*, 1966) and in the present small series several infections occurred after splenectomy. The findings in a large number of splenectomies in Hong Kong were similar (Cook *et al.*, 1963). The two patients who died suddenly in their villages some months after operation may have succumbed to overwhelming bacterial infections or to malaria. No clinical observations could be made during their fatal illnesses. Splenectomy alters the effective state of immunity to malaria, and in latent infections in experimental animals parasitaemia induced by splenectomy may persist for life (Garnham, 1963). Fatal *Plasmodium falciparum* malaria has been demonstrated after splenectomy in a previously immune chimpanzee (Rodhain and Jadin, 1964). *P. vivax* parasitaemia occurred in the postoperative period in one patient and some months after operation in two. Chloroquine tablets were given to each patient, with instructions that they be taken if fever occurred. Therefore little information concerning the hazards of malaria after splenectomy is provided. However, for cases from areas with endemic malaria and sporadic medical surveillance, splenectomy should probably be restricted to patients with disabling symptoms. Most persons with tropical splenomegaly are not greatly disabled despite their very large spleens and considerable anaemia.

The microscopical appearances of the liver biopsy specimens confirmed the absence of hepatic cirrhosis (Pitney *et al.*, 1967), so that the results of operation might be expected to be better than those of Chaudhuri *et al.* (1956) and Cook *et al.* (1963), where many patients had cirrhosis. This latter study also showed much less mortality after splenectomy in those patients without cirrhosis. Hepatomegaly is usually found in tropical splenomegaly and, as jaundice, wasting, and even oedema may occur, it is difficult to exclude cirrhosis other than by liver biopsy.

Summary

The results of splenectomy are described in 15 patients with tropical splenomegaly in New Guinea. Splenectomy was performed only in those patients with disabling symptoms due to anaemia or the size and weight of the spleen. There was one operative death due to haemorrhage, and two other patients died suddenly some months after splenectomy.

The main cause of anaemia in this disorder was an expanded plasma volume, which was reduced after splenectomy. Increased red cell destruction was also corrected by splenectomy. There was a sustained rise in haemoglobin values, and the surviving patients have remained well over a short follow-up period. It is suggested that, until more information is available concerning the natural history of the disorder and the long-term results of splenectomy in regions where malaria is endemic and suppressive therapy difficult to administer, splenectomy should be reserved for patients with disabling symptoms.

I wish to thank Professor W. R. Pitney, of the University of New South Wales, for helpful advice and criticism; Dr. A. R. Shepherd, who performed the splenectomies; the Wellcome Trust for the provision of equipment; and Dr. R. F. R. Scragg, Director of Public Health, Territory of Papua and New Guinea, for making available facilities for this work.

References

Atkinson, M., and Sherlock, S. (1954). *Lancet*, **1**, 1325.
Bowdler, A. J. (1963). *Ann. intern. Med.*, 58, 664.
Chaudhuri, R. N., Saha, T. K., Basu, S. P., Mukherjee, A. M., and Chaudhuri, M. N. R. (1956). *Indian J. med. Res.*, 44, 305.
Cook, J., McFadzean, A. J. S., and Todd, D. (1963). *Brit. med. J.*, **2**, 337.
Crawford, H., and de Gruchy, G. C. (1958). *Med. J. Aust.*, **1**, 657.
Dacie, J. V., and Lewis, S. M. (1963). *Practical Haematology*, 3rd ed. London.
Garnham, P. C. C. (1963). In *Immunity to Protozoa*, edited by P. C. C. Garnham, A. E. Pierce, and I. Roitt. London.
Hamilton, P. J. S., *et al.* (1965). *E. Afr. med. J.*, **42**, 196.
Lowdon, A. G. R., Stewart, R. H. M., and Walker, W. (1966). *Brit. med. J.*, **1**, 446.
McFadzean, A. J. S., Todd, D., and Tsang, K. C. (1958). *Blood*, **13**, 524.
Pitney, W. R., Pryor, D. S., and Tait-Smith, A. (1967). *J. Path. Bact.* In press.
Prankerd, T. A. J. (1963). *Brit. med. J.*, **2**, 517.
Pryor, D. S. (1967a). *Quart. J. Med.*, **36**, 321.
—— (1967b). Ibid., **36**, 337.
Rodhain, J., and Jadin, J. (1964). *Ann. Soc. belge Méd. trop.*, **44**, 531.
Veall, N., and Vetter, H. (1958). *Radioisotope Techniques in Clinical Research and Diagnosis*. London.
Weinstein, V. F. (1964). *Lancet*, **2**, 218.

Joint Haemorrhage in Haemophilia: Is Full Advantage Taken of Plasma Therapy?

ANITA M. ALI,* M.B., B.S.; R. H. GANDY,*† M.B., B.S.; MARGARET I. BRITTEN,* B.SC.
KATHARINE M. DORMANDY,* M.B., M.R.C.P., M.C.PATH.

Brit. med. J., 1967, 3, 828–831

Recurrent bleeds into joints and muscles are among the most typical and frequent of the haemorrhages sustained by the severely affected haemophiliac (Wilkinson *et al.*, 1961; Ramgren, 1962; Biggs and Matthews, 1966; Stuart *et al.*, 1966; and many others). Without immediate and competent treatment these bleeds are potentially crippling, leading to various degrees of functional disability (Jordan, 1965a); their frequency makes adequate schooling practically impossible (Britten *et al.*, 1966), thereby jeopardizing the boy's future career.

Despite the fact that plasma replacement therapy, given as soon as possible after the onset of bleeding, has for some years been the accepted treatment for musculoskeletal haemorrhage (Biggs, 1964; van Creveld, 1964; Hardisty and Ingram, 1965; Salzman and Britten, 1965), it was apparent that many haemophiliacs in the Metropolitan Regional Hospital Board Areas were receiving inadequate treatment or none at all. A survey was therefore undertaken to ascertain the extent to which this treatment was in fact being used in that area. An attempt was also made to correlate the outcome of bleeds with the therapy that had been received. This paper describes our findings during 1965 and 1966.

Materials and Methods

The patients and their parents who took part in this investigation were already in touch with us through our survey into the educational problems of haemophiliacs. A total of 210 patients under the age of 30 ("boys"), registered at many different hospitals and all suffering haemarthroses, agreed to co-operate.

---

* Department of Haematology, the Royal Free Hospital (North-western Branch), London N.W.3.

† Present address: Department of Pathology, the Combined Cambridge Hospitals, Tennis Court Road, Cambridge.

The boys were usually visited at home, with one or both parents present. A detailed medical history, with particular reference to the musculoskeletal system, was taken and the patient's joints were examined. The range of each joint was assessed on the active movements which the boy could accomplish without difficulty or pain. The degree of muscle-wasting was noted.

Haemophilia and Christmas disease were considered together. The patients were divided into groups according to age and the treatment received.

The age groups chosen were 0 to 5 years, 5 to 11, 12 to school-leaving, and school-leaving to 30. (School-leaving age was used in preference to a definite age, because the hazards of the schoolboy differ from those of the young adult.)

The treatment groups chosen were "no plasma" and "plasma." Boys were assigned to the no plasma group if they had never or only rarely received replacement therapy, and to the plasma group if they regularly or frequently received it. Their treatment was regarded as prompt if they received a rapid infusion of fresh-frozen plasma or its equivalent within 12 hours of the onset of a joint or muscle haemorrhage.

A system of grading, based on that of DePalma and Cotler (1956), was used for all joints into which there had been a haemorrhage. The assessment was clinical, as no radiological examinations were made. Thus:

Grade 1—joints into which there had been one or more bleeds but which showed no residual decrease in the range of movement and therefore no deformities which could be clinically observed.

Grade 2—joints showing slightly reduced range of movement but no appreciable joint dysfunction.

Grade 3—joints in which the reduced range of mobility interfered with function.

Grade 4—joints showing more advanced changes than in grade 3—that is, severe deformities.

Results

Of the 210 boys 196 sustained numerous episodes of joint haemorrhage; 131 were found to have deformities. Haemorrhage had occurred into 999 joints, of which 415 were deformed. Of the affected joints, 38% had sustained first bleeds before the boys had reached the age of 4, and 60% had done so by the age of 6.

A quarter of the boys under the age of 5, nearly half of the 5–11 group, and the majority of the older boys had deformities. Table I shows not only how early haemophilic deformities begin but how rapidly their severity increases during the years of growth. Several of the boys in the school-leaving to 30-year group had spent a period of their childhood confined to wheelchairs because of severe knee deformities. All of these had had orthopaedic treatment and were able to walk again.

Varying degrees of muscle-wasting, especially in the thigh and calf, were seen in most of the boys. Where there was gross quadriceps-wasting the boys appeared to have knee-bleeds with ever-increasing frequency unless the knee had been protected by a calliper or other appliance. Muscle haemorrhages accounted for five equinus deformities resulting from calf bleeds, one claw-hand after a forearm bleed, and one fixed flexion deformity of the left elbow after a haemorrhage into the biceps.

Though temporary immobilization, preferably by means of splints, is an important aid to recovery from haemarthroses and muscle bleeds, as is graded physiotherapy (France and Wolf, 1965), many of the boys had never had a joint splinted nor had they been taught suitable exercises to maintain the muscles controlling the affected joint.

TABLE I.—*Deformed Joints. Percentage of Lesions of Grades 2, 3, and 4 in Each Age Group.*

Deformities	Age Groups			
	0–4	5–11	12–SL*	SL–30
Percentage grade 2	80	58	48	52
" " 3	20	27	32	28
" " 4	0	15	20	20

* SL=School-leaving age.
N.B.—Grade 1 lesions are omitted because they are not deformities.

Plasma Replacement Therapy

Extent of Use

Table II shows the division of the boys into age and treatment groups. Seventy-one boys did not attend hospital for haemarthroses; 29 others went to hospital but were not infused, and 16 had had plasma only once or twice in their lives. Three boys had inhibitors to factor VIII; the histories of the remaining 16 classified as "miscellaneous" were vague.

TABLE II.—*Treatment Received by the Boys Up To the Time of the Survey*

Treatment	Age Groups				Total
	0–4	5–11	12–SL*	SL–30	
Plasma Prompt	7	6	12	4	29 } 75
Plasma Delayed	7	7	25	7	46
No plasma	12	48	30	26	116 } 135
Miscellaneous†	0	3	15	1	19
Total	26	64	82	38	210

*SL=School-leaving age.
† "Miscellaneous" includes boys known to have had some plasma therapy but for whom no detailed history could be obtained and 3 with inhibitors to factor VIII.

Of the 210 boys, only 75 had received plasma with any regularity; the treatment of 46 of these had been delayed, leaving only 29 who appeared to be receiving prompt and regular therapy.

Reasons for Delayed Treatment.—(a) Delay on the part of the patient or his parents in seeking hospital treatment: 55 boys did not go to hospital within 12 hours of the onset of a haemarthrosis; half of these waited several days or even longer. (*b*) *Delay in obtaining admission to hospital*: about 26% of the boys contacted their general practitioners before going to hospital. Sometimes this was because their hospitals insisted on a doctor's letter each time; others relied on him to arrange transport. Further delays occurred on arrival at many hospitals, where there were no short cuts through the time-consuming process of admission and a haemarthrosis was not regarded as an emergency. (*c*) *Delay in hospital before an infusion was given*: 16 boys were not treated on admission; of these, 14 waited several days.

Short-term Effects of Plasma Therapy

In addition to the rapid relief of pain and the faster reduction of swelling, plasma treatment considerably shortened the time "out of action." Thirty-nine boys gave estimates of the periods of time they were incapacitated by haemarthroses treated with plasma and those not so treated. A further 44, who did not receive plasma for joint bleeds, estimated the time missed with each episode. Of those treated, 72% were active in less than a week, and none were laid up for more than two weeks, whereas 52% of the untreated boys were out of action for two to four weeks and 7% for over four weeks. Only boys with very minor haemarthroses recovered untreated in less than a week.

Long-term Effects of Plasma Therapy

Fourteen boys, all under the age of 8, had received plasma treatment throughout their lives. Among their 40 affected joints there were only three deformed ones, two of which were in the same child. Both these boys had had treatment only after delays of two days. Two of the deformities were grade 2 and the third grade 3.

A detailed comparison was made between the numbers of new deformities which had developed in treated and untreated boys between the ages of 5 and school-leaving; this was the period during which the maximum number of deformities had been found to start. Our findings were:

Untreated boys: 1 deformity to every 7 joints with haemorrhage.
Treated boys: 1 deformity to every 39 joints with haemorrhage.

We obtained the above figures in the following way: All boys in the no-plasma group who sustained recurrent haemarthroses in more than one joint were considered, as were all similarly affected boys in the plasma group, provided that they had been receiving treatment for at least three years.

The average age of the 26 treated boys was 11.1 years (range 5–17), and they had been receiving treatment for an average of 4.5 years (range 3–7). Only four deformities had developed in the 156 affected joints. Three of these had occurred in boys who had received delayed infusions. The fourth, a grade 2 knee lesion, appeared to have been promptly treated for each haemarthrosis, but this joint had sustained many haemorrhages in a short period. The average age of the 50 untreated boys was 11.3 years (range 5–17). Records were made of all deformities that had developed in these boys in the 4.5 years before their examination for the survey. Thirty-six deformities had started in the 251 affected joints.

Haemarthroses occurred to approximately the same extent in the two groups both before and during the period studied; before that time the incidence of deformity had also been similar.

Thirty-three boys said that on one or more occasions aspiration had been used in the treatment of massive haemorrhage into a knee or ankle. In some cases joints had unfortunately been aspirated without plasma cover. Where plasma had been given in conjunction with aspiration some boys had felt great relief, but for others this procedure had been unsuccessful and painful.

Nearly half of the boys were not registered at a haemophilia centre, though there were 10 in the area investigated. Many of those who were registered had attended only for diagnosis and were treated at other hospitals or at home. One severely crippled boy of 20 had never been to any hospital for a haemarthrosis.

Discussion

Many authors have reported a big reduction in the incidence of deformity in patients receiving plasma replacement therapy (Biggs, 1964; Poulain, 1964; Ahlberg, 1965; Jordan, 1965b; Brinkhous *et al.*, 1966). As the results of our survey were similar, it was disturbing to find how few were the boys receiving prompt, or indeed any, plasma treatment for joint and muscle haemorrhages.

Since many of the affected joints examined had sustained first bleeds before the boys had even reached the age of 4, it is clear that the best therapy must be available from earliest childhood if permanent deformity is to be prevented. This applies equally in cases of muscle haemorrhages, as the deformities which follow these are usually severely disabling—none of those seen in the survey had been promptly treated.

Effective treatment involves the early administration of active therapeutic material. Day or night the patient or his parents must themselves be able to telephone the hospital to say he is coming for an infusion. As plasma infusions are given rapidly (Matthews, 1966) treatment can often be on an out-patient basis, thus causing minimal interruption to the boy's life. Evans (1967) has commented that most of the haemophilic boys at the Lord Mayor Treloar College, Froyle, Alton, Hampshire, where there are more than 30 over the age of 11, are absent from school with a haemarthrosis for hours instead of weeks now that they are receiving prompt plasma therapy.

At the time of the survey much of the frozen plasma issued to hospitals in the south-east of England was deficient in factor VIII, and therefore useless for the control of haemophilic haemorrhage (Bennett *et al.*, 1967). Because their own tests had shown the poor quality of this plasma, several haemophilia centres were making their own therapeutic materials (personal communications from R. M. Hardisty, 1966; C. A. Holman, 1966; and G. I. C. Ingram, 1966). All the 29 boys thought to be having prompt and effective treatment attended one of those centres. It seems likely that the use of inactive plasma, as well as delayed administration, was responsible for the lack of success of the therapy received by some of the boys.

Because haemophilia is a rare disorder, and its management is highly specialized, it is desirable that patients should be treated only at hospitals where every facility is always available. Many patients have found it worth while to go to a centre for treatment even when a considerable journey was involved. Where it would be impracticable for a boy to attend a haemophilia centre for routine treatment, his local hospital should co-operate closely with the centre where he is registered, so that advice can be easily obtained at any time (Dalrymple-Champneys *et al.*, 1967).

The majority of doctors have little chance to gain experience in the treatment of haemophilia. Many did not seem to appreciate the seriousness of joint and muscle bleeds, and were unaware of the great advances made for the treatment of these. Discouraged by the results of the conservative care given by many hospitals, general practitioners often merely advised bed-rest. It was evident during the survey that much needless suffering and crippling was occurring because doctors, parents, and patients did not know where to seek help.

This country has been well to the fore, both technically and clinically, in research into the problems of haemophilia, as was indicated in a leading article in the *British Medical Journal* (1966). It would indeed be sad if Great Britain were to lag behind in the treatment of the most frequent complications of the disorder. For practical reasons we had to limit the area studied, and have therefore made no mention of the position in other parts of the country, though we are well aware that a number of coagulation units are providing excellent care for their haemophilic patients. Now that cryoprecipitate factor VIII concentrate is becoming more readily available it should be easier to organize the provision of good therapy, and on a wider scale, than it was before 1966. It is essential that knowledge of the advantages of this treatment, and of where it can be obtained, should be more widespread among both doctors and patients.

Summary

The state of the joints of 210 haemophilic boys was clinically investigated in south-east England during 1965–6. Particular attention was paid to the treatment that had been received.

Prompt infusions of active plasma preparations had reduced (*a*) the duration of incapacity from haemarthroses by over half, and (*b*) the incidence of new deformities by four-fifths.

Without plasma therapy joint damage begins at an early age—one-quarter of the boys under 5 years had deformed joints. Overall, 131 boys had deformities involving 415 joints.

Only one-third of the 210 boys had received any plasma therapy; only one-seventh had had prompt treatment.

Some of the reasons why so few boys had had effective treatment were: (*a*) many doctors and parents were unaware of the benefits of plasma therapy for haemarthroses or of the need for prompt infusions; (*b*) few hospitals had arranged for patients' transport and speedy admission—few had issued instructions or given advice; and (*c*) many haemophiliacs attended hospitals which had no specialized coagulation units.

We wish to thank the many consultants, general practitioners, school medical officers, and school principals who have made this survey possible. We are especially grateful to Dr. Rosemary Biggs for her help in planning the survey and in interpreting the results. The co-operation of patients and their parents has been unlimited.

Financial support was given by the Medical Research Council and the Haemophilia Society.

Our preliminary findings were reported by K. M. D. to the Institute of Haemophilia during the 10th World Congress of the International Society for the Rehabilitation of the Disabled, Wiesbaden, September 1966.

REFERENCES

Ahlberg, A. (1965). *Acta orthop. scand.*, Suppl. No. 77, p. 74.

Bennett, E., Dormandy, K. M., Churchill, W. G. L., Coward, A. R., Smith, M., and Cleghorn, T. E. (1967). *Brit. med. J.*, **2**, 88.

Biggs, R. (1964). *Proc. roy. Soc. Med.*, **57**, 1171.

——and Matthews, J. M. (1966). *Treatment of Haemophilia and Other Coagulation Disorders*, edited by R. Biggs and R. G. Macfarlane, p. 129. Oxford.

Brit. med. J., 1966, **2**, 1608.

Brinkhous, K. M., Swanton, M., Webster, W. P., and Roberts, H. R. (1966). *Proceedings of Congress of the World Federation of Hemophilia*, Australia. In press.

Britten, M. I., Spooner, R. J. D., Dormandy, K. M., and Biggs, R. (1966). *Brit. med. J.*, **2**, 224.

Dalrymple-Champneys, W., Hunter, J. R., and Polton, K. R. (1967). Ibid., **2**, 440.

DePalma, A. F., and Cotler, J. (1956). *Clin. Orthop.*, **8**, 163.

Evans, E. S. (1967). *Proceedings of British Orthopaedic Association Clinical Meeting*, Spring, 1967, p. 54.

France, W. G., and Wolf, P. (1965). *J. Bone Jt Surg.*, **47B**, 247.

Hardisty, R. M., and Ingram, G. I. C. (1965). *Bleeding Disorders: Investigation and Management*, p. 78. Oxford.

Jordan, H. H. (1965a). *Acta orthop. belg.*, **31**, 640.

—— (1965b). *Proceedings of Institutes on Hemophilia* (National Hemophilia Foundation, N.Y.), p. 22.

Matthews, J. M. (1966). *Treatment of Haemophilia and other Coagulation Disorders*, edited by R. Biggs and R. G. Macfarlane, p. 70. Oxford.

Poulain, P. (1964). *Réadaptation*, No. 108, p. 27.

Ramgren, O. (1962). *Acta med. scand.*, **171**, 237.

Salzman, E. W., and Britten, A. (1965). *Hemorrhage and Thrombosis*, p. 38. Boston and London.

Stuart, J., Davies, S. H., Cumming, R. A., Girdwood, R. H., and Darg, A. (1966). *Brit. med. J.*, **2**, 1624.

van Creveld, S. (1964). *Nederlandse Hemofiliestichting*, p. 2. Utrecht.

Wilkinson, J. F., Nour-Eldin, F., Israëls, M. C. G., and Barrett, K. E. (1961). *Lancet*, **2**, 947.

Trial of Gastric Cooling for Haematemesis*

J. B. McFARLAND,† M.D., CH.M., F.R.C.S.; J. G. GOW,‡ M.D., CH.M., F.R.C.S.

Brit. med. J., 1967, **3**, 831–834

Gastric cooling as a method of controlling upper gastrointestinal haemorrhage was initially developed by Wangensteen *et al.* (1958). The temperature and the rate of flow of coolant which they employed produced an intragastric temperature of the order of 15° C. They suggested that this caused: (1) reduced gastric blood flow; (2) depressed acid/pepsin secretion and activity; and (3) decreased gastric motility.

In an extended clinical series they reported on the treatment of 75 patients by gastric cooling, with control of haemorrhage in 57 (76%) (Nicoloff *et al.*, 1962). This result is comparable to the figures analysed by Crampton *et al.* (1964), who added a further 123 reported cases and noted an overall control of haemorrhage in 72.6%. Unfortunately, cessation of haemorrhage cannot necessarily be equated with patients' survival, and in one of the large series included in this analysis (Wangensteen *et al.*, 1963) haemorrhage was controlled in 87% of cases but the hospital mortality was 57%.

Usually a commercial refrigerator formed the basis of the apparatus for gastric cooling. A refrigerated alcohol/water solution was pumped through an intragastric balloon. Mechanical complications with such apparatus have been described by Wangensteen (1962), Nicoloff *et al.* (1962), Richman and Anthony (1963), and Miller *et al.* (1963). Because of these complications a simplified water-circulating apparatus was used in this study.

Haematemesis is an alarming symptom of a serious situation. There is a definite place for a non-operative technique that would assist in its early management and allow time for an exact diagnosis to be made later. We here compare a trial of early gastric cooling with conventional methods of managing massive gastrointestinal haemorrhage.

Subjects, Materials, and Methods

The patients treated had been admitted urgently to a general hospital after a haematemesis or melaena. The condition was thought to be serious enough for the subject to be included in the series if one or more of the following features were present: (1) haematemesis in excess of 1,000 ml., observed by a competent medical witness; (2) fall in systolic blood pressure to 100 mm. Hg. or below for one hour or longer; and (3) acute fall in haemoglobin to below 10.2 g./100 ml. or haematocrit to below 30%.

The patient was admitted to a special unit in a surgical ward, and after he had been assigned to an age group (under or over 50 years) a random selection was made for treatment to include gastric cooling or to be by conventional methods.

The policy of the conservative management is indicated by the following points:

(1) Blood was replaced intravenously at a rate and to an amount indicated by the patient's condition. The blood pressure, pulse rate, haemoglobin, and haematocrit were used as guides, though less importance was given to the latter two in the later stages.

(2) Intravenous dextrose/saline was given slowly (500 ml. six-hourly), usually to keep an intravenous drip infusion open.

(3) A nasogastric tube was *not* used during conservative management and was introduced only if operation (or gastric cooling) was planned.

(4) The patient was encouraged to take milk-and-water orally during conservative management (and immediately after a period of gastric cooling).

(5) Sedation, usually by intramuscular injection, was used as indicated. The drug used was decided for each patient individually: morphine, Omnopon, and a combination of chlorpromazine 25 mg. with promethazine 25 mg. were most commonly given.

(6) Antibiotics, usually by injection, were given when specifically indicated or when cover appeared particularly valuable.

Half the patients in the series were managed conservatively. For the other half gastric cooling was used in addition.

A few days subsequent to this treatment a barium-meal or Gastrografin *x*-ray examination was carried out.

Gastric Cooling Apparatus

The cooling unit in this study was the Cryocycle hypothermia system (Fig. 1). This consisted, in principle, of a pump which circulated water at a rate of about 2 litres a minute in a closed system through copper pipes in an ice-bath, and by tubes to the intragastric balloon. A double balloon of extremely thin (condom) rubber was used with a thermistor lying between the balloons. The cooled water entered through the centre of the coaxial tube, was ejected laterally into the balloon, and returned through the outer tube.

---

* From a paper read at the Annual Meeting of the British Society of Gastroenterology held in London on 3–5 November 1966.

† Senior Lecturer in Surgery, University of Liverpool.

‡ Consultant Surgeon, Liverpool Regional Hospital Board.

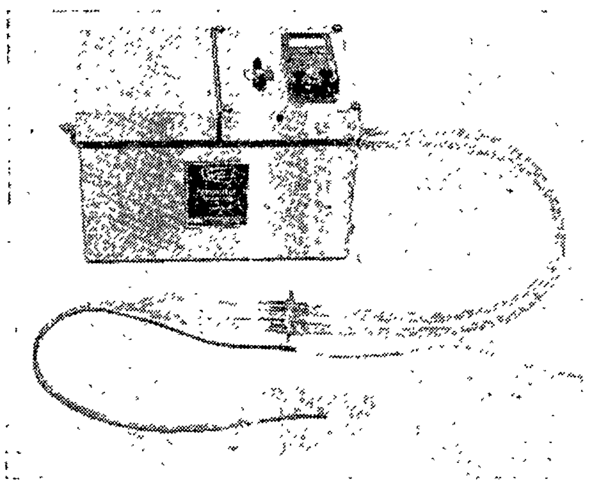


Fig. 1.—Photograph of the Cryocycle hypothermia system. A thermistor lies between the two thin walls of the double balloon, which has been filled with 800 ml. of water.

Technique of Gastric Cooling

When the decision to employ gastric cooling had been made the patient was usually sedated with promethazine 25 mg. and chlorpromazine 25 mg., given intramuscularly. A local anaesthetic spray of 4% lignocaine was used to numb the patient's throat. A nasogastric tube was passed and the patient's stomach was thoroughly lavaged with cold water. This was continued right up to the time for the gastric cooling balloon to be passed, when the nasogastric tube was withdrawn. Every effort was made to empty the stomach completely, especially to remove all blood clot and thus allow good contact between the balloon and the mucosa.

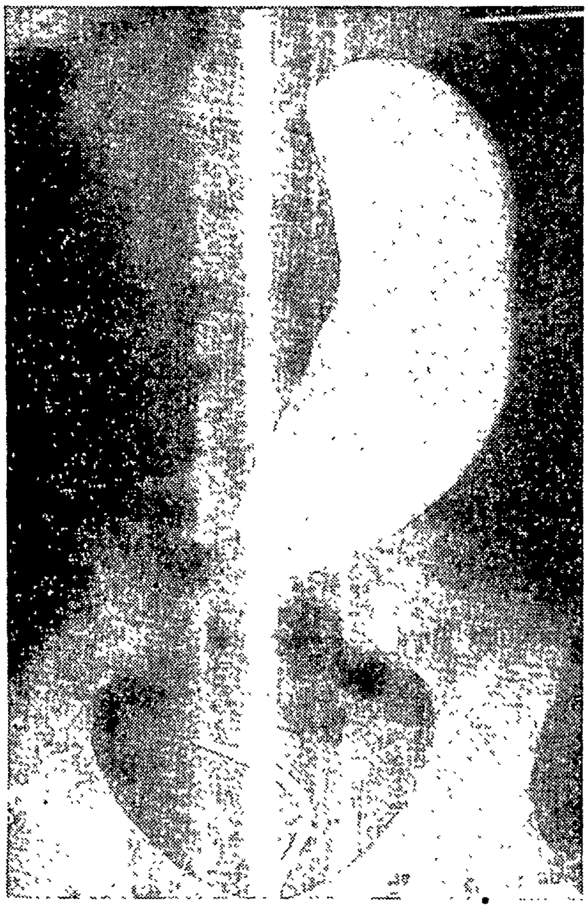


Fig. 2.—Radiograph showing a balloon filled with radio-opaque fluid in a normal stomach. Part of the thermistor lead may be seen in the stomach. The lower thermistor is in the rectum.

The length of the tube to be passed was gauged roughly against the patient, and the tube was then slowly but steadily introduced. It was most important to have the suction ready for immediate use from this point and to aspirate any regurgitated mucus or blood. The passage of the balloon was usually not difficult, but was of course easier in edentulous subjects. With the balloon and the tubes in position they were filled with 800 ml. of water in 50-ml. increments from a special syringe.

As a routine the position of the balloon was checked by one straight radiograph of the abdomen shortly after the beginning of treatment. The thermistor lead served as a guide to the position of the balloon. If more accurate visualization of the balloon was required a radio-opaque solution, such as Hypaque, could be introduced into it. Fig. 2 shows the *x*-ray plate obtained in this way from a normal-sized stomach.

When the gastric cooling was under way the pump circulated the water through the closed system of the tubes, the balloon, and the pipes in the bath. Supervision of the hypothermia machine required only that the bath was maintained with water and ice to a level covering the pipes. Carbon dioxide ice (" dry ice ") was added as a " booster " ; this was not essential, but it conserved the amount of ice used (over 1 cwt. (50.8 kg.) in 24 hours).

During the period of gastric cooling the intragastric, rectal, bath, inflow, and outflow temperatures were monitored (Fig. 3). Pulse rate, blood pressure, and respiration were recorded hourly ; electrocardiography was carried out ; haemoglobin and haematocrit estimations were done at regular intervals ; the bleeding- and clotting-times were measured once ; and the blood urea and electrolytes were estimated daily. Urine volume was recorded, checks being made on specific gravity and urea concentration.

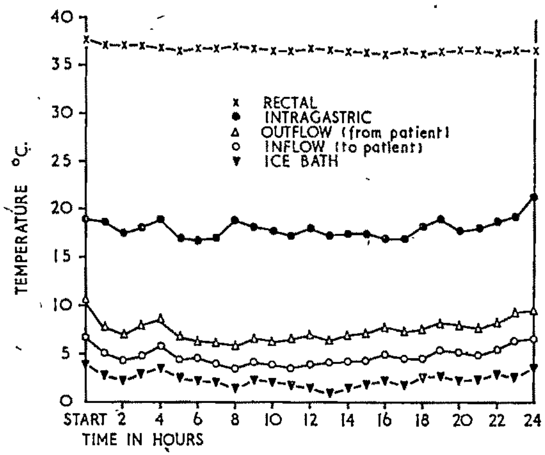


Fig. 3.—Graph of the temperatures during gastric cooling. This was compiled by averaging the figures for 10 cases early in the series.

In almost all cases gastric cooling was continued for 24 hours. Soon after it was under way the patient was covered by an electric blanket (in addition to ordinary blankets), and this was switched on as soon as any shivering or tendency of the rectal temperature to fall was noted. The level of external warming was aimed at limiting the fall in rectal temperature to only a few degrees, and sometimes a second electric blanket was required. At the completion of the period of gastric cooling the pump was switched off and the intragastric temperature allowed to level out with the body temperature. The balloon was emptied and removed.

Results

This paper describes the outcome in 44 patients treated within a two-year period. The apparent causes of the haemorrhage in this series are indicated in Table I.

Table II gives the overall outcome in the broad terms of complete recovery, successful operation, or death in each group. All hospital deaths are shown, and these are further summarized in Table III.

Table IV indicates the degree of success or failure of arrest of haemorrhage (indicated by absence of melaena, clear gastric contents, and haemoglobin level) in association with gastric cooling. This is for six patients under 50 years old (all successfully treated) and 16 over 50 years old. There was permanent success in 19 (86%) of the 22 cases.

TABLE I.—*Haematemesis: Diagnosis in 44 Cases*

	Gastric Cooling		Conservative Management		Total
Age Group:	Under 50	Over 50	Under 50	Over 50	
Gastric ulcer ..	1	9		4	14
Duodenal ulcer ..	2	4	4	6	16
No lesion on barium meal	3	2	2	4	11*
Varices		1		1	2
Carcinoma				1	1
Total	6	16	6	16	44

* This category includes 10 women, of whom two had taken salicylates, two were on corticosteroid therapy, and six remained undiagnosed. The one man had had a perforated duodenal ulcer six years earlier.

TABLE II.—*Eventual Outcome in the Series of 44 Patients*

Outcome	Gastric Cooling		Conservative Management		Total
	Under 50	Over 50	Under 50	Over 50	
Complete recovery..	5	10	6	11	32
Successful operation:					
Elective	1	1			2
Emergency ..		1		1	2
Death:					
No operation ..		3		1	4
Operation ..		1		3	4
Total	6	16	6	16	44

TABLE III.—*Causes and Times of the* 8 *Deaths in the Series of* 44 *Patients*

Gastric Cooling

A.B.: 64 years, male, cardiac infarction; during G.C.
C.D.: 56 years, male, hepatic failure; one month after G.C.
E.F.: 66 years, female, stroke and cardiac infarction; 12 days after G.C.
G.H.: 64 years, male, cardiac infarction; 11 hours after G.C.

Conservative Management

S.T.: 70 years, male, cardiac failure and continuing haemorrhage; four days
U.V.: 58 years, male, hepatic failure; 27 days
W.X.: 78 years, female, post-gastrectomy leak and cardiac infarction; 18 days
Y.Z.: 68 years, female, leak after near-total gastrectomy for carcinoma; 8 days

TABLE IV.—*Degree of Success or Failure or Arrest of Haemorrhage in 22 Patients Treated with Gastric Cooling*

Degree of Arrest	Under 50 Years Old			Over 50 Years Old				Total
	G.U.	D.U.	No Lesion on Ba Meal	G.U.	D.U.	No Lesion on Ba Meal	Varices	
Permanent ..	1	2	3	8	3	2		19
Arrest but delayed recurrence ..				1				1
Arrest but immediate recurrence..							1	1
Failure					1			1
Total.. ..	1	2	3	9	4	2	1	22

TABLE V.—*Degree of Success or Failure of Arrest of Haemorrhage in 22 Patients with Initial Conservative Management*

Degree of Arrest	Under 50 Years Old		Over 50 Years Old					Total
	D.U.	No Lesion on Ba Meal	G.U.	D.U.	No Lesion on Ba Meal	Varices	Ca.	
Permanent ..	4	2	3	3	3			15
Failure			1	3	1	1	1	7
Total.. ..	4	2	4	6	4	1	1	22

Table V indicates the comparable figures for the 22 cases initially treated conservatively. In this group there was permanent arrest of haemorrhage in 15 (68%) of the cases. In both groups failures were limited to patients over 50 years old.

In Fig. 4 it may be seen that the average for the total blood transfused to each patient in the gastric-cooling group is 8.6 units (540 ml. per unit) compared with 8.3 units in the conservatively managed group.

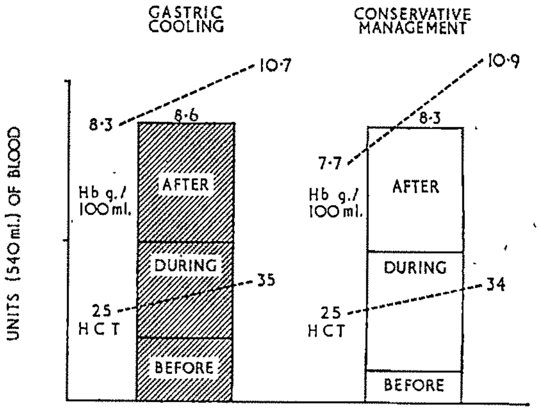


FIG. 4.—Comparison of the average amounts of blood transfused and the haemoglobin and haematocrit levels in the two groups of patients.

Evaluation of the Hypothermia Machine

The Cryocycle hypothermia system functioned very smoothly throughout the work. The plastic tubing, naturally, underwent some wear, but the second set was still being used at the end of the project. New balloons were used for each treatment; standard high-quality condoms proved ideal.

The most important temperature reading was that of the intragastric probe. If this remained steady and between 20 and 15° C. it was a good indication that coolant flow was proceeding satisfactorily. The average fall in rectal temperature was a few degrees only (as indicated in Fig. 3). However, it was possible for this to drift lower if external warming were not vigorous.

The hypothermia machine had the great advantage of being designed for gastric cooling only—that is, it was impossible when water was being circulated in the manner described for temperatures to fall below 0° C. This meant that the only immediate supervision necessary was that ice should be maintained in the bath.

Complications of Gastric Cooling

No catastrophic complications such as stomach rupture due to overdistension were encountered. This would seems to be almost impossible with the hypothermia machine used in this work.

Though cardiac infarction accounted for two deaths in patients who had gastric cooling this could quite reasonably be regarded as coincidental. Electrocardiography did not show any "injury potential" in association with gastric cooling.

Chest infection was the most common problem. During gastric cooling the intragastric balloon possibly gave some degree of left chest "splintage," though infection was not noticeably more marked on the left side. The patients were relatively immobilized in the supine position, and some inhalation of blood or mucus must have occurred quite often in spite of the care taken. In retrospect, moderate inclination of the upper trunk would probably have been wise.

When operations on the stomach were done urgently not long after gastric cooling had been under way there were no untoward findings in the gross or microscopical appearances of the stomach. Nor was there any evidence that postoperative healing was prejudiced by gastric cooling.

Discussion

In this study gastric cooling was carried out for a 24-hour period in all but a few of the cases so treated. This was because a review of the duration of treatment used by other workers (when they stated this) suggested this to be a reasonable time to control haemorrhage and minimize the chance of its immediate recurrence. It proved satisfactory to adhere to this period as a basis for comparative study, but probably a shorter period could be effective in some cases.

The definition of "massive" haemorrhage in terms of the blood loss, the patient's condition, and haemoglobin and haematocrit levels was arbitrary. It would not allow strict comparison with other reported series, but was a good practical guide for inclusion of patients in this series. Only after the patient had been accepted was the card indicating the method of treatment consulted.

Comparison between the two groups by examination of the "degree of arrest of haemorrhage" (Tables IV and V) would suggest that gastric cooling (three recurrences or failures) had a better success rate than the conservative group (seven failures), but statistical evaluation of these data (Table VI) indicates that any difference in the arrest of haemorrhage is not significant. Moreover, Table II shows that the eventual outcome (four deaths) was the same for each group.

TABLE VI.—*Statistical Evaluation of Data from Tables IV and V*

	Gastric Cooling	Conservative Management	Total
Permanent arrest	19	15	34
Degree of cooling	3	7	10
Total	22	22	44

$\chi^2 = 2{\cdot}07$. $P > 0{\cdot}10$.

In Fig. 4 the volume of blood transfused and the degree of anaemia show some minor differences (the conservative group had marginally lower haemoglobin levels at the start and throughout the period of review; less blood was transfused to those under 50 years—conservative group), but the overall *similarity* of the figures is striking. In particular an average of 8.6 units of blood was given to the gastric cooling group, while an average of 8.3 units was given to the controls.

It is evident that there is no significant difference between the two groups.

Summary

In a prospective study gastric cooling was used as an adjunct to initial conservative management of patients with serious upper gastrointestinal haemorrhage.

It has been shown that this method conferred no benefit on this group of patients compared with a similar group managed by expectant measures only.

This relative failure was not due to technical deficiencies; the hypothermia apparatus functioned smoothly and appeared to be superior to most earlier units.

The overall experience with this technique suggested that it may be useful when haemorrhage is persisting and there are strong reasons for avoiding operation.

This work was supported by a grant from the Medical Research Council. The Cryocycle hypothermia system, used throughout, was made available by Edward Weck and Co., Long Island City, New York. We are grateful also to the physicians and surgeons of Sefton General Hospital who referred cases and to Sister E. Edwards and Sister D. Markey for their expert nursing.

REFERENCES

Crampton, R. S., Cali, J. R., Yerys, P., Buetow, G. W., and Glaubitz, J. P. (1964). *Surgery*, **55**, 607.
Miller, R. E., Moscarella, A. A., and Fitzpatrick, H. F. (1963). *Arch. Surg.*, **86**, 272.
Nicoloff, D. M., Griffen, W. O., jun., Salmon, P. A., Peter, E. T., and Wangensteen, O. H. (1962). *Surg. Gynec. Obstet.*, **114**, 495.
Richman, A., and Anthony, D. (1963). *Amer. J. dig. Dis.*, **8**, 113.
Wangensteen, O. H., Root, H. D., Jenson, C. B., Imamoglu, K., and Salmon, P. A. (1958). *Surgery*, **44**, 265.
Wangensteen, S. L. (1962). *Surg. Clin. N. Amer.*, **42**, 1171.
—— Orahood, R. C., Voorhees, A. B., Smith, R. B., III, and Healey, W. V. (1963). *Amer. J. Surg.*, **105**, 401.

Lactobacillus casei C.S.F. Folate Activity

D. G. WELLS,* M.B., B.S.; H. J. CASEY,† A.I.M.L.T.

Brit. med. J., 1967, **3**, 834–836

Folic acid derivatives are essential components of enzyme systems required in the synthesis of several key precursors of both protein and nucleic acids. The effects of folate deficiency on human metabolism are potentially extremely severe (Woods, 1964).

It is known that the C.S.F. concentrates folate (Herbert and Zalusky, 1961). As the explanation for this is not understood and because of the recent interest in the relation between folate deficiency and neurological disease (Hansen *et al.*, 1964; Anand, 1964; Grant *et al.*, 1965), it was decided to study the C.S.F. folate activity in patients with neurological disease.

Materials and Methods

Samples of cerebrospinal fluid were obtained from patients in the following groups:

(1) *Hospital Controls:* The 30 patients in this group were admitted for investigation of neurological or psychiatric symptoms. However, in no instance was there evidence of active neurological disease. Several patients who had cerebrovascular accidents some months before admission were included in the control group. The C.S.F. was normal in respect of the total protein, cell count, and Pandy, Nonne–Apelt, and Lange tests.

(2) Patients with miscellaneous neurological diseases including: those with epilepsy being treated with anticonvulsants and those with multiple sclerosis and varied tumours of the nervous system.

The C.S.F. was centrifuged and the supernatant taken for analysis. Blood for the serum folate estimation was taken while the patient was fasting. The serum was separated within two hours from the time of venesection. Ascorbic acid (5 mg./ml.) was added to the C.S.F. and serum. Specimens were stored at −20° C. until analysis.

---

* Formerly Resident Pathologist, the National Hospital, Queen Square, London W.C.1.

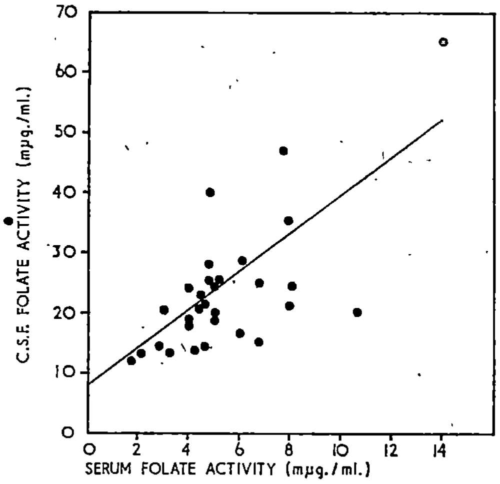
† Department of Haematology, the Hospital for Sick Children, Great Ormond Street, London W.C.1.

The serum folate levels were measured by microbiological assay with *Lactobacillus casei* (Waters and Mollin, 1961). The normal serum folate range is 5.9–21 mμg./ml. A serum folate of 4 mμg./ml. or above excludes severe folate deficiency. The C.S.F. folate levels were determined similarly, but the final dilution of the C.S.F. was one part in 160 as compared with one part in 80 for the serum folate estimation. If the colorimeter reading of the test sample did not correspond with the sensitive part of the pteroylglutamic acid curve the assay was repeated at an appropriate higher or lower dilution. Duplicate assays were performed on each C.S.F. and serum specimen, the mean figure being taken.

Results

Group 1

The range of C.S.F. folate activity in the 30 hospital control subjects was 12.6–67 mμg./ml. The mean C.S.F. folate level was 23.6 mμg./ml. (±2.0 mμg./ml. S.E.). The mean serum folate was 5.4 mμg./ml. (±0.46 mμg./ml. S.E.). The correlation between the C.S.F. and serum folate levels is shown in the Chart ($r=+0.7$; $P<0.001$). The calculated regression line has been drawn ($y=3.1\times+7.0$).



Relation between C.S.F. and serum *L. casei* folate activity.

Group 2

(A) *Epileptics Treated with Anticonvulsants* (10).—The mean C.S.F. folate level in 10 epileptic patients on anticonvulsant therapy was 16 mμg./ml. (± 2.1 mμg./ml. S.E.), which was significantly different from the mean C.S.F. folate level of the control subjects ($P<0.05$). The mean serum folate level was 4.7 mμg./ml. (±0.57 mμg./ml. S.E.). One-third of the patients had a C.S.F. folate level below 12.6 mμg./ml. Despite the effect of the anticonvulsants a correlation persisted between the serum and C.S.F. folate levels ($r=0.627$; $P<0.05$). The calculated regression line was $y=2.3\times+5.3$. Perhaps the most interesting epileptic patient studied was a woman who developed a cerebellar disorder with ataxia, nystagmus, and dysarthria while being treated with Epanutin and phenobarbitone. Intensive investigation (including air-studies) failed to suggest an alternative diagnosis to Epanutin intoxication. However, when the Epanutin therapy was curtailed no improvement resulted. Her serum and C.S.F. folate levels were 1 mμg./ml. and 4.2 mμg./ml. respectively. The serum vitamin B_{12} level was normal. Treatment with folic acid resulted in no objective improvement.

(B) *Multiple Sclerosis* (12).—The range of C.S.F. folate activity in the 12 patients with multiple sclerosis was 16–43 mμg./ml. The mean C.S.F. and serum folate levels were 21.6 mμg./ml. (±1.7 mμg./ml. S.E.) and 6.0 mμg./ml. (±0.83 mμg./ml. S.E.) respectively. The mean C.S.F. folate level was not significantly different from that of the control subjects ($P>0.05$). The correlation between the serum and C.S.F. folate activity in this small group was poor ($r=0.28$; $P>0.05$). Several of the patients were being treated with vitamin B_{12} injections and/or corticosteroids. This therapy or the underlying pathology may have been responsible for the lack of correlation.

(C) *Tumours of the Nervous System* (10).—The C.S.F. folate range in 10 patients with varied tumours of the nervous system was 7–27 mμg./ml. The mean C.S.F. folate level was 19 mμg./ml. (±1.9 mμg./ml. S.E.) while the mean serum folate level was 5.9 mμg./ml. (±1.1 mμg./ml. S.E.). The mean C.S.F. folate level was not significantly different from that of the control subjects ($P>0.05$). This group included patients with benign tumours and also those with malignant lesions. A patient with a low C.S.F. folate of 7 mμg./ml. and serum folate of 3.9 mμg./ml. had a spinal block due to metastases. When a laminectomy was performed tumour tissue was found invading the theca. In view of the known ability of tumour cells to metabolize folate it is not surprising that the correlation between the serum and C.S.F. *L. casei* folate activity was poor ($r=0.32$; $P>0.05$).

(D) *Miscellaneous Neurological Diseases.*—Smaller groups of patients suffering from polyneuritis (5), Parkinsonism (4), motor neurone disease (4), Friedreich's ataxia (1), tabes dorsalis (1), syringomyelia (1), trigeminal neuralgia (1), and acute necrotic myelitis (1) were also studied. Their C.S.F. folate levels with one exception fell within the range seen in the control subjects. The patient with a low C.S.F. folate of 12 mμg./ml. was an alcoholic with a peripheral neuropathy. His admission to hospital was prompted by the development of bilateral optic neuritis. A patient with neurological symptoms in whom no definite diagnosis could be made is of interest because she had a low C.S.F. folate level. She had pulmonary tuberculosis and was being treated with antituberculosis drugs (isoniazid, para-aminosalicylic acid, and streptomycin). She gave a short history of paraesthesia of her hands and feet, suggesting an early peripheral neuropathy. However, electromyographic studies showed no evidence of peripheral neuropathy. Her C.S.F. folate was 8 mμg./ml. and the serum level 1.3 mμg./ml. The serum B_{12} level was 660 μμg./ml. When her drug therapy was curtailed and her diet improved her symptoms were alleviated.

Discussion

It remains unexplained why folate deficiency does not cause a clearly defined neurological picture allied to that of subacute combined degeneration of the cord. Neurological disease associated with folate deficiency has now been documented by a few authors (Anand, 1964 ; Hansen *et al.*, 1964). Grant *et al.* (1965) have discussed this association and described three cases with mainly sensory signs and symptoms which improved after oral folic acid.

There is a positive correlation between the serum and C.S.F. folate activity. Despite this correlation it is reasonable to assume that the C.S.F. folate level will more accurately reflect the folate content of the nervous system than the serum level. It is therefore advantageous to assay the C.S.F. folate activity when investigating the relation between disorders of the nervous system and folate deficiency.

The major difficulty of investigating such a relation is that folate deficiency may be coincidental and quite unrelated to the nervous disorder. Therefore, before attributing a neurological disorder to folate deficiency it is essential to exclude other aetiological factors, including deficiency of vitamin B_{12}, pyridoxine, and thiamine.

As a group the epileptics showed the largest proportion of subnormal folate levels. Mannheimer *et al.* (1952) and Badenoch (1954) were the first to note the occurrence of megaloblastic anaemia in epileptic patients who were being treated with anticonvulsant drugs. More recently there have been reports of folate deficiency in many non-anaemic drug-treated epileptics (Hawkins and Meynell, 1958 ; Klipstein, 1964 ; Malpas *et al.*, 1966 ; Reynolds *et al.*, 1966). The findings in our small group of epileptics are in agreement and also show that evidence of disturbed folate metabolism may be detected in the C.S.F. This is of interest, as Reynolds *et al.* (1966) have postulated that the interference with folate metabolism may be related to the therapeutic action of anticonvulsants, and at the same time may be responsible for some of the mental symptoms that occur in these patients.

One of the epileptic patients being treated with phenobarbitone and Epanutin subsequently developed a cerebellar syndrome which failed to resolve when the Epanutin was curtailed. Permanent neurological dysfunction resulting from Epanutin has been described by several authors, including Morris *et al.* (1956) and Putnam and Rothenberg (1953). Rats and cats when subjected to prolonged intoxication showed the loss of the Purkinje cells and degenerative cell changes in the cerebellum (Kokenge *et al.*, 1965). The patient, described above, was found to have a C.S.F. folate level of 4.2 mμg./ml. It is suggested that the toxic effect of Epanutin is due to its interference with folate metabolism.

Sobotka *et al.* (1958), by means of a microbiological assay utilizing a thermophilic bacillus, found raised C.S.F. folate levels in 34 out of 42 cases of multiple sclerosis studied. The C.S.F. folate levels in the 12 multiple sclerosis patients studied all fell within the range seen in the control subjects. Of 10 patients with varied tumours of the nervous system, only one had a low C.S.F. folate level. This patient had a spinal block due to metastases. It is probable that the tumour cells were metabolizing the C.S.F. folate.

The C.S.F. folate level in five patients with polyneuritis of different aetiology with one exception fell within the range seen in the control subjects. The exception was an alcoholic with a severe peripheral neuropathy and evidence of an early hepatic cirrhosis. Folate deficiency in combination with a deficiency of other vitamins has already been noted in cases of alcoholic peripheral neuropathy by Fennelly *et al.* (1964). No improvement resulted when the patient was given oral folic acid.

The association of folate deficiency and tuberculosis has been noted by Roberts *et al.* (1966). They concluded that folate deficiency was not due to the chemotherapy but to the disease process itself, or a poor diet. Whether the paraesthesiae and dysaesthesia in the case described were due to the folate deficiency cannot be answered, as the symptoms may have been the presenting feature of a disease, such as multiple sclerosis, which spontaneously remitted.

Summary

The serum and C.S.F. *Lactobacillus casei* folate activity has been assayed in 30 hospital control patients. A positive correlation between the C.S.F. and serum folate activity has been shown to exist.

The C.S.F. folate activity has been assayed in miscellaneous neurological diseases. Drug-treated epileptic patients showed a high proportion of subnormal C.S.F. levels. Groups of patients with multiple sclerosis, miscellaneous tumours, etc., were found to have a mean C.S.F. folate level which did not differ significantly from that of the control group.

The association between neurological disorders and folate deficiency is discussed.

It is a pleasure to thank Professor J. N. Cumings and Dr. R. M. Hardisty for their help and advice in the preparation of this manuscript.

REFERENCES

Anand, M. P. (1964). *Scot. med. J.*, **9**, 388.

Badenoch, J. (1954). *Proc. roy. Soc. Med.*, **47**, 426.

Fennelly, J., Frank, O., Baker, H., and Leevy, C. M. (1964). *Brit. med. J.*, **2**, 1290.

Grant, H. C., Hoffbrand, A. V., and Wells, D. G. (1965). *Lancet*, **2**, 763.

Hansen, H. A., Nordqvist, P., and Sourander, P. (1964). *Acta med. scand.*, **176**, 243.

Hawkins, C. F., and Meynell, M. J. (1958). *Quart. J. Med.*, **27**, 45.

Herbert, V., and Zalusky, R. (1961). *Fed. Proc.*, **20**, 453.

Klipstein, F. A. (1964). *Blood*, **23**, 68.

Kokenge, R., Kutt, H., and McDowell, F. (1965). *Neurology (Minneap.)*, **15**, 823.

Malpas, J. S., Spray, G. H., and Witts, L. J. (1966). *Brit. med. J.*, **1**, 955.

Mannheimer, E., Pakesch, F., Reimer, E. E., and Vetter, H. (1952). *Med. Klin.*, **47**, 1397.

Morris, J. V., Fischer, E., and Bergin, J. T. (1956). *Brit. med. J.*, **2**, 1529.

Putnam, T. J., and Rothenberg, S. F. (1953). *J. Amer. med. Ass.*, **152**, 1400.

Reynolds, E. H., Milner, G., Matthews, D. M., and Chanarin, I. (1966). *Quart. J. Med.*, **35**, 521.

Roberts, P. D., Hoffbrand, A. V., and Mollin, D. L. (1966). *Brit. med. J.*, **2**, 198.

Sobotka, H., Christoff, N., and Baker, H. (1958). *Proc. Soc. exp. Biol. (N.Y.)*, **98**, 534.

Waters, A. H., and Mollin, D. L. (1961). *J. clin. Path.*, **14**, 335.

Woods, D. D. (1964). *Proc. roy. Soc. Med.*, **57**, 388.

Gritti–Stokes Amputation in Atherosclerosis: a Review of 237 Cases

PETER MARTIN,* V.R.D., M.CHIR., F.R.C.S.; STUART RENWICK,† M.B., F.R.C.S., F.R.A.C.S.
E. MAELOR THOMAS,‡ F.R.C.S.

Brit. med. J., 1967, 3, 837–838

Operation

For the past 15 years we have used the Gritti–Stokes amputation extensively for threatened or established gangrene in atherosclerosis because the anatomy of the collateral circulation in limbs gangrenous from atherosclerosis makes primary healing usual. This is because the femoro-popliteal artery is nearly always obstructed, in which circumstance the distal part of the limb receives its blood supply through the collateral vessels which bypass this vessel. Collateral vessels normally pass in the intramuscular planes, but where there are no such planes they are forced into subcutaneous tissues (Fig. 1). So when the femoro-popliteal artery is blocked the collaterals are found in among the muscles where these surround the femur above or the tibia and fibula below; but in the region of the knee joint, where the bones are not so surrounded, they are forced into the subcutaneous tissues. Flaps fashioned from skin supplied by such enlarged collaterals can be expected to heal better than flaps not so nourished (Martin and Wickham, 1962). Mortality and morbidity have been low, and in addition a useful stump results. Others have advocated this operation (Jones, 1961; Middleton and Webster, 1962; Nayman, 1964; Lishman, 1965).

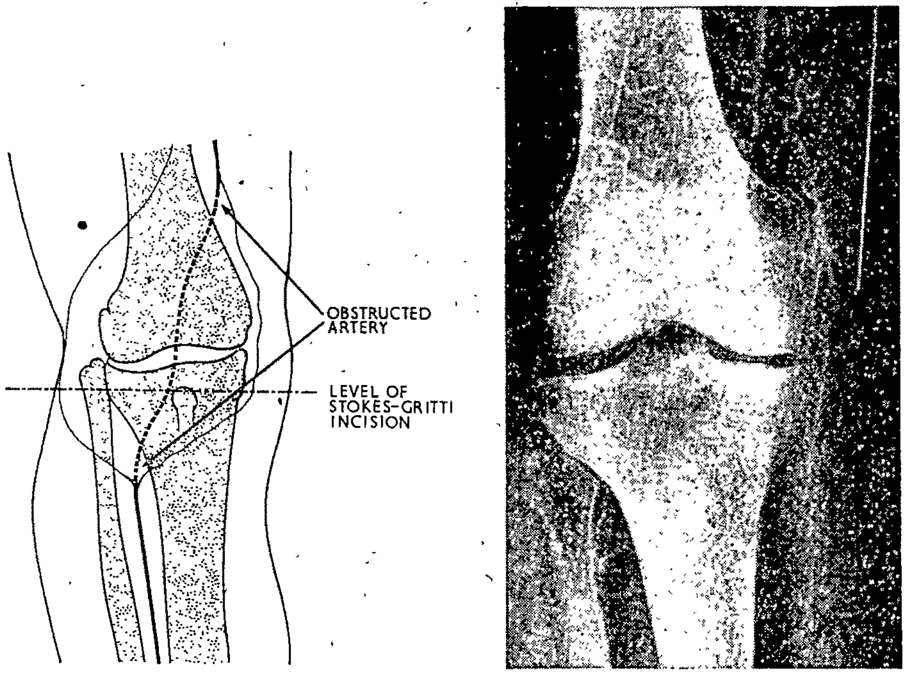


FIG. 1.

The U-shaped incision begins at the adductor tubercle, passes downwards, and then across the mid part of the tibial tubercle. It then ascends on the outer aspect of the lower end of the femur to a point corresponding to the adductor tubercle on the inner aspect. The incision goes down to bone. The two ends of this incision are joined behind the knee by an incision convex downwards, its lowest part about 1 in. (2.5 cm.) distal to its extremities. The knee joint is then acutely flexed and the lateral and cruciate ligaments of the joint are divided. The tibia dislocates forwards, the posterior capsule and the ligaments are divided, and then from in front the vessels and nerves in the popliteal fossa are also divided. The vein—but not the artery, which is already thrombosed—requires a ligature. The sciatic nerve may need a ligature. From the back the hamstring muscles are divided, and the amputation is completed.

The end of the femur is then sawn through at the level of the adductor tubercle. The articular surface of the patella is sawn off. With a bradawl, holes are bored through the lower end of the patella and the posterior lip of the femur so that the patella can be stitched with stout silk to keep it in place over the end of the femur, and to the popliteal ligament is sewn the hamstring tendons so that their extension function is preserved. The wound is sutured in one layer, and a suction-drain is inserted through one angle (Fig. 2).

The drain is removed, without disturbing the dressing, on the second day, and the dressings on the tenth day after operation. The patient is allowed up on the second day and to walk with crutches as soon as he can manage. Within two weeks he should be measured for his pylon. Little blood is lost, postoperative shock is slight, and for some reason phantom limb is not conspicuous.

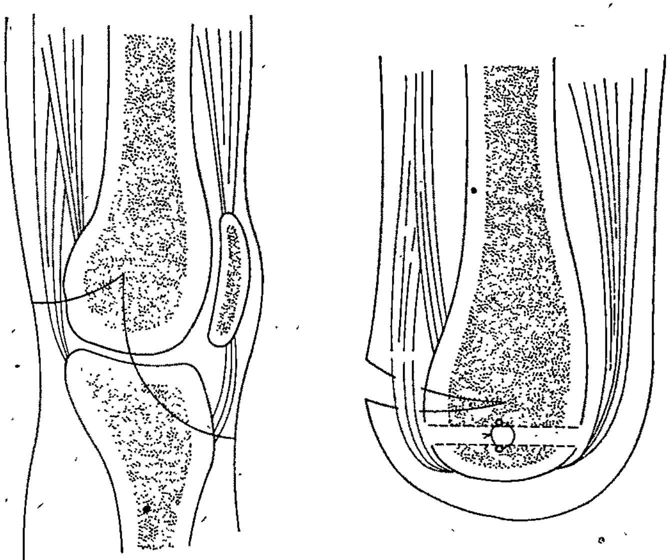

THE INCISION
THE STUMP

FIG. 2.

---

* Surgeon, Hammersmith Hospital, London W.12, and Chelmsford Hospital.
† Registrar, Hammersmith Hospital, London W.12.
‡ Major, R.A.M.C., Honorary Registrar, Hammersmith Hospital, London W.12.

Patients

Gritti–Stokes amputations have been done on 237 occasions between 1957 and 1966 at the Hammersmith and Chelmsford and Essex Hospitals. During this period 20 primary mid-thigh amputations and 21 below-knee amputations were performed for all varieties of vascular disease. Mid-thigh amputations were done when there was infection, sometimes by gas-forming organisms, and when non-infected gangrene of the limb extended to the level of the upper third of the tibia. Below-knee amputations were rarely done for arteriosclerotic gangrene. Bilateral amputations were done on 20 patients.

The average age of patients was 67 years, with a range from 41 to 89 years. Ten per cent. of the patients had had a previous cerebrovascular episode, and 87% had evidence of ischaemic heart disease. Forty-four (20%) suffered from diabetes. The ratio of male to female patients was 5 to 1.

Indications.—The operations were performed for gangrene, rest pain, or indolent ischaemic ulceration.

Results

There were 14 deaths in the first two weeks after amputation, a mortality rate of 5.9%. Primary healing occurred in 176 patients (78.8%). In 27 healing was delayed by minor skin sepsis but was eventually complete, giving a total healing rate of 91%.

In 17 patients (7.7%) sepsis or failure to heal led to a higher amputation, and we have one patient with an unhealed ulcer who will probably come to higher amputation. Two patients have wound sinuses with radiological evidence of osteomyelitis, but they use their prostheses without discomfort. One patient has a mobile patella, probably due to incomplete removal of the cartilage from the joint surface of this bone.

These results are summarized in the Table.

Results in 223 Amputations in which Patient Survived 14 *Days or Longer*

Complete healing	Primary healing	176	(78·8%)
	Delayed healing	27	(12·2%)
Incomplete healing	Stump sinus	2	(1·3%)
	Persistent ulcer	1	
	Failure needing re-amputation	17	(7·7%)

Subsequent Use of the Stump.—During the past 12 months we have fitted seven patients with an immediate prosthesis in association with the Limb Fitting Centre at Roehampton. All these patients were using their stumps for walking within 14 days of amputation. They will form part of a later communication from Roehampton.

Of the remaining 230 patients 123 (55%) were fitted with a prosthesis which they use. At least 29 (12.5%) were recorded as having returned to gainful employment.

Discussion

The operative mortality in this series was 5.9%, which is in close agreement with that reported by others of between 6 and 8% (Middleton and Webster, 1962 ; Lishman, 1965). This low mortality rate is probably due to the fact that the operation is easily and rapidly performed, that there is minimal loss of blood, and that there is no injury to muscle substance. The mortality for mid-thigh amputations is much higher, as Lishman (1965) showed, varying from 18 to 42% (Gilchrist, 1961 ; Ham *et al.*, 1964 ; Otteman and Stahlgren, 1965 ; Lishman, 1965).

The healing rate was 91%—78% by first intention. Others have reported primary healing rates for this operation varying between 76 and 90% (Middleton and Webster, 1962 ; Nayman, 1964 ; Lishman, 1965). The reported healing rates for mid-thigh amputation vary from 53 to 72% (Dale and Jacobs, 1962 ; Ham *et al.*, 1964).

Reamputation at a higher level was necessary in 7.7% of patients. This contrasts markedly with a reamputation rate of between 29 and 38% for below-knee amputations (Tolstedt and Bell, 1961 ; Dale and Jacobs, 1962 ; Lishman, 1965).

As regards disarticulation through the knee, we have been disappointed because primary healing failed to occur in the few of which we have had experience. This may be due to the fact that the skin incision traverses skin which does not enjoy the liberal blood supply found with a Gritti–Stokes incision. Furthermore, the only account of a series of disarticulations that we have seen recorded only 15 patients with primary healing out of 27 patients undergoing operation (Taylor, 1967). In addition, we have evidence that some of the successful cases would in fact have been better if part of the condyles of the femur had been removed to avoid pressure on the skin covering them. If the technique of disarticulation is going to be altered so that the condyles do in fact have to be removed to some extent, then this operation will approximate very closely to the Gritti–Stokes amputation here described. We await with interest reports of amputation by disarticulation.

It is also interesting to note that in the interim report from Roehampton of the results of immediate fitting of prostheses the only type of amputation which was successful in every case was the Gritti–Stokes, though certainly the numbers were small.

Thus the Gritti–Stokes amputation has a low mortality, a high healing rate, and a low reamputation rate. The stump, too, is a useful one.

Rehabilitation is facilitated by the availability of a lightweight articulated prosthesis. This is partially ischial and partially end-bearing, the latter factor ensuring proprioception. The knee joint can be arranged so that flexion is at the same level as that of the opposite side.

If bilateral amputation becomes necessary the Gritti–Stokes amputee can get about in the house on his knees or with rockers and can turn over in bed, which a bilateral mid-thigh amputee cannot do.

Summary

The results of 237 Gritti–Stokes amputations for atherosclerotic gangrene are presented. Primary healing occurred in 78.8%, with a total healing rate of 91%. A mortality of 5.9% and a reamputation rate of 7.7% compare more than favourably with similar series of below-knee or mid-thigh amputations. The immediate fitting of a prosthesis on the operating-table should promote earlier mobility and lower the mortality rate still further.

REFERENCES

Martin, P., and Wickham, J. E. A. (1962). *Lancet*, **2**, 16.
Jones, R. N. (1961). *Brit. med. J.*, **2**, 1496.
Middleton, M. D., and Webster, C. U. (1962). Ibid., **2**, 574.
Nayman, J. (1964). *Med. J. Aust.*, **1**, 441.
Lishman, I. V. (1965). *J. roy. Coll. Surg. Edinb.*, **10**, 212.
Gilchrist, A. R. (1961). Ibid., **6**, 159.
Ham, J. M., Mackenzie, D. C., and Loewenthal., J. (1964). *Aust. N.Z. J. Surg.*, **34**, 97.
Otteman, M. G., and Stahlgren, L. H. (1965). *Surg. Gynec. Obstet.*, **120**, 1217.
Dale, W. A., and Jacobs, J. K. (1962). *Ann. Surg.*, **155**, 1011.
Tolstedt, G. E., and Bell, J. W. (1961). *Arch. Surg.*, **83**, 934.
Taylor, G. W. (1967). *Proc. roy. Soc. Med.*, **60**, 69.

Medical Memoranda

Familial Myasthenia Gravis

Brit. med. J., 1967, 3, 839–840

Myasthenia gravis is described in textbooks of medicine and neurology as a disease of the third and fourth decades of life. Its occurrence in infancy and childhood is rare. During 1900–65 only 54 cases in 22 families have been reported. To find the disease in more than one generation in the same family is rarer still, only four such instances so far having been recorded. Myasthenic symptoms persisting from the time of birth (congenital myasthenia) is also rare. The following four cases of myasthenia gravis in a brother, sister, and two children of an unaffected sister are of interest from these various aspects of the disease.

CASE REPORTS

Case 1.—A man aged 28 attended the Medical College Hospital, Calicut, for drooping of the upper lids, difficulty in focusing near objects, and blurring of vision of two years' duration. On direct questioning he admitted that he had had slight drooping of the eyelids for at least 12 years. He denied any weakness in the limbs or difficulty in swallowing. The history of his past illness showed nothing contributory. One of his sisters, aged 17 (Case 2), had had the same complaints since the age of about 5 years, as also had two nephews (Cases 3 and 4).

General physical examination showed nothing contributory. Bilateral ptosis was present. The ocular movements were almost completely absent in all directions in both eyes. He could not look to one side or the other without turning his head. The pupils were normal. There was no other abnormality in the central nervous system. Examination of the other systems did not reveal any abnormality. Laboratory investigations were negative. The *x*-ray picture of the chest was normal. About 20 minutes after he was given neostigmine subcutaneously (2.5 mg. mixed with 0.5 mg. of atropine) he could lift his eyelids normally and the ocular movements were restored to complete range. The effect lasted for about three hours. He was put on neostigmine bromide 10 mg. thrice daily and ephedrine 30 mg. twice daily. He has since remained significantly improved.

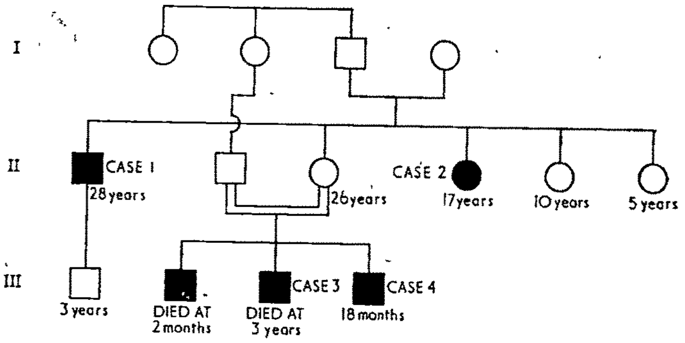
Case 2.—A 17-year-old unmarried girl, sister of Case 1, had had ptosis and restricted movements of the eyeballs from the age of 12 years. The disability was worse towards the evening. From the age of 15 tiredness and weakness of both upper limbs were also noticed. General examination did not reveal any abnormality. Ptosis was present on both sides. Movements of the eyeballs were very restricted in all directions. The pupils were normal. The muscles of the upper limbs showed diminution in motor power not limited to any specific muscle groups. There was no wasting. The deep reflexes were sluggish. Physical examination did not reveal any other abnormality in the central nervous system or any other system. *X*-ray examination of the chest showed widening of the superior mediastinum consistent with a thymic shadow. Other investigations were negative. As in Case 1, there was prompt relief of symptoms and restoration of ocular movements and disappearance of ptosis after neostigmine injection. The patient improved from the regular administration of neostigmine bromide 10 mg. thrice daily.

Case 3.—A 2-year-old boy, son of a normal sister of Cases 1 and 2, was noticed to have ptosis from birth. The parents found that he could not look to one side or the other without turning his head. The extremities were floppy. He was not yet steady in his walk and tended to fall. Physical examination showed bilateral ptosis, restriction of ocular movements in all directions, and hypotonia of the limb muscles. The deep reflexes were sluggish. No other abnormality was detected. The *x*-ray picture of the chest was normal. The ocular movements and the strength of the muscles improved and the ptosis disappeared after the injection of 1.25 mg. of neostigmine. The parents were advised to give the child 5 mg. of neostigmine bromide twice daily. He was doing well, but 11 months after the first admission he had an attack of pneumonia and died.

Case 4.—An 18-month-old boy, younger brother of Case 3, was brought to us immediately after that brother had died of bronchopneumonia. The cases, as stated by the parents, were similar. The boy was found to be weak and slow in his movements and to have had bilateral ptosis since birth. The weakness became more pronounced towards the evening, when the ptosis was also more prominent. Physical examination showed hypotonia of muscles, ptosis, external ophthalmoplegia, and sluggish deep reflexes. An *x*-ray picture of the chest was normal. There was prompt response to a subcutaneous injection of 1.25 mg. of neostigmine, with disappearance of ptosis and external ophthalmoplegia.

FAMILY TREE

The family tree is shown in the Chart. The affected members are shown in black. The members of generation I were examined and all were found to be normal. In this generation there were no marriages between relations. The history did not suggest the presence of similar illness in the previous generation. The disease presumably made its first appearance in generation II, to which Cases 1 and 2 belong. The other members of generation II were examined and found to be normal. The unaffected sister of Cases 1 and 2 and her husband are first cousins. They had three male children in generation III. All were affected by the disease. Their first child died at the age of 2 months. We did not see the child, therefore the case is not reported here. Case 3 died at the age of 3 years. Case 4 is still alive and is being followed up. The 3-year-old son of Case 1 is normal.



FOLLOW-UP

Cases 1, 2, and 3 came under our observation in August 1963 and Case 4 in September 1964. Case 3 died in July 1964. Cases 1, 2, and 4 are still being followed up. They are on maintenance treatment with neostigmine and ephedrine. Case 2 married recently, and it will be of interest to observe the children of the marriage.

COMMENT

The myasthenic syndrome has often been reported in neonates born of myasthenic mothers since Strickroot *et al.* (1942) reported the case of a mother with myasthenia gravis whose newborn child developed signs of generalized weakness on the third day of life and died on the seventh day from respiratory failure. Since in these cases the symptoms are transient and are probably due to a curare-like substance transferred through the placenta it is not correct to include these cases as familial myasthenia gravis. The first report of familial incidence of myasthenia gravis is that of Oppenheim (1900). Celesia (1965) reported the cases of a brother and sister suffering from myasthenia, and reviewed all the cases of familial myasthenia gravis recorded in the literature up to that time, bringing the total number to 54, distributed among 22 families.

The four cases reported here bring the total so far to 58 cases in 23 families. Since in these cases the lesion is mostly confined to the ocular muscles the problem of differentiation from ocular myopathy (Kiloh and Nevin, 1951) arises. But the tendency of the disability to worsen towards evening and the favourable response to the administration of neostigmine favoured the diagnosis of myasthenia gravis.

Certain other observations may be made in these cases. They represent individuals of two generations. In only four of the 22 previously reported families were two generations affected. Peters (1906) reported the cases of two sisters, two brothers, and the father. Noyes (1930) reported cases of a brother, sister, and father ; Eaton (cited by Levin, 1949) the cases of a father and son ; and Foldes and McNall (1960) the cases of two sisters and their mother. The present report is the fifth instance of familial myasthenia gravis affecting more than one generation. Celesia (1965) observed that in instances where more than one generation is affected by the disease the onset is in adulthood. Our cases, however, prove otherwise, for Cases 3 and 4 showed myasthenic symptoms from birth.

The first case of congenital myasthenia was reported by Bowman (1948). Levin (1949) considered three types of myasthenia gravis in children. They are the transient neonatal myasthenia, the familial myasthenia occurring in siblings, and the ordinary or acquired myasthenia. Acquired non-familial myasthenia is rare in childhood ; but among 41 cases of familial myasthenia limited to one generation, in 20 the onset of the disease was in infancy and in 12 in childhood or adolescence (Celesia, 1965). All our four cases had their onset before the age of 16 years, thus proving the early age of onset in familial myasthenia. This difference of the familial cases from the non-familial ones may be of importance from the genetic point of view.

Levin (1949) used the term "congenital myasthenia" to describe the form of myasthenia which begins at birth (or before), and is characterized by a mild onset, marked external ophthalmoplegia, partial ptosis, and symmetrical weakness of the involved muscle groups. In contrast to the usual myasthenia gravis it is not progressive and does not show remissions. There is a dramatic response to the administration of neostigmine. Though the basic defect is the same the disease may be different from the myasthenia gravis described by Erb (1879) and Goldflam (1893). Among the cases of familial myasthenia gravis reported there are only six patients in four families in whom the disease was present from birth and hence qualify as congenital myasthenia. These were reported by Levin (1949, two cases in a family), Osserman (1961, three cases in two families), and Walsh and Hoyt (1959, one case in a family with four affected members). In all these cases ptosis, ophthalmoplegia, and generalized weakness were the prominent symptoms. Our Cases 3 and 4 are the seventh and eighth cases of congenital myasthenia gravis among the familial myasthenics recorded to date. Though Levin thought it probable that these cases would show marked improvement in course of time, one of our patients died at the age of 3 years from an intercurrent respiratory infection.

So far there is only one report of thymus enlargement in familial myasthenia gravis. At necropsy Marinesco (1908) noticed persistence of the thymus, and the histopathological features suggested hyperplasia. In our Case 2 the x-ray picture of the chest showed widening of the superior mediastinum consistent with enlargement of the thymus.

Our thanks are due to Dr. R. Ananthanarayanan, Principal, Medical College, Calicut, and to Dr. M. Thankam, Superintendent, Medical College Hospital, Calicut, for allowing us to report these cases.

C. B. C. WARRIER, M.D., B.SC., M.R.C.P.,
Assistant Professor.
T. D. G. PILLAI, M.R.C.P.ED.,
Associate Professor.
Department of Medicine,
Medical College,
Calicut, India.

REFERENCES

Bowman, J. R. (1948). *Pediatrics*, **1**, 472.
Celesia, G. G. (1965). *Arch. Neurol. (Chic.)*, **12**, 206.
Erb, W. (1879). *Arch. Psychiat. Nervenkr.*, **9**, 336.
Foldes, F. F., and McNall, P. G. (1960). *J. Amer. med. Ass.*, **174**, 418.
Goldflam, S. (1893). *Dtsch. Z. Nervenheilk.*, **4**, 312.
Kiloh, L. G., and Nevin, S. (1951). *Brain*, **74**, 115.
Levin, P. M. (1949). *Arch. Neurol. Psychiat. (Chic.)*, **62**, 745.
Marinesco, G. (1908). *Sem. méd. (Paris)*, **28**, 421.
Noyes, A. P. (1930). *R.I. med. J.*, **13**, 52.
Oppenheim, H. (1900). *Diseases of the Nervous System*, translated by Edward E. Mayer, 2nd ed., p. 650. Philadelphia.
Osserman, K. E. (1961). *Myasthenia Gravis : Second International Symposium Proceedings*, edited by H. R. Viets, p. 307. Springfield, Illinois.
Peters (1906). *Ärztever., Rostock*, **5**, 242.
Strickroot, F. L., Schaeffer, R. L., and Bergo, H. L. (1942). *J. Amer. med. Ass.*, **120**, 1207.
Walsh, F. B., and Hoyt, W. F. (1959). *Amer. J. Ophthal.*, **47**, No. 5, pt. 2, 28.

Self-inflicted Oleogranuloma of Breast

Brit. med. J., 1967, **3**, 840–841

While oleogranuloma of the breast is a well-recognized condition in the Orient, it must be unusual to encounter a case in Britain. The following case of bilateral granulomata of the breasts in an English woman is especially interesting, in that the condition was self-inflicted after she had read an article in the lay press which mentioned that Japanese women have had petroleum jelly injected into their bosoms to increase their size.

CASE REPORT

An unmarried woman aged 26, the mother of twins aged 6 years, was concerned about the flatness of her chest and consulted a plastic surgeon who, 10 years previously, had removed a tattoo from her arm. As she had recently been under psychiatric treatment, it was thought unwise to advise operation at that time. She therefore decided to treat herself by making multiple injections of warm, molten petroleum jelly into each breast, using a 20-ml. syringe and intramuscular needles which she had purchased for this purpose. Pain was not experienced at the time of the injection, but several days later she described tenderness and discomfort in both axillae. This was followed during the next few months by a severe reaction, more marked on the right side, and the breasts became nodular, painful, and inflamed, and finally sinuses formed exuding petroleum jelly (Fig. 1).

Mammograms showed extensive cystic changes in the breasts, presumably due to grease globules (Fig. 2). *Treatment :* Bilateral simple mastectomy was advised but rejected by the patient. It was therefore decided to try to evacuate the grease globules through several small incisions. Each breast was operated on separately, with an interval of three months between operations.

At operation some of the oleogranulomata were so well defined that they could be dissected free intact (Fig. 3). Other areas of the breast had diffuse fibrotic changes with infiltration of grease, and the best that could be done here was to extrude as much of the petroleum jelly as possible. The wounds were closed and a small corrugated rubber drain was inserted. Postoperative antibiotic therapy was given, though bacterial culture of the excised tissue was sterile. The wounds healed by first intention and the breasts have remained free from further discharge. As expected, the breasts were still quite flat and the patient was still seeking mammoplasty.

Histology of the removed lumps showed the typical appearances of oleogranulomata, there being multiple cystic areas surrounded by dense fibrous tissue and foreign body giant cells (Fig. 4).

COMMENT

As early as 1903 Gersuny suggested that paraffin waxes of high melting-point could be used as a subcutaneous implant to alter surface contours. It was soon found, however, that in a proportion of cases the late results were far from satisfactory owing to the formation of oleogranulomata, followed by ulceration of the overlying tissues and persistent discharging sinuses.

While this method of mammoplasty has been abandoned by medically qualified persons, occasionally one comes across such a case as that described, but this is more common in the East (Tinckler and Stock, 1955).

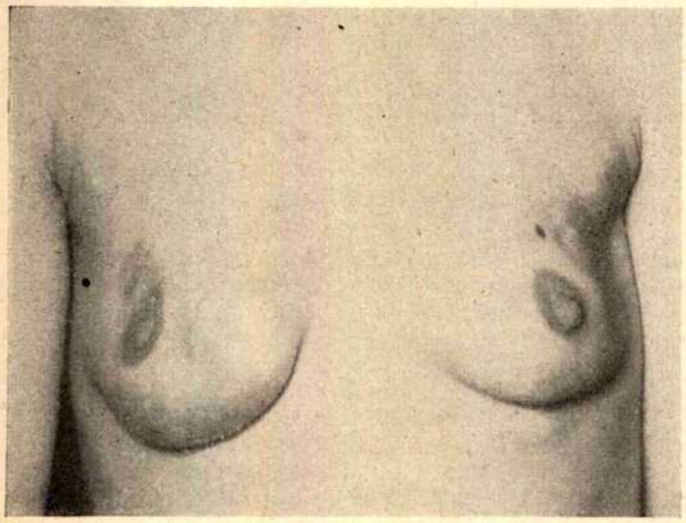


FIG. 1.—Induration and sinuses in both breasts after an intramammary injection of petroleum jelly.

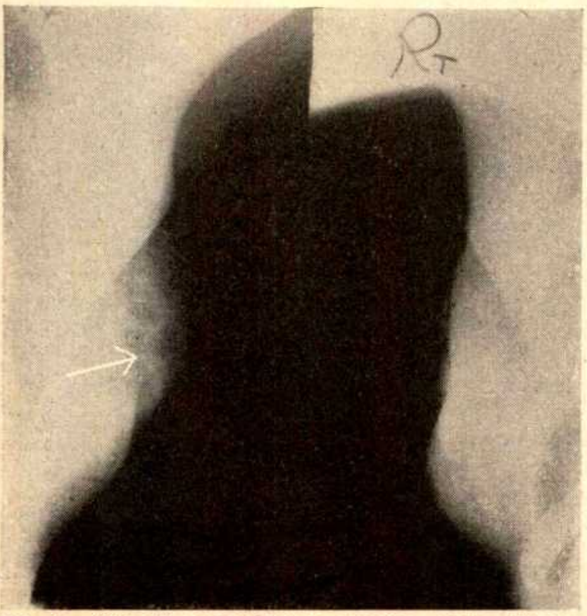


FIG. 2.—Bilateral mammograms: extensive cystic changes shown on left side (arrowed) presumably due to grease globules.

Histologically there is no difference between the oleogranuloma so formed and that encountered as a result of accidental injection with a high-pressure spray gun. Another less abstruse cause of oleogranulomata is the injection of haemorrhoids with phenol in almond oil, a procedure which is not without its hazards.

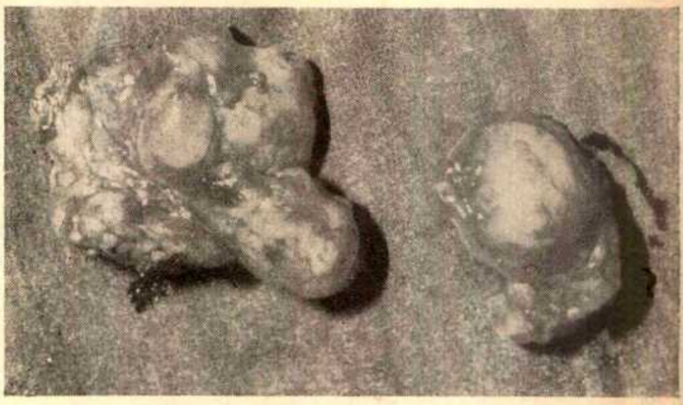


FIG. 3.—Two oleogranulomata dissected intact from the breast.

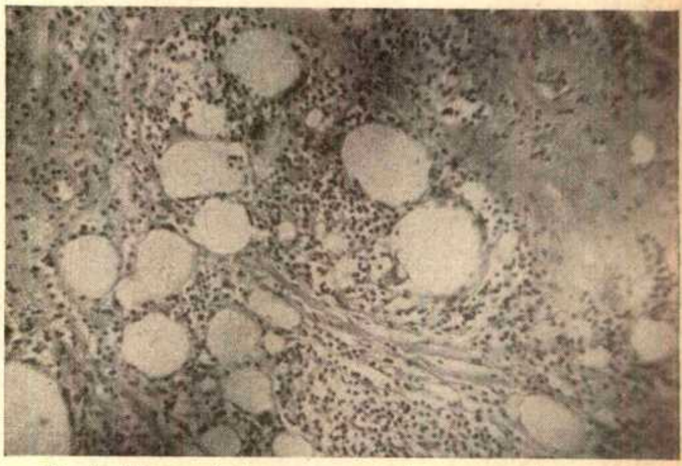


FIG. 4.—Microscopical appearance of oleogranuloma (low power).

Oleogranulomata in the main are themselves relatively harmless except for the mechanical difficulties they may cause, depending on their site. If, on the other hand, ulceration of the overlying skin occurs with the formation of a persistent discharging sinus, then neoplastic change sometimes occurs at the edge of the ulcer so formed (Vinogradov, 1936).

We would like to thank Professor F. E. Stock for his help and criticism in the preparation of this paper, and Mr. J. Cosbie Ross for allowing us to report it.

R. B. CROSBIE, M.B., B.SC., F.R.I.C., F.R.C.S., F.R.C.S.ED.,
Senior Surgical Registrar, Royal Southern Hospital, Liverpool 8.
H. D. KAUFMAN, CH.M., F.R.C.S., F.R.C.S.ED.,
Senior Surgical Registrar, Broadgreen Hospital, Liverpool 14.

REFERENCES

Gersuny, R. (1903). *Zbl. Chir.*, **30**, 1.
Tinckler, L. F., and Stock, F. E. (1955). *Aust. N.Z. J. Surg.*, **25**, 142.
Vinogradov, D. (1936). *Langenbecks Arch. klin. Chir.*, **187**, 69.

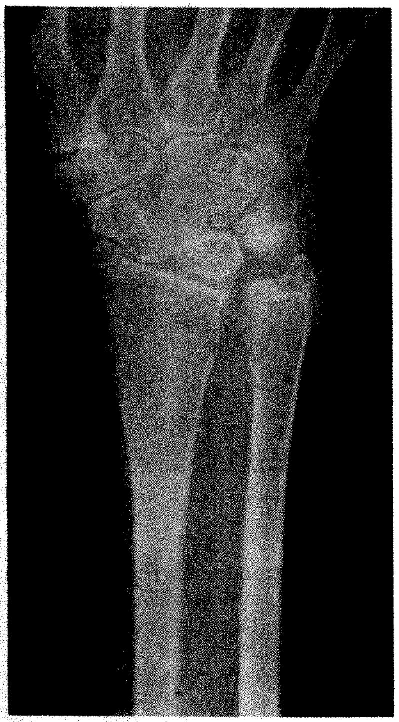
Oldest Pituitary Dwarf?

Brit. med. J., 1967, 3, 842

The oldest presenting age of idiopathic pituitary dwarfism in a series reported by Albert *et al.* (1953) was 41. Faurbye (1946) reported the case of a 61-year-old woman and Hawley (1963) the case of a 67-year-old man. We describe the case of a man with hypopituitary dwarfism who first became ill at the age of 77 years, responded excellently to hormonal replacement therapy, and subsequently developed a carcinoma of the oesophagus.

CASE REPORT

The patient was admitted to hospital on 21 July 1965 with a history of increasing dyspnoea, swelling of the ankles, weakness, constipation, and increased sensitivity to cold. He had never shaved or experienced libido, there was no relevant past history, nor was there any family history of dwarfism. He was born on 12 February 1888 in Melbourne and had lived a life of relatively unrestricted activity successfully managing a small plant nursery for many years. In appearance he was a gnome-like man, slightly drowsy, with waxy wrinkled skin and a high-pitched voice. Body hair was absent and the testes and penis were prepubertal in size and appearance; his total height was 134 cm., pubic-to-floor 68 cm., and span 134 cm. Further examination showed nothing abnormal apart from a body temperature of 36.1° C., a bradycardia, and sluggish tendon reflexes.



Radiograph of left wrist showing persistence of the epiphysial lines in the radius and ulna.

On admission, serum electrolytes were: sodium 121 mEq/l.; potassium 4.4 mEq/l.; chloride 87 mEq/l.; CO_2 combining power 25 mEq/l. Other relevant investigations were: serum urea 72 mg./100 ml.; haemoglobin 13.3 g./100 ml.; white cell count 5,000/cu. mm.; E.S.R. 34 mm. in one hour (Westergren); serum cholesterol 312 mg./100 ml.; protein-bound iodine 2.4 μg./100 ml.; 24-hour ^{131}I thyroid retention 17%; E.C.G.—sinus bradycardia low voltages and flat or inverted T waves; urinary 17-ketosteroids 1.8 mg./24 hours; 17-hydroxycorticosteroids 4.8 mg./24 hours; urinary gonadotrophins absent at 4.0 mouse units per day; *x*-ray film of skull—normal-sized sella turcica with no other abnormality; skeletal survey—persistence of the epiphysial lines in the radius and ulna (see Fig).

Over the next two days he became stuporous, and a diagnosis of hypopituitarism with water intoxication was confirmed by a serum sodium of 102 mEq/l. and a serum chloride of 74 mEq/l. Treatment was begun with fluid restriction, cortisone acetate 12.5 mg. b.d., and triiodothyronine 100 μg./day. Within 48 hours he became restless and disorientated, with visual hallucinations and a raised temperature. Clinical examination did not reveal an infective process, and a diagnosis of an acute brain syndrome due to cortisone was made. Cortisone was decreased, fluids were further restricted, and large doses of chlorpromazine, and subsequently a combination of haloperidol (Serenace) and benzhexol (Artane), were used. Acute delirium persisted for three days, despite correction of serum electrolytes, and then gradually improved. His further course was complicated by the development of an iron-deficiency anaemia and marked peripheral oedema. The faeces were positive for occult blood, but contrast *x*-ray films at this time revealed no definite abnormality of the gastrointestinal tract. After blood transfusion there was a marked diuresis and general improvement.

At the time of his discharge from hospital, six weeks after admission, he was alert and cheerful, no abnormality was detectable in the cardiovascular or central nervous systems, and the serum electrolytes were normal. He was maintained on prednisolone 1 mg. t.d.s. and L-thyroxine 0.1 mg. a day, and remained very well until 12 months after discharge, when he complained of dysphagia, indigestion, and loss of 1 st. (6.4 kg.) in weight over a period of six weeks. Barium-meal examination revealed a constriction and filling defect at the lower end of the oesophagus. Biopsy showed a poorly differentiated squamous-cell carcinoma of the oesophagus invading the mucosa and muscle layers.

COMMENT

The diagnosis of hypopituitary dwarfism in this man was established by his history and investigations. In the absence of any sign of abnormality of the pituitary fossa it would seem reasonable to assume that this is "idiopathic." It is remarkable that at least seven decades elapsed before medical attention was required for the treatment of this degree of pituitary insufficiency. It is also of interest that although there was epiphysial fusion on *x*-ray examination there was also persistence of the epiphysial lines in the radius and ulna comparable to the skeletal age standard for 18 years in the radius and 17 years in the ulna (Greulich and Pyle, 1959). The case reported by Faurbye (1946) had similar radiographs, while Hawley's (1963) case showed widespread failure of fusion of the epiphyses throughout the skeleton.

The reason for his deterioration, resulting in admission with water intoxication due to corticosteroid deficiency at this particular time, remains uncertain, but the presentation is very similar to Hawley's (1963) case. The development of an acute brain syndrome has been seen by one of us (F. I. R. M.) in several severely hypopituitary adults started on doses of cortisone greater than 25 mg./day, and it is likely that this dose was excessive in this patient.

So far as we can determine this man is the oldest patient recorded in the medical literature with idiopathic hypopituitarism and dwarfism. The development of a carcinoma in the oesophagus some 12 months after the beginning of replacement therapy with corticosteroids and thyroxine at the age of 77 years is of interest. As a barium-meal examination at the time of his original admission was normal, the possibility that there was some aetiological relation between the substitution therapy and the progress of his carcinoma deserves consideration.

We should like to thank Dr. J. H. Bolton for his kind permission to report this case.

H. L. CAPLAN, M.B., B.S., M.R.A.C.P.,
Registrar, Department of Psychiatry, University of Melbourne, Royal Melbourne Hospital.
F. I. R. MARTIN, M.D., M.R.A.C.P.,
Endocrinologist, Royal Melbourne Hospital.

REFERENCES

Albert, A., Underdahl, L. O., Greene, L. F., and Lorenz, N. (1953). *Proc. Mayo Clin.*, 28, 698.
Faurbye, A. (1946). *Acta psychiat. scand.*, 21, 245.
Greulich, W. W., and Pyle, S. I. (1959). *Radiographic Atlas of Skeletal Development of the Hand and Wrist*, p. 118. Stanford, Calif.
Hawley, R. R. (1963). *J. clin. Endocr.*, 23, 1058.

Adenomyoma of Stomach

Brit. med. J., 1967, **3**, 843

Gastric adenomyoma is a rare cause of pyloric obstruction. It was first recognized radiologically as a possible cause of benign pyloric stenosis by Campbell (1949). The histological features of the tumour were first described by Magnus-Alsleben (1903), who reported five cases discovered incidentally at necropsy. Since then 23 additional cases have been published. Four cases examined radiologically showed evidence of a benign pyloric lesion (Wass, McCloskey, and Sullivan, 1951 ; Cimmino, 1955 ; Goldberg and Margulis, 1966). Two of the standard radiological textbooks do not mention adenomyoma as a cause of pyloric obstruction (Shanks and Kerley, 1958 ; Lumsden and Truelove, 1965). The lesion is important clinically because of its histological similarity to heterotopic pancreatic tissue, which it may also mimic radiologically.

CASE REPORT

A 39-year-old housewife presented with a 10-year history of recurrent attacks of epigastric pain and vomiting. Pain was not relieved by antacids, was unrelated to meals, and was made worse when she ate meat and fatty foods. Her appetite was good except during the intermittent vomiting attacks. There was no history of shoulder pain, haematemesis, melaena, or weight loss. Clinical examination revealed some epigastric tenderness, but no palpable masses or other abnormality.

Investigations.—Haemoglobin 13.4 g./100 ml.; white cell count 4,700 cu. mm. ; erythrocyte sedimentation rate 10 mm. in one hour ; blood group A rhesus-positive. Barium meal: a small ulcer niche was demonstrated on the mid-third of the lesser curve of the stomach ; there was some delay in initial gastric emptying ; there was a constant narrowing of the pyloric antrum with two persistent niches of barium ; a pyloric filling defect was constant despite changes of position and palpation ; peristalsis was normal in the area ; the oesophagus and duodenal cap were normal. The appearances were unchanged on re-examination after one month.

Operative Findings.—A firm mass was palpable in the anterior wall of the pyloric antrum. A small benign lesser-curve ulcer was present. The distal two-thirds of the stomach was resected and a gastroduodenal anastomosis performed. Recovery was uneventful.

Pathological Findings.—There was marked narrowing of the pyloric antrum by a thickening of the submucosa and muscle for 3 cm. The submucosa was firm and grey, and up to 0.5 cm. thick. The muscle coat in the area was 1.2 cm. thick. Macroscopic spaces were visible in the submucosa and underlying part of the muscle coat. The histological appearances were those of an adenomyoma. Examination of various areas of the tumour showed areas of Brunner's glands and ducts lined by columnar epithelium surrounded by connective tissue and muscle bundles. A track was seen running from the submucosa into the gastric lumen. The lesser-curve ulcer was small, chronic, and benign.

COMMENT

Benign tumours of the stomach are rare and present with a variety of symptoms.

This patient's symptoms were suggestive of peptic ulcer with intermittent pyloric obstruction. The previously reported cases of adenomyoma have had various symptoms, including vague indigestion, epigastric discomfort, and chest pain. An epigastric tumour was palpable in one case (Gruzdeff, 1909). Adenomyoma has been described in association with infantile hypertrophic pyloric stenosis (Wass *et al.*, 1951). The lesion has always been found on the anterior wall of the pyloric antrum. On barium meal examination four cases showed pyloric narrowing and a constant filling defect.

A central umbilication, often described as being typical of leiomyoma or neurofibroma, which may also occur in the pylorus, was found in one case (Cimmino, 1955).

The pyloric niche in the present case corresponded to the track demonstrated histologically. Ducts opening into the pyloric antrum have not been previously described in adenomyoma and have been referred to as being typical of heterotopic pancreatic tissue (Lapidari, 1937). There is a close relation between these two lesions. Both originate from primordial epithelial buds which may develop in varying degrees of differentiation, resulting in the eventual histological spectrum of adenomyoma, aberrant pancreas, and hyperplasia of Brunner's glands (Clarke, 1940). The essential histological feature is the presence of differentiated and undifferentiated glandular tissue in the submucosa and mucosa of the pyloric antrum (Stewart and Taylor, 1925). The lesion is classified according to which cell type predominates: undifferentiated glandular epithelium and muscle whorls in adenomyoma, Brunner's type differentiated epithelium, or pancreatic type acini. Aberrant pancreas is the commonest of these. It is seen more often in males (Copleman, 1963) and produces pyloric obstruction in 25% of cases which occur in adults (Palmer, 1951). It is usually intramural and almost half the lesions are in the distal third of the stomach.

Apart from pyloric obstruction due to peptic ulceration with pylorospasm or fibrosis and the characteristic deformity due to pyloroplasty, there are many benign causes of pyloric stenosis. A pyloric mucosal polyp usually has a pedicle and is mobile. A congenital mucosal diaphragm, due to failure of canalization of the embryonic foregut (Conway, 1965), and the focal type of hypertrophic pyloric stenosis, the features of which have been reviewed by Seaman (1966), may both cause eccentric pyloric narrowing.

Much rarer lesions producing pyloric narrowing include eosinophilic gastroenteritis, which is associated with changes in the small intestine and responds to steroids (Wolf and Khilnani, 1966). Gastric sarcoidosis, tuberculosis, eosinophil granuloma, and tertiary syphilis may present with pyloric narrowing, usually in association with systemic manifestations of the disease, which assist in the diagnosis.

In the case described the lesion was thought on barium meal examination to be due to aberrant pancreas. Histology confirmed the diagnosis of gastric adenomyoma. The patient remained asymptomatic over a two-year period.

JAMES G. MCNULTY,* M.B., F.F.R.,
Senior Registrar, Department of Radiology,
Royal Free Hospital, London W.C.1.

---

* Present address: Department of Radiology, St. Thomas's Hospital, London S.E.1.

REFERENCES

Campbell, R. J. C. (1949). *Brit. J. Radiol.*, 22, 284.
Cimmino, C. V. (1955). *Radiology*, **65**, 73.
Clarke, B. E. (1940). *Arch. Path.*, **30**, 143.
Conway, N. (1965). *Brit. med. J.*, **1**, 970.
Copleman, B. (1963). *Radiology*, **81**, 107.
Goldberg, H. I., and Margulis, A. R. (1966). *Amer. J. Roentgenol.*, **96**, 382.
Gruzdeff, D. A. (1909). *Med. Obozr. Mosk.*, **71**, 805.
Lapidari, M. (1937). *Arch. ital. Chir.*, **47**, 432.
Lumsden, K., and Truelove, S. C. (1965). *Radiology of the Digestive System.* Oxford.
Magnus-Alsleben, E. (1903). *Virchows Arch. path. Anat.*, **173**, 137.
Palmer, E. D. (1951). *Medicine (Baltimore)*, **30**, 81.
Seaman, W. B. (1966). *Amer. J. Roentgenol.*, **96**, 388.
Shanks, S. C., and Kerley, P. (1958). *A Textbook of X-ray Diagnosis*, vol. 3. London.
Stewart, M. J., and Taylor, A. L. (1925). *J. Path. Bact.*, **28**, 195.
Wass, F. J., McCloskey, B. J., and Sullivan, E. J. (1951). *Amer. Surg.*, **17**, 844.
Wolf, B. S., and Khilnani, M. T. (1966). *Gastroenterology*, **51**, 542.

Spontaneous Rupture of Uterus at 22 Weeks' Pregnancy

Brit. med. J., 1967, 3, 844

CASE REPORT

The patient, a woman of 35, had had no children after 11 years of marriage. In January 1966, when 22 weeks pregnant, her uterus ruptured spontaneously. At operation twin foetal sacs were found free in the peritoneal cavity.

Her previous gynaecological history was complicated. A year before the uterus ruptured, after 10 weeks' amenorrhoea, she was said to have passed grape-like tissue during a vaginal bleed. Microscopy was not carried out, and this tissue was presumed to be hydatidiform mole. During the next four months she had intermittent episodes of vaginal bleeding but no proper period. A diagnostic curettage was therefore done, when fresh products of conception were evacuated; she continued to bleed, and eight days later a further curettage had to be performed. At this operation the uterus was perforated. Shortly afterwards she had a normal period.

Five months later she presented with amenorrhoea of 14 weeks' duration, and a pregnancy consistent with 18 weeks' gestation was felt. This proceeded normally, apart from the discrepancy between the uterine size and period of amenorrhoea.

The day after a visit to the antenatal clinic at 22 weeks she was admitted complaining of sudden and severe abdominal pain, with vaginal bleeding. There was no history of trauma or uterine contractions. On examination there were no signs of circulatory collapse. The abdomen was distended, with tenderness all over. The uterus could not be delineated either abdominally or per vaginam. There was some vaginal blood loss.

A diagnosis was made of intraperitoneal bleeding from either ruptured uterus or ectopic pregnancy. At laparotomy twin foetal sacs, each about the size of a 22-week pregnancy, were found free in the peritoneal cavity, which contained about 750 ml. of blood. The uterus had contracted to the size of a 16-week pregnancy, and in the midline of the fundus was a tear through which a finger could be passed. The foetal sacs and blood were removed, and, since the patient had had no children, a simple suture of the tear was performed.

Her recovery was normal. A hysterogram six months later showed a small filling defect in the fundus. In September 1967 the patient was 30 weeks pregnant, and so far all was well.

COMMENT

Rupture of the pregnant uterus before the onset of contractions of labour or abortion is rare. Published reports are few. The above case presented the combination of twin pregnancy with a previous uterine perforation and possible hydatidiform mole. The largest collection of spontaneous rupture of the apparently normal uterus is that of Felmus *et al.* (1953). Of their 121 cases a quarter had had previous uterine instrumentation. In three cases trophoblastic invasion of the myometrium was given as the immediate predisposing cause. One-third of their cases ruptured before the sixth month of gestation. In the above case the uterus had ruptured in the midline of the fundus, where a perforation would most likely be. Characteristically, the pregnant uterus ruptures through the body; the uterus in labour ruptures through the lower segment.

It is unusual for the foetus to be extruded completely through the rupture. In the present case both sacs were free in the peritoneal cavity. Because of this the uterus had been allowed to retract and thereby diminish the extent of the tear. This probably lessened the bleeding and would explain the patient's good general condition. Most reports describe the patient as being shocked.

The treatment of choice is hysterectomy, the subtotal operation being done if speed is necessary. Two cases of repeated rupture of the uterus in a subsequent pregnancy have been described after simple suture of the tear (Lazarević, 1932; Wenner, 1949).

I would like to thank Miss Lois E. Hurter for permission to publish this case.

D. E. R. BATEMAN, F.R.C.S., M.R.C.O.G.,
St. Thomas's Hospital, London S.E.1.

REFERENCES

Felmus, L. B., Pedowitz, P., and Nassberg, S. (1953). *Obstet. gynec. Surv.*, 8, 155.
Lazarević, V. (1932). *Zlb. Gynäk.*, 56, 1291.
Wenner, R. (1949). *Gynaecologia (Basel)*, 128, 38.

Diaphysial Aclasia with Compression of the Spinal Cord

Brit. med. J., 1967, 3, 844–845

In their review of 1,102 patients with diaphysial aclasia Stocks and Barrington (1925) found that only 7% had vertebral osteochondromata. If these occur within the spinal canal they can cause compression of the spinal cord or the cauda equina. The first case was described by Ochsner and Rothstein (1907), but since then very few cases have been recorded. Slepian and Hamby (1951) could find only nine certain cases of cord compression. They added a further case, and three more cases have been reported (Cannon, 1954; Gokay and Bucy, 1955; Larson, Dodge, Rushton, and Dahlin, 1957). This makes a total of 13 cases, and, since diaphysial aclasia is not a very rare condition (Jaffe, 1958), cord compression is an unusual complication.

CASE REPORT

A schoolgirl aged 16 presented with a sudden onset of clumsiness of the right hand, which rapidly increased. This was followed a month later by weakness of the right knee.

On examination she had typical generalized diaphysial aclasia. The neurological examination showed wasting and weakness of the intrinsic muscles of both hands and weakness of the flexors and extensors of the right elbow and wrist. Abduction and adduction of the right shoulder were also weak. The reflexes in the right arm were weak or absent. There was a mild spastic paresis of the right leg, but both plantar responses were flexor. There were no abnormal sensory signs apart from poor position sense in the fourth and fifth fingers of the right hand.

Investigations.—Radiographs of the cervical spine, including tomograms, showed exostoses arising from the spinous processes and laminae of the fifth and sixth cervical vertebrae (Fig. 1). A myelogram showed a posterior filling defect at the level of the fifth cervical vertebra (Fig. 2). Lumbar puncture showed nothing abnormal apart from a protein of 58 mg./100 ml.

Operation.—Exostoses were found on the back of both the laminae of the fifth cervical vertebra. A laminectomy of the fifth and sixth cervical vertebrae was performed and two exostoses were found on the front of the lamina of the fifth cervical vertebra (0.5 and 0.75 cm. in diameter) and one larger exostosis (1 cm. in diameter) on the front of the lamina of the sixth cervical vertebra. These were indenting the dura mater. Histology showed that they were typical osteochondromata.

After operation she developed retention of urine, which cleared within three weeks, and a month after operation she had almost normal power in all four limbs. During the next year she had intermittent episodes of mild weakness of the right leg and both arms, but has had no further neurological symptoms for the past three years.

She also suffered from congenital mitral incompetence, which was first noted at the age of 3 but had produced no symptoms.

DISCUSSION

This patient was younger than the others recorded, who have all been past the age of skeletal growth. In all other respects she represents the typical features of this unusual complication of diaphysial aclasia. The osteochondromata pressing on the spinal cord were small and arose from the deep surface of the laminae. All the previous cases have had similarly small osteochondromata within the spinal canal, apart from the case described by Gökay and Bucy (1955). That patient had a large retroperitoneal osteochondroma arising from the bodies of the second to the fifth lumbar vertebrae, with a dumb-bell extension through the neural canal between the third and fourth lumbar vertebrae which compressed the cauda equina.

Neurological recovery after removal of the osteochondroma is usually complete. In the case reported here there was some slight and variable neurological disability for a year after operation. The cause of this was unknown, but recovery was finally complete. Laminectomy and removal of the osteochondroma should therefore be performed as soon as the diagnosis is established by radiography. In one case (Larson *et al.*, 1957) the tumour was thought to be a chondrosarcoma. The possibility that the pressure may result from an increase in size of an exostosis undergoing malignant change is a further indication to explore the spinal canal promptly.

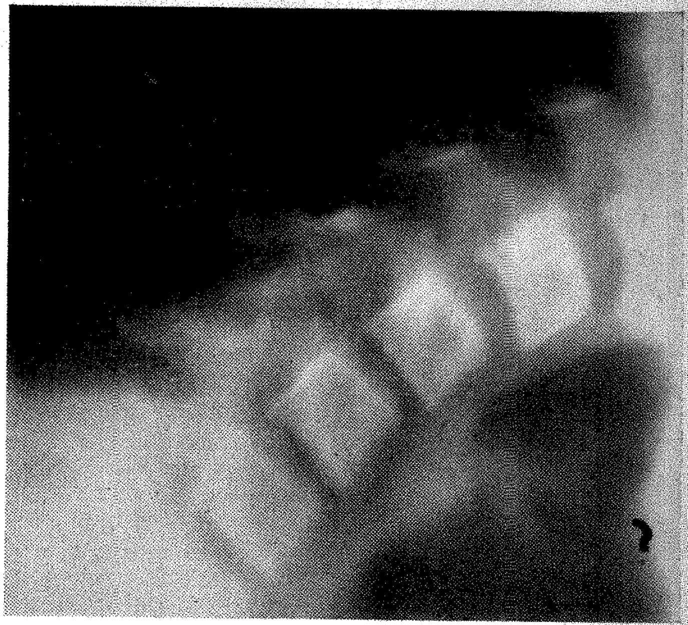


FIG. 1.—Lateral tomogram of cervical spine showing exostoses arising from the deep surfaces of the laminae of the fifth and sixth cervical vertebrae.

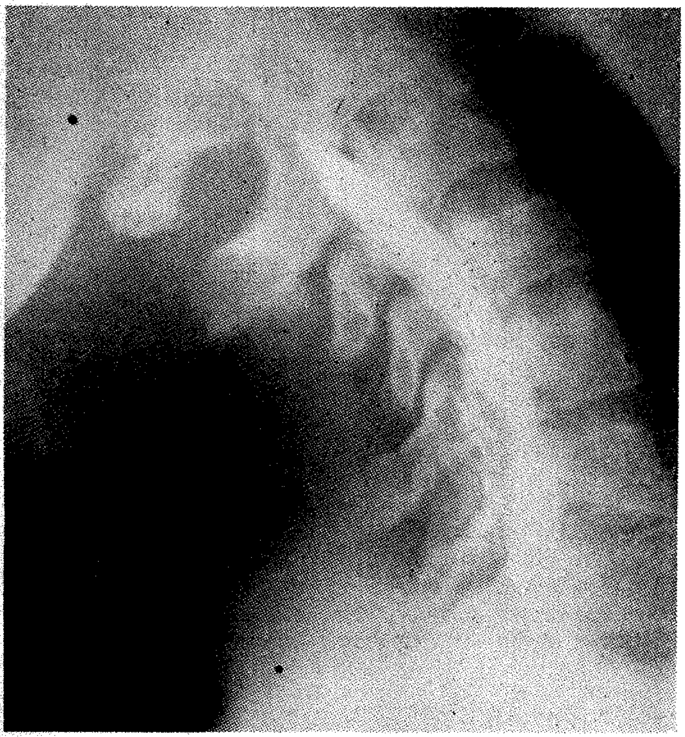


FIG. 2.—Cervical myelogram showing a posterior filling defect at the level of the fifth cervical vertebra.

I am grateful to Mr. J. N. Aston and Mr. R. Campbell Connolly for their permission to report this case. The photographs were kindly supplied by the Department of Medical Photography, St. Bartholomew's Hospital.

P. J. STILES, M.B., B.S., F.R.C.S.,
Orthopaedic Department,
St. Bartholomew's Hospital,
London E.C.1.

REFERENCES

Cannon, J. F. (1954). *Amer. J. hum. Genet.*, **6**, 419.

Gokay, H., and Bucy, P. C. (1955). *J. Neurosurg.*, **12**, 72.

Jaffe, H. L. (1958). *Tumours and Tumourous Conditions of the Bones and Joints*, p. 151. Philadelphia.

Larson, N. E., Dodge, H. W., Rushton, J. G., and Dahlin, D. C. (1957). *Proc. Mayo Clin.*, **32**, 728.

Ochsner, E. H., and Rothstein, T. (1907). *Ann. Surg.*, **46**, 608.

Slepian, A., and Hamby, W. B. (1951). *J. Neurosurg.*, **8**, 529.

Stocks, P., and Barrington, A. (1925). *Hereditary Disorders of Bone Development, Diaphysial Aclasis*, Part I, p. 30. London.

Current Practice

TODAY'S DRUGS

With the help of expert contributors we publish below notes on a selection of drugs in current use.

Immunization Schedules

Immunization schedules are intended to serve as guide lines for those responsible for ensuring that children are collectively and individually protected against certain communicable diseases. Suitable vaccines are available for immunization against diphtheria, tetanus, whooping-cough, poliomyelitis, measles, smallpox, and tuberculosis, but as they cannot be given together it is desirable to arrange a simple programme of immunization, taking into account what is safe, effective, practical, and most likely to result in the immunization of the maximum number of children. A number of factors have to be considered when constructing such a programme.

Combined and Simultaneous Vaccination

The number of injections to be endured by the child, the number of clinic visits to be paid by the mother, and the administrative costs to be met are reduced as a result of the incorporation of diphtheria, tetanus, and pertussis vaccines (D.T.P.) into one effective trivalent vaccine. In addition, simultaneous administration of oral poliomyelitis vaccine (O.P.V.) with D.T.P. further increases the efficiency of the immunization service without reducing the safety and efficacy of the vaccines.

Number of Vaccinations

A single administration of a live vaccine, such as measles, smallpox, or B.C.G., usually produces lasting immunity against the corresponding disease, but a single administration of trivalent O.P.V. may not result in simultaneous development of immunity against all three types of poliovirus. Second and third feedings are necessary in order to give each of the three types of poliovirus an opportunity of colonizing the intestines.

A single injection of pertussis vaccine containing killed organisms and of diphtheria and tetanus toxoids does not provide protection ; three adequately spaced injections are required.

Intervals between Vaccinations

Adequate antibody responses to the three components of D.T.P. are not obtained unless a minimum of four weeks elapses between successive injections ; even better results are obtained when the intervals are increased to six weeks or longer. Intervals of four to six weeks should also elapse between successive feedings of O.P.V., the reason being that one type of poliovirus may be prevented from establishing itself in the intestines while one or both of the other types are still multiplying, a process which may last four to six weeks after the initial infection was produced.

It is common practice in this country to allow six weeks between administration of measles, smallpox, and B.C.G. vaccines, although in some tropical countries measles and smallpox, or B.C.G. and smallpox, are given simultaneously.

Age of Immunization

The optimum age for administration of any vaccine is determined by a variety of factors.

The antibody response of infants to *diphtheria toxoid* and *oral polio vaccine* improves with age as the child's immunological mechanisms mature and transplacentally transmitted maternal antibodies are eliminated from the circulation. These factors argue in favour of delaying immunization until the child is 6 to 12 months of age ; but *whooping-cough* is a particularly severe disease during infancy, and therefore a strong case can be made for early administration of D.T.P. Most authorities now recommend that the course of D.T.P. with O.P.V. should commence between the ages of 2 and 6 months.

Residual maternal antibodies render live *measles vaccine* ineffective in most children under 6 months of age and in some until they are almost 1 year old. As a child becomes responsive to live vaccine so also does he become susceptible to measles. Routine vaccination should therefore be carried out after the age of 10 months, but should not be delayed long after the age of 12 to 15 months, particularly when a measles epidemic is expected. In some practices a dose of inactivated measles vaccine is given four to six weeks before the live vaccine.

Primary *smallpox* vaccination will "take" at any age from birth, but the risk of post-vaccination encephalitis, although low in infants vaccinated during the first year of life, is even less among those vaccinated during the second year. Smallpox vaccination should therefore be postponed until the second year of life.

All tuberculin-negative children in close contact with a case of *tuberculosis* should be B.C.G. vaccinated irrespective of their age. Routine immunization of tuberculin-negative children is otherwise carried out at the age of 11 or 12 years, thus ensuring that they are tuberculin-positive during puberty and adolescence, when the risk of tuberculosis would otherwise increase.

Booster Doses

The antibody titres produced by a course of D.T.P. and O.P.V. in infancy wane with time but are readily boosted by further administration of the vaccines a year later. A further booster dose of diphtheria and tetanus toxoid and of oral polio vaccine is required at school entry in order to maintain a high state of immunity. By the age of 5 whooping-cough is rarely a serious disease, and the pertussis component renders triple vaccine particularly reactogenic in these older children.

Practical Considerations

Immunization schedules should be simple to remember, easy to administer, and, when followed, prove to be safe and effective. A schedule involving three vaccination visits during both the first and second years of life would read:

Age	Vaccines	No. of Vaccinations
3 to 6 months ..	Commence course of three administrations D.T.P. + O.P.V.	Three at intervals of not less than four weeks
1 to 2 years ..	Measles vaccination, smallpox vaccination, booster D.T.P. + O.P.V.	Three at intervals of not less than four weeks
First year at school	Booster D.T. + O.P.V.	One
8 to 12 years ..	Booster D.T. + O.P.V.	,,
12 years	B.C.G. for the tuberculin negative	,,

Chlorocresol should not be added to solutions for intrathecal or epidural injection or when volumes over 15 ml. are to be injected at a time.

REFERENCES

[1] Davis, H., *Quart. J. Pharm.*, 1934, **7**, 379.
[2] Briggs, A. M., and Callow, D. E., ibid., 1941, **14**, 127.

ANY QUESTIONS?

We publish below a selection of questions and answers of general interest.

Drugs and Renal Calculi

Q.—*What drugs in common use give rise to a risk of stone formation in the kidney in persons with normal renal function?*

A.—Drugs only rarely produce kidney stones. Those that do so do by altering calcium metabolism—for example, vitamin D—or by making the urine alkaline—for example, carbonic anhydrase inhibitors such as acetazolamide—or by modifying urate excretion—for example, the thiazide group of diuretics. Vitamin D is harmful in this way only when given in a high range of dosage, such as 1 to 5 mg. a day (40,000 to 200,000 i.u.). Doses of this magnitude are necessary in the treatment of hypoparathyroid tetany and for various forms of metabolic bone disease, but they should not be given for the prophylaxis of rickets, when doses of 10–100 µg. a day are adequate and harmless.[1] All forms of vitamin D, such as vitamin D_3 and dihydrotachysterol, introduce a similar danger.

With the danger from the vitamin D compounds should be considered the similar danger with all calcium salts, such as lactate, gluconate, and so forth, since large doses of these, sometimes given as ingredients of antacids, can produce renal calcification and stones even with normal renal function. The acetazolamide type of drugs may cause renal calcification, perhaps by reducing citrate output and alkalinizing the urine. They are commonly used only for glaucoma, but in this situation they may be essential and produce a therapeutic dilemma. A high fluid intake may be sufficient to prevent this complication.

Thiazide drugs act differently by virtue of their curious effect on uric acid metabolism. They frequently cause uric acid crystalluria with renal symptoms. I have known a large staghorn uric acid stone formed in a woman addicted to chlorothiazide, which irrationally she took to reduce her weight. High fluid intake and alkalinization with potassium salts, such as citrate or bicarbonate, are suitable methods of therapy when the drug cannot be changed for another diuretic not having this effect on uric acid.

We are not considering here the problem of urinary secretions from the crystallization of drugs, such as can occur with large doses of sulphonamides.

REFERENCE

[1] Dent, C. E., *Prescribers' Journal*, 1966, **5**, 17.

Treatment of Chronic Brucellosis

Q.—*What is the best treatment for long-standing brucellosis?*

A.—Tetracycline is still the sheet anchor in the treatment of long-standing brucellosis. Ampicillin, which, being a bactericidal agent, might be expected to be superior, failed when given in reasonable doses to two patients who subsequently responded promptly to tetracycline.[1] Spink,[2] from his extensive experience, recommends that tetracycline 0.5 g. should be given six-hourly for at least three weeks. It may be necessary to repeat this course once or twice, but treatment beyond that is not likely to be successful. Better results may be obtained if in addition streptomycin 0.5 g. is given twice a day intramuscularly for the first two weeks of treatment.

The Herxheimer-like reactions which may occur early in treatment can be controlled by prednisolone 15 mg. six-hourly intramuscularly, and this usually results in a prompt defervescence of symptoms.[3 4] It is also possible that corticosteroids affect the host-parasite relationship in some way which facilitates antibiotic activity. Combined tetracycline-streptomycin therapy with prednisolone for the first five days of treatment probably offers the greatest chance of eradicating the chronic disease.

REFERENCES

[1] Farid, Z., Bassily, S., and Omar, M. S., *Lancet*, 1964, **2**, 763.
[2] Spink, W. W., ibid., 1964, **2**, 161.
[3] Magill, G. B., Killough, J. H., and Said, S. I., *Amer. J. Med.*, 1954, **16**, 810.
[4] Joffe, B., and Diamond, M. T., *Ann. intern. Med.*, 1966, **65**, 564.

Sterilizing Procaine Solution

Q.—*How should a procaine solution (2 or 3% in water) for injection be sterilized? Is steaming for 10 minutes sufficient?*

A.—The official pharmacopoeial method of sterilizing procaine hydrochloride injection is autoclaving at 115° C. (10 lb. per sq. in. (0.7 kg. per sq. cm.)) for 30 minutes. This method can be guaranteed to produce sterility, but it probably has a wide margin of safety. If this process cannot be carried out, steaming, preferably in the presence of a bactericide, could be used as an alternative.

Davis[1] stated about several injections, including procaine hydrocloride, that "even in the presence of contamination much worse than that obtaining during any dispensing operations, sterile products can readily be obtained by exposure to streaming steam at atmospheric pressure for one hour." He showed that a 2% procaine hydrochloride solution contaminated with a suspension of *B. subtilis* and *Cl. sporogenes* was sterile after 60 minutes' steaming. Briggs and Callow[2] showed that solutions of procaine hydrochloride have some bactericidal action on *B. typhosa* and *Streptococcus haemolyticus*, and that the effect is increased by chlorbutol and sodium metabisulphite.

If steaming were to be used it would be advisable to add 0.1% of chlorocresol, as in the official injection, and to continue the steaming for 30 minutes. That would probably give as wide a margin of safety as autoclaving. Ordinary pharmaceutical cleanliness should be observed in preparing the solution—for example, the utensils should be clean and should be rinsed with freshly distilled water. The solution should also be made with freshly distilled water and should be sealed and sterilized as soon as possible after preparation.

Worm Infestation in Dogs

Q.—*What treatment will eradicate roundworm and echinococcus infestation in dogs and thus eliminate the danger of these parasites being transmitted to children?*

A.—Tapeworms (including echinococcus) and roundworms (ascarids) are the most common helminths of dogs.

For routine purposes small oral doses of arecoline are effective against tapeworms, and one of the piperazine compounds or diethyl carbamazine citrate is indicated to combat roundworm infestation.[1 2] A periodic examination of the faeces will point out carrier animals. The elimination of external parasites by regular bathing with an insecticide will ensure freedom from the tapeworm *Dipylidium caninum*, since this tapeworm has both fleas and lice as its intermediate host.

REFERENCES

[1] *The Universities Federation for Animal Welfare Handbook on the Care and Management of Laboratory Animals*, 1967, 3rd edition. Edinburgh and London.
[2] *Pharmaceutical Society British Veterinary Codex*, 1965. London.

Notes and Comments

"Arc Eye."—Dr. T. K. ELLIOTT (Sutton Coldfield) writes: Having had to deal with cases of "arc eye" for more than 20 years, may I be permitted to comment on the answer to this question ("Any Questions?" 26 August, p. 543)? While I would agree that adrenaline or, preferably, phenylephrine drops are usually effective for mild cases, more severe cases may require a preparation containing a local anaesthetic such as ½% pantocaine (amethocaine) eye ointment. Indeed, susceptible cases known to have been exposed to an overdose of ultraviolet light are, after initial treatment, usually given a tube of eye ointment to take home, because it is almost the only application which will prevent them having a sleepless night owing to intense pain in the eye.

Dr. M. W. ROBINSON (Chief Medical Officer, Associated Electrical Industries Limited, Power Group, Trafford Park, Manchester 17) writes: Out of a population at risk of approximately 2,000—that is, welders, fitters, and by-standers—our surgery attendances in this works number approximately 800 per annum. Some actually suffer "arc eye" (flash), and others are exposed to and fear the condition. All are treated immediately with adrenaline 1/4,000 eye drops, and are cured within 24 hours, except for a few—perhaps 10%—who require further treatment. They are given an astringent lotion, and they recover in a further 24 hours. This treatment is standard practice when electric-arc welding is carried out. Very rarely is a local anaesthetic required.

Clinicopathological Conference

A Case of Polycythaemia with Aortic Stenosis

DEMONSTRATED AT THE ROYAL POSTGRADUATE MEDICAL SCHOOL

Clinical History

Professor E. G. L. **Bywaters**: The patient (Case No. 205812, P.M. 11594), who was 61 at the time of his death, was first referred to the radiotherapy department of Hammersmith Hospital from Dr. Hollings of Kingston Hospital in 1957 with a diagnosis of polycythaemia rubra vera, having been investigated there for an epistaxis.

Examination showed a plethoric man with a rough systolic murmur over the aortic area radiating up to the neck. The blood pressure was 190/150 mm. Hg. The spleen and the liver were palpable, 2 and 4 cm. respectively beneath the costal margin. Investigations confirmed the polycythaemia, with a haemoglobin of 22.5 g./100 ml., packed cell volume 70%, red blood cells 8.3 million per cu. mm., platelets 350,000, white blood cells 13,000 per cu. mm. The differential count showed 90% neutrophils, 2% eosinophils, 6% lymphocytes, and 2% large monocytes. The blood volume was 8.7 l. (114 ml./kg.) and the red cell volume 5.6 l. (73 ml./kg.) body weight both increased from the upper limit of normal—85 to 35 ml./kg. respectively. The bone marrow showed hyperactivity and the E.C.G. showed left ventricular hypertrophy. These findings were thought to be consistent with a diagnosis of polycythaemia rubra vera and aortic stenosis, and the man was treated with 6 mc. ^{32}P.

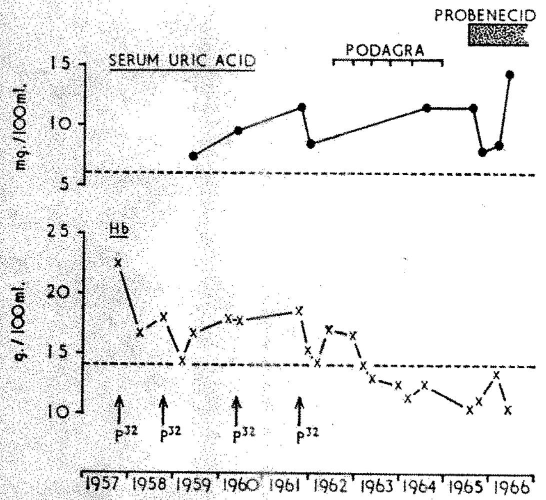


Chart showing progress of patient 1957–66.

In April 1958 he suffered an acute loss of consciousness followed by transient right-sided facial weakness and was admitted to St. Bartholomew's Hospital with a diagnosis of probable cerebral thrombosis. In November 1958 he was readmitted to Hammersmith Hospital. At that time there were no abnormal neurological findings, the liver and spleen were not palpable, the blood pressure was raised at 240/170 mm. Hg, and the chest *x*-ray showed left ventricular enlargement. The haemoglobin was 18 g./100 ml., the red blood cells 5.7 million per cu. mm., packed cell volume 54%, white blood cells 8,000 per cu. mm. with platelets 426,000 per cu. mm. In view of persistent signs of polycythaemia he was given a further injection of ^{32}P (8 mc.). In 1959 he was readmitted again (third admission) for check-up, but the blood volume this time was relatively normal—6.1 litres (73 ml./kg.), as was the red blood cell volume—2.7 l. (32 ml./kg.), haemoglobin 16.6 g./100 ml., packed cell volume 48%. The uric acid at this time was found to be raised at 7.7 mg./100 ml., and blood urea 42 mg./100 ml.

In 1960 he had become increasingly plethoric and was admitted for the fourth time. The liver and spleen were no longer palpable, haemoglobin 17.8 g./100 ml., packed cell volume 53%, and serum uric acid still raised at 9.5 mg./100 ml. He was given a further dose of ^{32}P (5.9 mc.).

The next year, 1961, he was admitted for the fifth time, at this moment being symptom-free. The blood pressure had come down to 170/110 mm. Hg, there was an aortic systolic murmur and the heart was not thought to be enlarged. The haemoglobin was 18.4 g./100 ml., packed cell volume 55%, serum uric acid 11.6 mg./100 ml., with urea 46 mg./100 ml. He was given a fourth and final injection of ^{32}P (6 mc.).

Onset of Gout

The next year he developed gout, and in the ensuing two years suffered six attacks of typical podagra responding to colchicine. In 1963 he had a grand mal attack treated with phenobarbitone, and in 1964 was referred to the rheumatology unit.

At this time, seven years after his original admission, he was relatively well, with a blood pressure of 160/105 mm. Hg. The liver and spleen were both palpable at 4 and 10 cm. from the costal margin respectively, and a loud systolic murmur was heard in the aortic area. Small lumps were found on the ears, but crystals were not obtained from these on puncture. The serum uric acid before treatment was found to be 12 mg./100 ml., with a haemoglobin of 12.4 g./100 ml. and a urea of 49 mg./100 ml. Before he could be started on uricosuric therapy he went off to South Africa for a holiday for three months, and we saw him again only on his return, when he was admitted again in July 1965 (for the sixth time). This time he had developed heart failure, and was complaining of dyspnoea and ankle swelling. Examination showed him to be cyanosed, plethoric, and dyspnoeic, with basal râles and oedema of the legs. The jugular venous pressure was elevated to 10 cm., there was a mid-systolic murmur loudest in the fourth left interspace, and the apex beat was outside the midclavicular line in the sixth space. The pulse was 120, the blood pressure 110/60 mm. Hg., and there was a triple rhythm. The liver was enlarged to 10 cm. below the costal margin and the spleen to 3 cm. There was no evidence of arthropathy or tophus formation. Chest *x*-ray revealed cardiomegaly and interstitial pulmonary oedema ; the E.C.G. showed left ventricular hypertrophy. The blood urea was 60 mg./100 ml., the serum uric acid 11.6 mg./100 ml. Blood cultures were negative. The

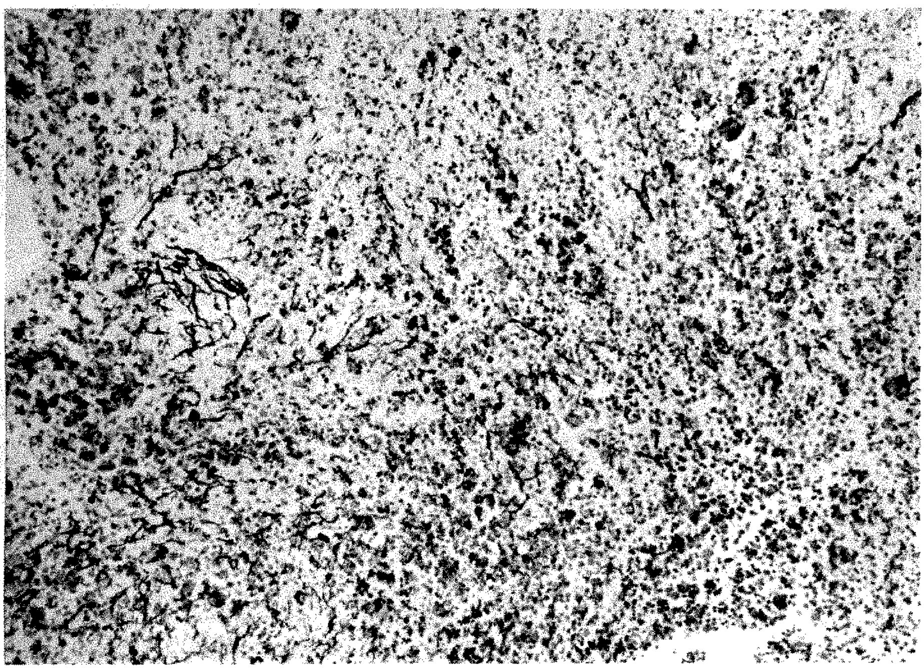
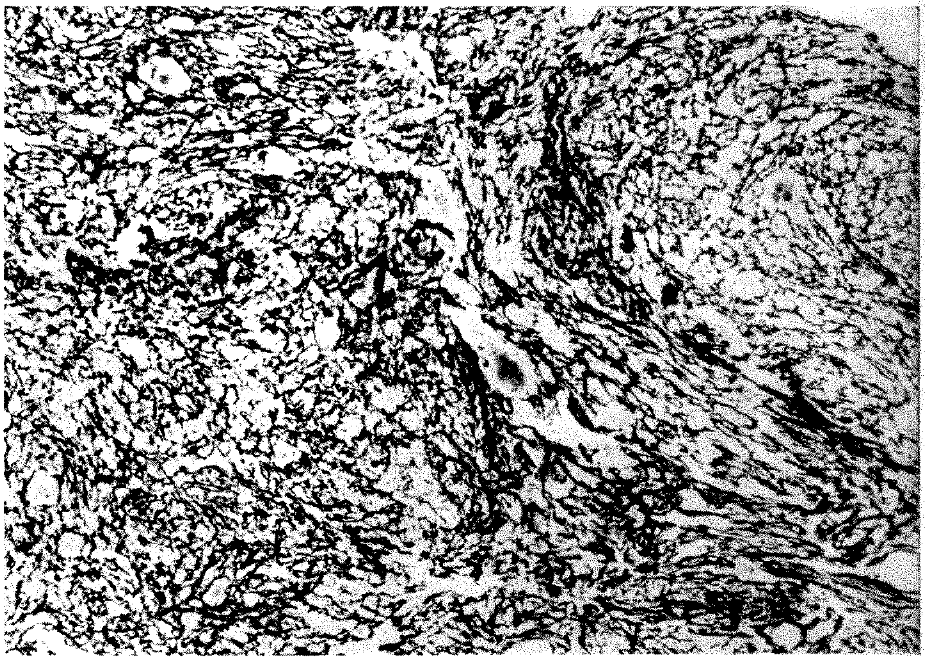


FIG. 1.—Vertebral bone marrow. Hypercellular marrow with scanty reticulin fibres. (Reticulin stain. ×115.)

FIG. 2.—Femoral bone marrow. Markedly increased reticulin fibres with parallel coarse fibres. Cells are unstained. (Reticulin stain. ×115.)



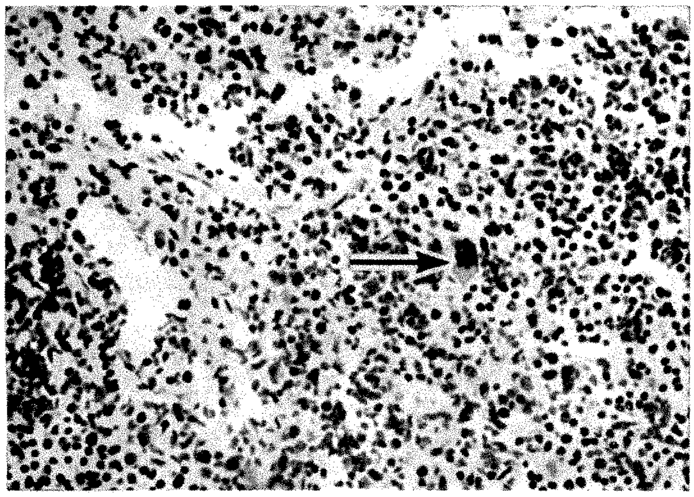


FIG. 3.—Lymph node. A cell of the megakaryocyte series (arrowed) lies near a lymph follicle. (H. and E. ×270.)

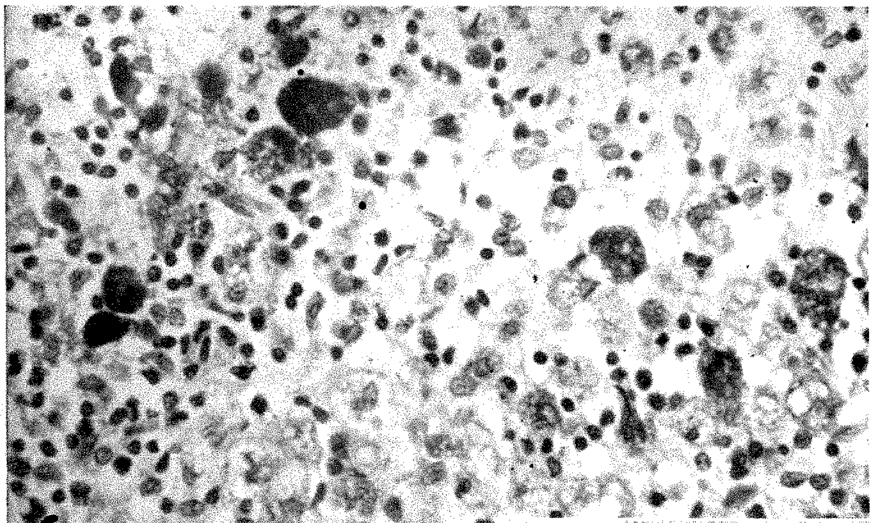


FIG. 4.—Splenic pulp. Many cells with foamy cytoplasm; in some this is strongly P.A.S. positive. (P.A.S. ×430.)

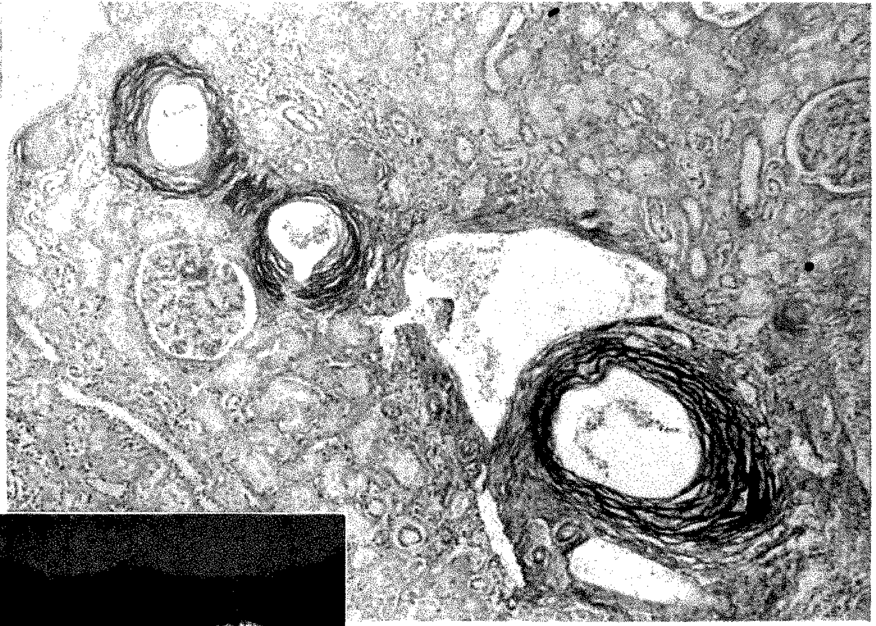


FIG. 5.—Kidney. Elastic reduplication. This may be a senile change or due to hypertension. (Elastic van Gieson. ×430.)

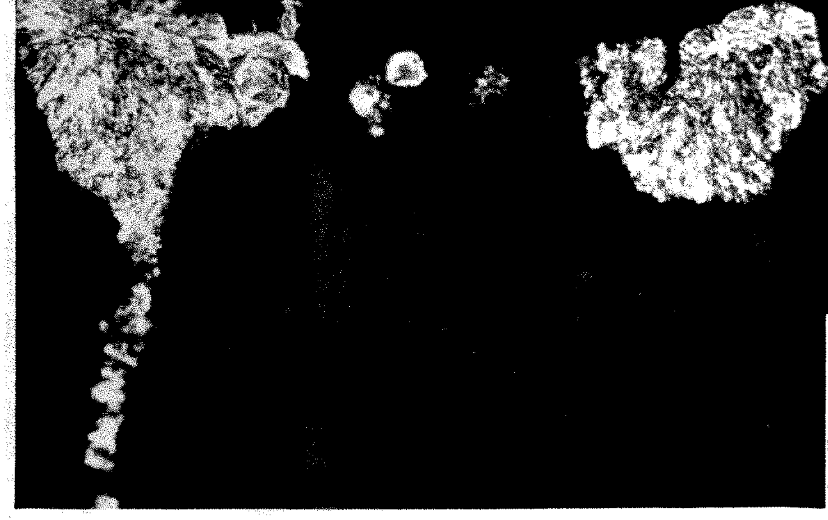


FIG. 6.—Cartilage. Birefringent urate deposits photographed with partly crossed polaroids.

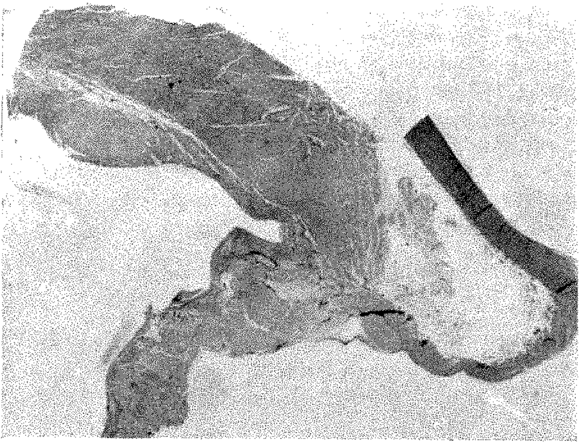


FIG. 7.—Aortic valve. Grossly thickened calcified cusp of aortic valve. (H. and E. ×3.25.)

haemoglobin was 10.2 g./100 ml., and the red blood cells 3.8 million per cu. mm. The packed cell volume was 32%, white blood cells 22,000 per cu. mm. with 98% neutrophils and platelets 155,000. The red cell volume was 2.3 l. (34 ml./kg.) plasma volume 4.2 l. (34 ml./kg.), plasma volume 4.2 l. (62 ml./per kg.), the latter being slightly raised, presumably due to his heart failure, the total blood volume therefore being 6.5 l. (97 ml./kg.).

Renal function was at this time relatively good, with a concentration and dilution of urine between 1010–1019 specific gravity. The mean uric acid excretion for 24 hours in the urine was 670 mg. The plasma iron clearance, using ^{52}Fe, showed 39.5 minutes (normal 70–140 minutes)—that is, an increased clearance. Surface counting over the screen gave no evidence of extramedullary erythropoeisis. A bone marrow biopsy showed marked hyperplasia of all elements, with slight megaloblastic change and low iron stores.

Onset of Heart Failure

At this point, therefore, though the polycythaemia had been brought under control by the phosphorus injections as shown by a relatively normal red blood cell volume, he had developed cardiac failure, and this was the major clinical problem. We were uncertain of the cause of the failure but thought it to be due to a combination of aortic stenosis, hypertension, and ischaemic heart disease. Treatment with digitalis and mersalyl produced some improvement despite a transient attack of atrial flutter with 2:1 block. Blood volume studies gave no reason for further treatment of his polycythaemia. While he was in the ward another grand mal attack occurred, presumably due to cerebral thrombosis. An electroencephalogram showed minimal left-sided abnormality.

He was discharged and remained free from cardiac failure and of attacks of gout on treatment with probenecid as a uricosuric drug and colchicine although the serum uric acid did not fall below 7.9 mg.%.

Last Admission

However, in 1966 he was readmitted for the seventh and last time in severe congestive cardiac failure. The pulse was irregular at an apical rate of 100 beats per minute, with extra-systoles. The blood pressure was 110/70 mm. Hg., the jugular veins were congested to the angle of the jaw and showed cannon waves. Sacral and leg oedema was present, the spleen and the liver were enlarged, the haemoglobin was 10.4 g./100 ml., white blood count 18,000 per cu. mm. with 90% neutrophils, and the packed cell volume 33%. The electrocardiogram showed ventricular extra-systoles, the blood urea was 85 mg./100 ml., the serum uric acid 14.4 mg./100 ml., and the serum potassium 4.8 mN/l.

He was treated with bed rest, low salt intake, digoxin, frusemide and continued probenecid, with added potassium tartrate. Five days after admission supraventricular tachycardia occurred, not correctable by intravenous injections of lignocaine. Direct current shock under general anaesthesia restored sinus rhythm but later the same day he developed cardiac arrest and resuscitative measures were unsuccessful.

Clinical Diagnosis

(1) Polycythaemia rubra vera (successfully treated); (2) secondary gout (treated, but with poor success as regards serum uric acid levels); (3) congestive cardiac failure, due mainly to aortic stenosis.

Haematology

Dr. S. M. LEWIS: We know that in a significant number of patients with polycythaemia the condition eventually progresses to myelosclerosis. We know that this is not a sudden process, it is a gradual change; the patient doesn't have polycythaemia one day and myelosclerosis the next day. In this case there was a gradually developing anaemia, the spleen began to enlarge, so that by 1965 there was no doubt that he had evidence of early myelosclerosis although not yet the full-blown picture. A peripheral blood film in 1965 showed a red cell appearance significantly different from earlier films. Oval poikilocytes were present—the sort of poikilocytes which begin to make an appearance at an early stage of myelosclerosis. Haematologically at least there was no doubt about the development of myelosclerosis.

Professor C. C. BOOTH: Could I ask you one question—were there any macrocytes or multilobe polymorphs in that last film?

Dr. LEWIS: There were no multilobe polymorphs. Had there been, I would not have been surprised. There were some sideroblasts present in the bone marrow at the late stage—an interesting complication. There were certainly macrocytes; some of them were polychromatic macrocytes, indicative of a high reticulocyte count, and there were possibly minimal changes of megaloblastic anaemia as well.

Post-mortem Findings

Dr. D. EVANS: The body was that of an elderly male of normal nutrition, with central cyanosis. There were bilateral inguinal herniae. The seventh rib was fractured.

The *spleen* (1,800 g.) was firm with a dark red pulp, inconspicuous Malpighian follicles, and scattered grey-white nodules 2–6 mm. in size with ill-defined outlines. There was soft red marrow in the shaft of the whole of the right femur. There was no lymphadenopathy.

The *heart* (690 g.) showed left ventricular hypertrophy (2.1 cm.). The aortic valve was bicuspid, with heavily calcified irregular rigid cusps forming a slit-like opening 2.3 cm. long. The tricuspid valve was 14.0 cm. in circumference; the other valves were normal. There was non-occlusive coronary artery atheroma.

The *lungs* were oedematous. The liver (2,700 g.) had a nutmeg appearance.

The *kidneys* were of equal size (150 g.) and had finely nodular subcapsular surfaces.

There was white frosting over the articular cartilage in the right metatarsophalangeal joint, but none in the hips or knees.

On microscopy the *marrow* (Fig. 1) was cellular, with normal erythropoietic components. The reticulin pattern was variable, ranging from normal through increased to "fibroblastic" (Fig. 2).

Extra medullary haemopoiesis was present, as evidenced by megakaryocytes in the liver, spleen, and lymph nodes (Fig. 3) but quantitatively it was slight.

Foamy phagocytes were present in the spleen (Fig. 4), some showing P.A.S. positive cytoplasm. The kidneys showed non-specific scars and marked elastosis of the intralobular arteries consistent with but not diagnostic of benign hypertension (Fig. 5). Doubly refractile urate crystal deposits could be shown in cartilage (Fig. 6). Calcific aortic stenosis was confirmed (Fig. 7), and interstitial myocardial fibrosis was present. There were heart failure cells in the lungs.

So this patient had suffered from polycythaemia rubra vera with secondary hyperuricaemia leading to clinical gout. Following repeated treatments with radioactive phosphorus the polycythaemia became controlled but evidence for progression of the disease into a myelosclerotic phase was equivocal. The aetiology of his cardiac failure was a combination of hypertension and aortic stenosis, the latter occurring on the basis of a congenital bicuspid aortic valve which became calcified later in life.

Pathologist's Diagnosis

(1) Polycythaemia rubra vera.
(2) Secondary gout.
(3) Calcific aortic stenosis on congenitally bicuspid valve.
(4) Congestive heart failure.
(5) ? Benign hypertension.

Discussion

Professor BYWATERS: The several problems here fall fairly clearly into three or four different categories. I think we might discuss first of all whether there was myelosclerosis present or not, and what we could expect to see if there were.

Dr. LEWIS: The point against myelosclerosis was, as Professor Bywaters remarked, that there was little evidence of extramedullary haemopoiesis as measured by surface counts after injection of radioactive iron. But we found at necropsy that there was evidence of some extramedullary haemopoiesis. It is my impression that a significant degree of extramedullary haemopoiesis does not usually occur in uncomplicated polycythaemia vera, and when it does occur this is evidence in favour of myelosclerosis. Plasma iron clearance was particularly rapid, but we don't know what the patient's red cell survival rate was, and I do not think that the observation of rapid plasma iron clearance helps to distinguish myelosclerosis from polycythaemia.

Dr. C. L. COPE: Could you explain what plasma iron clearance is—I don't think everybody's quite clear.

Dr. LEWIS: Plasma iron clearance is the time taken for a small dose of intravenously administered radioactive iron to disappear from the circulation. Normally it goes to the bone marrow, where it will be utilized for the production of further red cells or kept there as part of iron stores. Essentially it is a reflection of erythropoietic activity. It is more rapid than normal in polycythaemia. In myelosclerosis it is sometimes slower than normal but in other cases of myelosclerosis it may be rapid.

Professor BOOTH: May I just interrupt here—I'm getting totally confused. The issue seems to be, had this patient what you term uncomplicated polycythaemia rubra vera or had he myelosclerosis ? What we need to know is what criteria you would use to differentiate between these two.

Dr. LEWIS: As I said earlier the distinction is very difficult at the stage of the disease where it is in transition. Undoubtedly the patient initially had polycythaemia. He had a high red cell count with a very high red cell volume and a polymorph leucocytosis but relatively few metamyelocytes and no myelocytes in circulation ; and his spleen was not palpable. These are the features of polycythaemia vera. On the other hand the peripheral blood film showed poikilocytosis, which is a striking feature of myelosclerosis and is a reflection of marrow abnormality.

Features of Myelosclerosis

Professor BOOTH: In other words there are two main features of myelosclerosis ; one, the anatomical abnormality within the bone marrow, namely fibrosis with an increased reticulin pattern, and the other a functional abnormality of some sort seen in the peripheral blood. Dealing with the anatomical abnormality, does Dr. Evans think it was present ?

Dr. EVANS: I find it almost as difficult as Dr. Lewis does. I can't agree about the absence of extramedullary haemopoiesis in uncomplicated polycythaemia rubra vera. Minot in 1923[1] recognized that a severe degree may sometimes occur. In our cases of polycythaemia rubra vera the amount of extramedullary haemopoiesis I found here is present in every one. In other words, one finds histological evidence of extramedullary haemopoiesis in polycythaemia rubra vera even if it is functionally unimportant.

Professor BOOTH: In fact, then, the degree of reticulin pattern that you showed us in those very beautiful pictures could be found in a patient with uncomplicated polycythaemia.

Dr. EVANS: It has been shown to occur not only in patients with polycythaemia rubra vera but also in patients with other conditions.[2] Chronic myeloid leukaemia and even blast cell leukaemias can show a fibroblastic type of pattern. I don't think it is specific.

Dr. LEWIS: But it is a matter of degree.

Dr. EVANS: Partly.

Professor BOOTH: Dr. Wheby, would you like to give us the American view on this.

Dr. M. S. WHEBY: I can't give the American view but I can give my own view. There is no good way to resolve the issue —it is a problem in semantics. This points to the convenience of the concept of a "myeloproliferative syndrome."

Effect of ^{32}P

Dr. EVANS: May I ask whether any of these changes he has may be related to the ^{32}P treatment ?

Professor BYWATERS: What would Dr. Lewis expect this fairly successful ^{32}P treatment to produce ?

Dr. LEWIS: No changes in the red cell morphology, which remains normal. That is, if one is assuming that the ^{32}P treatment itself is not influencing the development of myelosclerosis.

Dr. CELIA OAKLEY: I am not quite clear why he was anaemic. If it was due to the ^{32}P, why did he still have extramedullary haemopoiesis ? He had a funny-looking blood film and calcific aortic stenosis—was there any evidence of mechanical intravascular haemolysis in that film ?

Dr. LEWIS: He had polychromasia and a reticulocyte count of 9% at one stage.

Professor BOOTH: Unless the red cell turnover was measured you can't really answer this.

Dr. LEWIS: I do not have any record of a red cell survival study. The presence of polychromasia might suggest that there was an increased red cell destruction. Alternatively, it could equally well be due to extramedullary haemopoiesis.

Professor BOOTH: The other question I wanted to ask was whether there was any megaloblastic change at the end. You suggested there were some intermediate megaloblasts in the bone marrow. Now this is a very interesting point, because if polycythaemia in its uncomplicated phase is compared with myelofibrosis the polycythaemic patient doesn't usually develop folic acid deficiency. The patient with myelofibrosis very frequently has a low serum folate and may develop frank megaloblastosis with an anaemia that can then respond to folic acid. In other words, there is an actively turning over marrow in myelofibrosis which can, as in haemolytic anaemia, induce a folic acid deficiency. Did you have any folate studies ?

Dr. LEWIS: I have no record of one.

Professor BYWATERS: I wonder if we could ask Dr. Evans whether there was much evidence of continuing haemolysis. The suggestion Dr. Oakley made was a very good one: I don't think we looked at haptoglobins in his plasma at all.

Dr. EVANS: Iron stains on the liver and spleen were negative.

Professor BYWATERS: So there is really little evidence for continuing haemolysis and the verdict on the myelosclerosis is that there might have been a little bit of it.

Dr. LEWIS: Yes, I think this is well put, and in fact, had this patient survived, there is evidence, I think, that he might have gone on to develop a much more clear-cut myelosclerosis.

Gout

Professor BYWATERS: I think perhaps the next point is this man's gout; it was an expected phenomenon and it behaved properly; the only thing that didn't go according to expectation were his serum uric acid levels which treatment with probenecid didn't reduce to normal, as it should do; because of this we were considering starting him on allopurinol, but we didn't get round to it because of his heart failure. I think, therefore, that the failure of probenecid was probably due to the slight renal functional impairment and this again was probably related to the fibrosis associated with the changes of essential hypertension. The kidneys, however, were not decreased in size.

Dr. EVANS: The only abnormal feature of the kidneys was the presence of the small scars.

Dr. E. D. WILLIAMS: Could I ask whether the development of gout can be correlated with the severity of the polycythaemia, or whether there is a great individual variation suggesting maybe an inherited predisposition to gout?

Professor BYWATERS: There is a good direct relationship of packed cell volume to serum uric acid level if only those polycythaemic patients who have a good renal function are considered; if renal function is impaired, rather erratic increases in serum uric acid occur which do not correlate so well with packed cell volume.

Dr. WILLIAMS: What about the development of clinical gout?

Professor BYWATERS: Clinical gout is an accident that frequently occurs in patients who have high levels of serum uric acid due to increased formation of urate and/or due to decreased output; that is with a body pool of urate increased from the normal level of one gramme of urate up to five, ten, or twenty grammes. We didn't measure this man's body pool, but we have every belief that it was increased and that his turnover was increased, as it is in all these patients. But there is no specific hereditary gouty tendency in this type of secondary gout, which is rare compared with primary gout: furthermore there is no predilection for males as there is in primary gout.

Professor BOOTH: And presumably there is no family history either.

Professor BYWATERS: There was no family history.

Dr. LEWIS: There was a review by Lynch about four years ago[3] on uric acid levels in blood dyscrasias and he suggested that in polycythaemia—pure uncomplicated polycythaemia—uric acid levels were generally lower than the levels in what he termed myeloid metaplasia, which undoubtedly included early myelosclerosis.

Professor BYWATERS: I think it depends upon the amount of purine turnover that's going on.

Dr. LEWIS: The point that Lynch made was that in polycythaemia the factor causing the elevation of uric acid is an increased number of red cells in circulation. In myeloid metaplasia on the other hand there may be considerable destruction of haemopoietic cells at the sites of extramedullary haemopoiesis, cells which are never delivered into circulation.

Professor BOOTH: And when a patient develops myelofibrosis does the gout get better?

Professor BYWATERS: I don't think we have any information on that point—in general I think it is a later stage in the disease and the gout will tend, therefore, to be worse because there is likely to be some renal impairment.

Professor BOOTH: Was there any evidence of gouty infiltration of the kidney?

Dr. EVANS: No, we fixed the kidney in alcohol and examined sections under polaroids, but there were no urate or uric acid deposits there. I don't think the mechanism by which gout affects the kidneys is known. The type of scar present here is non-specific though seen quite frequently in patients with gout.

Professor BYWATERS: It is the usual type of gouty kidney; whether it's related to the gout or not I don't know, but only a comparatively few cases show tophi in the kidney. Tophi in the kidney are thought to be much more important and more frequent than they really are. I think you're quite right that the real lesion in the typical case of gout with renal impairment is fibrosis.

Heart Failure

Professor J. GOODWIN: If I may, I would like to ask the pathologist about essential hypertension. You were obviously a little hesitant about diagnosing this, and since the patient had two diseases known to be associated with hypertension—gout and polycythaemia—I wonder if you would like to comment on that point and the possible other causes for his hypertension. There are, however, just two cardiac points I would make. One is, as Dr. Oakley said, this obviously wasn't a digitalis arrhythmia because the patient went back to sinus rhythm. Now if there is a digitalis tachycardia, as she's pointed out, very commonly the patient either won't revert to sinus rhythm with counter shock, or—much worse—he will develop serious conduction defects, heart block or even asystole. So counter shock, which is a very valuable means of treating resistant arrhythmias, is largely contraindicated in a patient with an unquestioned arrhythmia due to digitalis. I think the response of the patient to counter shock shows that this definitely was not a digitalis arrhythmia despite the fact that the cardiogram showed quite a lot of digitalis effect, much more, in fact, than it had on the previous occasion.

The other point I would like to make is a very small one, and that is that one is realizing more and more as time goes by that isolated calcified aortic stenosis commonly has a congenital aetiology; the lesion is not rheumatic or degenerative, as has often been thought in the past. This is still, I think, not always appreciated, and if I'd been a little brighter when I saw him first I might have diagnosed *congenital* aortic stenosis, but we were preoccupied with other factors. I think everything fits in. I'm a little surprised that he didn't have ischaemic heart disease due to coronary occlusion in view of the gout, polycythaemia, hypertension, and the fall in his blood pressure, which hasn't really been adequately explained but might have been due to myocardial infarction. His heart failure could be explained on the basis of the aortic stenosis, for as the valve becomes more heavily calcified so it becomes more rigid and thus the effective orifice becomes reduced. Together with an ageing myocardium I think probably there was quite enough to account for the heart failure.

Professor BOOTH: Dr. Evans, what about the hypertension?

Dr. EVANS: One of the criteria, left ventricular hypertrophy, is obviously invalid in the presence of aortic valve disease. Diagnosis depends then on what one's assessment is of the state of the small vessels, particularly in the kidney. Here we have an elderly man, and elderly people get a senile elastosis of the small vessels in the kidney with some elastic duplication. My own feeling was that this was rather more severe than I expected, and this is possible evidence that he did have a benign hypertension, but it's purely a question of opinion on the quantitative significance of the changes.

Professor BOOTH: Dr. Wheby reminded me that hypertension and polycythaemia go under the heading of Gaisböck's syndrome—what about this?

Dr. EVANS: I think the polycythaemia there is not polycythaemia rubra vera, is it?

Dr. LEWIS: As far as I am concerned it really is rather meaningless, but the name has been applied to this combination. A group of these patients studied at Johns Hopkins were found to have so-called "stress" polycythaemia or relative polycythaemia related to a shrinkage of plasma volume. But, in fact, approximately 30% of patients with polycythaemia do have hypertension.

Blood Volume

Dr. OAKLEY: May I offer an alternative explanation for the drop in blood pressure? There is a third contributor to the blood "pressure" which is often not spoken about very much and that is the blood volume. When he was polycythaemic he had an increased circulating blood volume—when the polycythaemia was subsequently treated his blood pressure fell and blood volume studies were then repeated and the comment made that no further treatment was needed. This was because the blood volume had fallen to normal, and with it his blood pressure, and perhaps this is the best explanation for the loss of his hypertension.

Professor BYWATERS: The high viscosity of the blood in polycythaemia increases the work of the heart.

Professor R. STEINER: I don't think we can accept this story of aortic stenosis becoming severe in the last few weeks or months. In retrospect when we looked at his old films it was realized that he had calcific aortic stenosis in 1958.

Professor GOODWIN: But you can't quantitate it, can you?

Professor STEINER: No.

Dr. A. BRECKENRIDGE: There is another relationship—we showed that approximately 30% of patients with untreated hypertension had a raised uric acid, but of course these were not the patients that over-produce uric acid—they're the ones that under-excrete it.[4] I think this is another facet to this very complicated problem.

Professor BOOTH: So if he'd had essential hypertension in addition to everything else this would have encouraged the retention of uric acid too. The other thing that interested me was the intensity of the fibrosis of the myocardium in a patient with apparently patent coronary arteries.

Dr. EVANS: This type of fine fibrosis lying in between the muscle fibres one tends to find with severe hypertrophy of the left ventricle, particularly when there is an associated aortic valve stenosis.

Professor BOOTH: So that your diagnosis of hypertension, ischaemic heart disease, plus aortic stenosis is all quite correct.

Dr. OAKLEY: All patients with severe aortic stenosis have ischaemic heart disease (but not necessarily coronary artery disease).

Dr. BRECKENRIDGE: In recent surveys it has been shown that patients with a raised uric acid have an increased incidence of ischaemic heart disease.

Professor BOOTH: Thank you. Any other points?

Professor GOODWIN: Can hyperuricaemia account for the myocardial fibrosis?

Dr. EVANS: I don't know in this particular instance whether there was any uric acid in the heart.

Professor BYWATERS: It would not produce a generalized fibrosis. Certainly tophi have been described in the mitral valve—this is quite likely to occur—it might possibly be found that crystals are present because of the calcific fibrosis, but I don't think it contributes anything.

Professor BOOTH: And really we have quite enough to explain it already. Thank you all.

We are grateful to Professor J. P. Shillingford and Dr. E. D. Williams for assistance in preparing this report, and to Mr. W. Brackenbury for the photomicrographs.

REFERENCES

[1] Minot, G. R., and Buckman, T. E., *Amer. J. Med. Sci.*, 1923, **166**, 469.
[2] Burston, J., and Pinniger, J. L., *Brit. J. Haematol.*, 1963, **9**, 172.
[3] Lynch, E. C., *Arch. Int. Med.*, 1962, **109**, 639.
[4] Brechenridge, A., *Lancet*, 1966, **1**, 15.

NEW APPLIANCES

Substitute for Gauze Swabs during Surgery: Preliminary Report

Mr. I. G. SCHRAIBMAN, Western Infirmary, Glasgow, writes: Most surgeons will be familiar with the numbing fear experienced when the scrub nurse, after some minutes of increasingly frenzied burrowing among the drapes, announces that the operative and postoperative swab counts do not tally. This may result in prolongation of the anaesthetic, disruption of theatre and radiology department schedules, and at very least the generation of considerable warmth in the theatre. If the error passes unremarked, the surgeon may well be accorded the distinction of appearing anonymously in the annual review of one of the medical defence societies.

The human factor can never be eliminated, and the risk will remain so long as obscuring fluids have to be mopped from the operative field.

It seemed reasonable to suppose that the risk could be lessened if the number of objects to be counted was limited; but as gauze swabs can be used only once the number used (and therefore the risk) is in proportion to the bloodiness of the procedure. For the number of swabs to be limited, therefore, they would have to be reusable, and in line with current post-mortem practice it was decided to use polyurethane sponges instead of swabs.

Ordinary commercial polyurethane foam sponge was purchased and cut with a sharp knife to the required size. The actual sizes selected were arbitrary—namely, 6 by 4 by 1½ in., 4 by 2 by 1½ in., and 2 by 2 by 1 in. (15 by 10 by 3.8 cm., 10 by 5 by 3.8 cm., and 5 by 5 by 2.5 cm.). Three of the first and six each of the latter were used for a major operation—for example, gastrectomy or colectomy—but only the two smaller sizes for smaller procedures—for example, hernias and varicose veins. For potentially infected operations—for example, where the bowel was to be opened—two separate sets of sponges were used, the contaminated ones being removed together with contaminated instruments and drapes, when the dirty part of the procedure was completed.

The sponges were wrapped in paper packets and sterilized by a standard theatre autoclaving procedure. Before use samples of the centre of some sponges were cultured but revealed no growth.

The absorptive capacity was increased by prior wetting of the sponge with saline. When the sponge was full of blood it was wrung into a measuring jug kept solely to register blood loss. It was then rinsed in normal saline and wrung out again ready for use. Sponges could be autoclaved four to six times before irreparably losing their shape and fluid-holding capacity.

It is now planned to impregnate the sponges with a radioactive substance for *x*-ray visualization.

Sponges were used in 19 major and 23 minor procedures without untoward effects. There were no unexpected wound infections and no sponges were lost. The only situation in which the gauze swab was to be preferred was for friction dissection, mounted on a forceps, as sponges would tear.

Polyurethane sponges have three advantages over gauze swabs: (1) as they are reusable a finite and limited number of them is required, regardless of the length or bloodiness of the operation; (2) a reasonably accurate running total of blood loss can be kept; and (3) commercially made sponges may be marketed at about half the price of gauze swabs on a unit for unit basis. The cost decreases with each reautoclaving, and, of course, the do-it-yourself variety come cheaper.

Book Reviews

Facts on New Growths

Prevention of Cancer: Pointers from Epidemiology. The Rock Carling Fellowship, 1967. By Richard Doll, O.B.E., D.Sc., M.D., F.R.C.P., F.R.S. (Pp. 143; illustrated. 7s. 6d.) London: Nuffield Provincial Hospitals Trust. 1967.

At the front of this book we are told that "The Rock Carling Fellowship was founded as an annual memorial to the late Sir Ernest Rock Carling," and once a year a book comes out to help us to keep in mind the life and works of this great man. This year the man of choice to write the book was W. R. S. Doll, and he has done his task well.

He has put down a lot of sound sense on that group of ills which we call new growths. The work is not, as some books have been, just a list of things that can cause lumps and bumps in rats and mice. To start with, Doll tells us the sort of facts that we should seek when we want to know if some forms of new growth are due to the air we breathe, the soil we dwell on, our food and drink, how we make love, the weed that some of us smoke, or what we use in our work. He then goes on to tell us how we should judge the facts that we have found and what they mean. He points out that in the long run the best proof may come from what takes place when we stop the use of a thing or change our way of life. To show this, he cites the case of a group of men, a lot of whom used to smoke; more of these men, in view of what they heard or read, had the good sense to give it up (or change to a pipe) than the rest of the men in the land. It may well be that the man in the street did not have the same chance to learn the true facts of the case. As time went by, it was found that the first group of men were, year by year, less prone to die from new growths in their lungs; while in the rest the rates for such deaths went up and up. This seemed to Doll to be fresh proof that new growths of the lungs can be caused by what men smoke.

Doll then lists some facts which may lead us to think that quite a few types of new growth can be due to things in the world round us, and he tells us how we can get rid of some of them and keep some in check. He does not want to ban those which do us more good than harm. He warns us that no dose of these things is so small that we can be sure that it is quite safe.

There are tests by which we can find out that a man has a new growth as soon as its strange cells start to grow and are shed. Doll tries to make us think out how we can tell if these tests will in fact help to save lives, or at least spare men pain and grief in the last part of their lives.

At the back of the book are six good maps, drawn in a new and clear way by Miss P. Cook, which show that the rates at which some kinds of new growths are found are not the same in all parts of the world, and that the change from place to place may be quite large.

To sum up in a few brief words, one would have to go a long way to find a book which was as well worth its price as this one, and most of us would gain if we were to read it.

I will now tell you why I have set out my views on Doll's book in such a strange style, which I hope he will not mind. At much the same time as I was asked to write this piece I had read, in proof, a new book[1] by an old friend, all in words with but one beat in them. I was struck by the fact that it helped me to make my thoughts more clear when, in turn, I tried to write in this way. Though, of course, I would not say that one should print one's work in this form at all times, I think it might help more men who write if they were to try it, too, at the stage when they set out their thoughts for the first time.

R. A. M. CASE.

REFERENCE

[1] Hogben, L., *Whales for the Welsh*, 1967. London.

Facets of Radiotherapy

Modern Trends in Radiotherapy 1. Edited by Thomas J. Deeley, M.B., Ch.B., F.F.R., D.M.R.T. and Constance A. P. Wood, M.A., M.R.C.P., F.F.R. (Pp. 382+xiii; illustrated. 85s.) London: Butterworth. 1967.

The only way a practising physician today can keep abreast of the times is to attend scientific meetings and read the medical literature. The latter is so enormous that the problem of selecting what to read depends upon interest and knowledge, as well as the ability to select, to skim, and to avoid.

In this book Dr. Deeley and Dr. Constance Wood have invited experts in the many facets of radiotherapy to record their own particular experience. There are 44 pages of references, mainly to articles written by the contributors. The book thus winnows the literature for our benefit. The first six chapters discuss the fundamental applications of radiobiology, including fractionation, oxygen, and combined therapy using chemotherapeutic agents. The next four chapters discuss boron capture therapy, fast neutron therapy, and Professor J. S. Mitchell's researches on the use of tritium-labelled compounds. Then Dr. Deeley pauses and inserts his own chapter on controlled clinical trials, and I assume that its insertion here is deliberate. It is chapter 11 in the centre of the book—the fulcrum, keeping the balance and reminding us that the true objective of all this is greater success, scientifically assessed, in the treatment of disease.

Dr. E. C. Easson writes on the management of Hodgkin's disease and allied diseases, and Dr. D. A. G. Galton a fascinating and instructive chapter on trends in the therapy of leukaemia, which is hardly a trend in radiotherapy. Similarly, the last chapter on the detection of tumours using isotopes does not absolutely fulfil the qualification of radiotherapy, which is the treatment of disease by ionizing radiation. The therapeutic use of radioiodine and radiophosphorus is of concern to the radiotherapist, but the chapter on pituitary implantation by G. F. Joplin and M. Hartog concerns only endocrine diseases which are highly specialized, and no mention is made of its value in the treatment of advanced carcinoma of the breast, which is a daily problem for the radiotherapist. One notable omission in the book is an account of the indications for the use of remote loading devices, which can be of tremendous value from the point of view of protection, provided the fractionation is radiobiologically effective. It is important that a technique should not be pigeon-holed too closely as a trend in a physiological exercise of wide applicability but limited interest.

It is interesting that the chapters on chemotherapy, boron capture, telecurie apparatus, electron therapy, and heavy particles all come from abroad, and, while it is interesting to learn what our colleagues are doing, it is unlikely that the facilities will be available in this country on any scale unless private means are available for buying the expensive apparatus involved. This does not minimize the contribution to knowledge which work with various particles provides, particles whose elementary life period appears very short as new ones are detected and marshalled.

The book is an attempt to relate progress through a vast field, and, while improvements in clinical results are not commensurate with technical advances, scientific accuracy of application of these irradiations does eliminate one complicating factor in our studies. The hope of the future must lie with greater knowledge of the relationship of dose to effect, which is a problem of fundamental radiobiology. The book makes fascinating reading and must be studied by all who are concerned with radiotherapy or radiobiology.

I. G. WILLIAMS.

Physiology as the Basis of Surgery

Scientific Foundations of Surgery. Edited by Charles Wells, C.B.E., S.Pk., F.R.C.S., Hon. LL.D., and James Kyle, M.Ch., M.B., F.R.C.S., F.R.C.S.I. (Pp. 629+xix; illustrated. £6 6s.) London: William Heinemann. 1967.

Not long ago a book entitled *The Scientific Foundations of Surgery* might have been expected to include a great deal of regional anatomy and some descriptive pathology but little else. By contrast this impressive volume consists almost entirely of physiology and the undefined territory which lies between general pathology, biochemistry, and cell biology. Moreover it comprises not merely the clinical applications (though these are not neglected) but also in generous measure the fundamentals of these sciences.

Thus, the first chapter deals at some length with the basic physiology of the heart, the mechanism of the coronary circulation, the control of blood pressure, the methods of assessing heart performance, and the interpretation of electrocardiographs. This is followed by sections dealing with the disturbances of function resulting from heart diseases and those brought about by surgical attack on the heart. Other chapters deal similarly with the physiology of the respiratory, alimentary, urinary, endocrine, and nervous systems, and with related questions of applied physiology. There are also chapters on genetics in relation to clinical medicine, on allergy and immunity, and on the physical and chemical basis of cancer chemotherapy. Naturally, the fluid balance receives full attention, and there are good accounts of the physiology of haematopoiesis, of the metabolism of iron, of the serum proteins, and of defects of haemostasis.

Altogether the book contains nearly a hundred sections by 130 contributors, the majority British surgeons, with some physicians and laboratory workers, and a small but distinguished group of surgeons from the United States and Canada. The writing is vigorous, succinct, and lucid and the general standard of presentation is uniformly high. This is a book to be prized.

CHARLES ILLINGWORTH.

Respiratory Disease in Childhood

Disorders of the Respiratory Tract in Children. Edited by Edwin L. Kendig, jun., M.D. (Pp. 834+xxiii; illustrated. £9 2s.) Philadelphia and London: W. B. Saunders. 1967.

The ambitious aim of this work is to provide an answer to almost any question about respiratory disease in childhood which could be asked by paediatricians or their residents, by chest physicians, radiologists, general practitioners, or by medical students. This is stated by the editor in his preface, and in a foreword Dr. Amos Christie writes that Dr. Kendig has brought together in this timely volume all that is currently known of those conditions of the chest which are unique to the paediatric age group.

Dr. Kendig and his 28 associated contributors have certainly made a determined attempt to justify these remarks. Starting with sections on the functional basis of respiratory physiology, the history, physical examination, diagnostic and therapeutic procedures, and the age factor in respiratory tract disease, the book continues with disorders of the newborn, followed by disorders of the nose, mouth, pharynx, larynx, and ear, then infections of the upper and lower tract, then non-infectious disorders of the lower tract, other diseases with a prominent respiratory component, and, finally, traumatic disorders.

The sections on asthma, tuberculosis, and cystic fibrosis stand out among the practical clinical subjects in their exposition, but all the conditions described are well done. Even the rarities like thesaurosis, alveolar microlithiasis and proteinosis, milk-related pulmonary haemosiderosis, pertussoid eosinophilic pneumonia, and dysautonomia receive attention.

There are some minor criticisms. No mention is made of the enanthem of infective mononucleosis; in the treatment of pneumococcal pneumonia the old-fashioned recommendation that "antimicrobial therapy should be continued for several days after defervescence and until clearing is present on the *x*-ray" is unfortunately perpetuated; in considering hydrothorax it is stated that sleeping in the semi-erect posture may provide some comfort but is not very practical for small children and infants—one wonders why not, seeing that our patients in these age groups with hiatus hernia are regularly nursed in their sentry boxes; the clinical description of respiratory syncytial virus infection is too scanty to be of value. Finally, four pages devoted to pictures of various tuberculin tests seems excessive and there is no mention of the intradermal jet technique, which is likely to be the method of choice in the future both for tuberculin testing and for giving B.C.G. There is no reference to the value of isoniazid-resistant B.C.G.

However, all paediatricians and chest physicians will find something of interest and value in this book and the extensive bibliographies enhance its usefulness. It is well produced and the printing and typography are excellent. There are 834 pages (including 44 for the index), 66 tables, and more than 350 figures. Unfortunately some of the figures are very poor, particularly those depicting intra-oral conditions, for which coloured plates are really required, and some of the *x*-rays and sections are indistinct. Fig. 64.2 is upside down and Fig. 41.15 on p. 412 should read 41.12.

If the non-essential figures and tables had been omitted the book would have been cheaper to produce and no less valuable to the reader.

WILFRID GAISFORD.

Mixing Medicine and Morality

The Anxiety Makers. Some Curious Preoccupations of the Medical Profession. By Alex Comfort. (Pp. 208; illustrated. 30s.) London: Thomas Nelson. 1967.

The main part of this book consists of descriptions and excerpts from past writings on sexual behaviour and morality. There is only a brief reference to classical literature, and the author passes swiftly to sexual manuals, such as *Geneanthropeia,* by Giovanni Sinibaldi (1642), a professor of medicine in Rome, which appeared in English in 1658 as *Rare Verities, the Cabinet of Venus Unlocked*—a mixture of classical and mediaeval folklore. The material was reprinted, little altered, in 1771 under the title *La Génération de l'Homme, ou Tableau de l'Amour Conjugal,* by Nicolas Venette, Dean of the Faculty at La Rochelle, a book designed to teach us how "to preserve our health through moderate use of the pleasures of marriage." Most of this was a mixture of sense and nonsense, on the whole designed to titillate, but by the 19th century sex had become a source of deep anxiety to medical writers. Comfort concentrates his fire on William Acton's (1857) treatise on the *Function and Disorders of the Reproductive Organs in Youth, in Adult Age and in Advanced Life,* but he fully describes the epidemic of anxiety about masturbation which raged through the 18th and 19th centuries. Normal women were described as having no sexual desires; intercourse was hazardous at all times and extremely dangerous during pregnancy and menstruation; masturbation was a prime cause of insanity; venereal disease and pregnancy were a just penalty for misdemeanours. Comfort devotes a chapter to constipation and inner cleanliness, with special reference to Arbuthnot Lane, his kink, and his colectomies.

We must agree with Comfort's thesis, which is that doctors have in the past made totally erroneous statements about the effects of masturbation, sexual intercourse, continence, contraception, constipation, etc., and until recent years at any rate have failed to collect scientific evidence on these topics. Speaking in their capacity as doctors, they have pronounced on the morality of premarital intercourse, abortion, contraception, and artificial insemination, when morality is not their proper business. Worst of all, they have mixed and muddled up medical and moral judgements. Granted all this, sexual anxiety is and has been widespread in communities which have been without benefit of doctors, and psychosexual evolution in industrial communities with social security services can hardly be left completely undirected.

The picture of young people's behaviour today, presented in Nell Dunn's *Up the Junction* and Christiane Rochefort's *Josyane and the Welfare,* is not an attractive one, and while Comfort has performed a useful service in demonstrating past errors he leaves us with little guidance for the future.

L. J. WITTS.

Neuroradiological Topics

Pneumoencephalography and Cerebral Angiography. By Bernard S. Epstein, M.D. (Pp. 349+xiii; illustrated. £7 10s.) London: Lloyd-Luke. 1966.

Dr. Epstein is a prolific writer on neuroradiological topics and is well known on both sides of the Atlantic. One can be sure that anything he writes is to the point and stems from his own very wide experience.

This new book is divided into four large chapters: normal pneumoencephalogram and angiogram, congenital malformations, vascular lesions, and brain tumours. The first half of the first chapter dealing with pneumographic anatomy appealed most to the reviewer. The intricacies of the basal cisterns are not easy to understand; although there are several accounts in various textbooks this is one of the clearest. Not only are the radiographs well chosen but the photographs of the author's own dissections of the brain are very well selected.

The section on tumours is the largest. This is a most difficult subject to tackle comprehensively, and it is sometimes not easy to marry up the various pneumographic and angiographic pictures associated with any particular lesion.

The illustrations throughout the book are generally speaking clear, and although the last figure is numbered 219 there are in fact about three times this number of pictures. All the illustrations are small, the largest being less than 2½ in. (6 cm.) square. While this has the advantage of packing a great many into a small space and several pictures on to the same page, it sometimes makes interpretation difficult, particularly for the uninitiated.

References are appended at the end of each subsection of a chapter. In all there are something over 1,000, divided into about 50 sections. They are up to date and well selected for the most part, but unfortunately there are hardly any from the French schools.

JAMES BULL.

Recognizing Haemoglobinopathies

An Introduction to the Haemoglobinopathies. And the Methods Used for their Recognition. By H. E. Hutchison, M.D., F.R.C.P. (Glasg.), F.C.Path. (Pp. 88 + vii ; illustrated. 30s.) London : Edward Arnold. 1967.

This book comprises in 80 pages basic information on haemoglobinopathies which include diseases arising from abnormal haemoglobins as well as the thalassaemias, which are the outcome of an inability to form enough normal adult haemoglobin.

The introduction gives fundamental facts on the structure of haemoglobin and there is a discussion of the physiological human haemoglobins as well as of abnormal variants. The distribution of the haemoglobinopathies and their clinical and haematological diagnosis are discussed, and there are also excellent explanations of their inheritance and of the nature of the anaemias. Arising from this, a section of the book allows the laboratory worker to look up the basic methods he requires. In the next edition the author when describing the amino-acids of the α and β chains of haemoglobin A might take account of recent work in which some of the residues described as being of aspartic and glutamic acid are now known to be residues of asparagine and glutamine respectively. Also, the only method for electrophoresis used is starch gel electrophoresis, and many laboratories would find it useful to have instruction referring to other techniques such as paper and cellulose acetate electrophoresis.

There is no doubt that this book will have a considerable appeal to a wide circle of clinicians as well as laboratory workers, and it is highly recommended.

H. LEHMANN.

"Labour Movement at its Best"

The Manor House Hospital. A Personal Record. By Samuel James Woodall, M.A., M.R.C.S., L.R.C.P., D.P.H. (Pp. 214 + x ; illustrated. 40s.) London : Routledge & Kegan Paul. 1966.

In September 1914 a British surgeon, Dudley Wright, volunteered to take a surgical unit to France and very soon opened a hospital in Yvetot. A year later the hospital was taken over by the French Red Cross and the English supporters of the hospital decided to open a hospital near London "for the treatment of disabled soldiers and sailors from our own Services." Manor House, situated in North End, Hampstead, was purchased, repaired, and extended and the new hospital was opened on 29 September 1917 by Field Marshal Sir William Robertson. The London Committee adopted the title of "The Industrial Orthopaedic Society" and every regular subscriber became eligible for treatment there if necessary.

The first few years were difficult but the Ministry of Pensions helped, and gradually the hospital grew in importance. New buildings were erected and it became successfully established. Several factors contributed to this, not least among them the emphasis on rehabilitation and the cultivation of a friendly atmosphere. Although many large sums were contributed by well-to-do persons, a large part of the income came from thousands of industrial workers who gave one penny a week. Paid organizers were stationed in different areas of the country and the number of such subscribers rose from 24,000 in 1921 to 300,000 in 1945. The members of some large trades unions joined *en masse* and many Labour leaders took great interest in the hospital—Ernest Bevin, Viscount Alexander, J. H. Thomas, Sir Ben Smith, and Mr. Ramsay MacDonald. The last mentioned said "that such institutions as the Manor House Hospital, which represented the mind of the working people, were characteristic of the Labour movement at its best." A great factor in the hospital's success was the personality of the first resident surgeon—Ambrose Woodall—who served from 1924 till 1958. He was well-qualified, experienced, tactful, and hard-working, and, having a clear vision of what was needed, wisely advised the lay committees on essential matters. He was also an expert on the medico-legal aspect of compensation cases and this added to the reputation of the hospital. His achievements were publicly recognized by the conferment of a knighthood in 1931 and by his elevation to the peerage in 1945.

The writer of this history—Samuel James Woodall—was the brother of the resident surgeon and served as physician to Manor House Hospital for many years ; to him Lord Chorley pays a moving tribute in the foreword.

When the National Health Service began in 1948 the Manor House Hospital (with the exception of the dental and ophthalmic departments) remained outside the control of the State. No reason for this is specifically given in the book, but careful readers will no doubt judge for themselves.

ZACHARY COPE.

Books Received

Review is not precluded by notice here of books recently received.

Cancer Research Today. By I. Berenblum, M.D. (Pp. 151 + xii ; illustrated. 30s. Paper 17s. 6d.) Oxford : Pergamon. 1967.

The Year Book of Nuclear Medicine. Volume 2. Edited by James L. Quinn, III, M.D. (Pp. 384 ; illustrated. 75s.) London : Lloyd-Luke. 1967.

Patients and Their Doctors. A Study of General Practice. By Ann Cartwright. (Pp. 295 + vii. 40s.) London : Routledge & Kegan Paul. 1967.

Pulmonary Insufficiency and Respiratory Failure. By Giles F. Filley, M.D. (Pp. 162 + ix ; illustrated. 52s. 6d.) London : Henry Kimpton. 1967.

Grenzen des Normalen und Anfänge des Pathologischen im Röntgenbild des Skelets. 11th edition. By Professor E. A. Zimmer. (Pp. 640 + viii ; illustrated. DM. 134.) Stuttgart : Georg Thieme. 1967.

Das Lebensschicksal der Einnierigen. By Dr. Heinz Rockstroh. (Pp. 113 ; illustrated. £1 3s. 11d.) Berlin : Volk und Gesundheit. 1967.

Progress in Biochemical Pharmacology. Vol. 2. Drugs Affecting Lipid Metabolism. Part 1. Edited by D. Kritchevsky, R. Paoletti, and D. Steinberg. (Pp. 520 + xii ; illustrated. sFr./DM. 120.) Basel and New York : S. Karger. 1967.

Progress in Biochemical Pharmacology. Vol. 3. Drugs Affecting Lipid Metabolism. Part 2. Edited by Kritchevsky, R. Paoletti, and D. Steinberg. (Pp. 532 + xii ; illustrated. sFr./DM. 120.) Basel and New York : S. Karger. 1967.

Selected Papers of George Hevesy. (Pp. 447 + ix. 90s.) Oxford : Pergamon. 1967.

Pyelonephritis. Forschungsergebnisse 1966. Edited by Professor H. Losse and Dr. M. Kienitz. (Pp. 387 + xi ; illustrated. DM. 48.) Stuttgart : Georg Thieme. 1967.

Wasser- und Elektrolyt-Fibel. By Dr. Bruno Truniger. (Pp. 154 + xii. DM. 16.80.) Stuttgart : Georg Thieme. 1967.

Kreislaufstillstand und Wiederbelebung. By Dr. Martin Stauch. (Pp. 80 + vii ; illustrated. DM. 7.30.) Stuttgart : Georg Thieme. 1967.

Diabetes Mellitus im Kindesalter. By Dr. A. Rosenkranz. (Pp. 191 + xii. DM. 8.) Stuttgart : Georg Thieme. 1967.

Internationales Symposium der Sozialisatischen Länder über Rehabilitation. Halle, 1964. Edited by Professor K. Renker, Dr. I. Vas, and Dr. W. Zimmeck. (Pp. 298. £2 0s. 3d.) Leipzig : Georg Thieme. 1967.

Die Sklerodermie und ihr Nahestehende Bindegewebsprobleme. By Professor G. W. Korting and Dr. H. Holzmann. (Pp. 155 + vi ; illustrated. DM. 48.) Stuttgart : Georg Thieme. 1967.

Ursachen und Erscheinungsformen der Akzeleration. By Professor Amneliese Sälzler. (Pp. 200. £2 0s. 1d.) Berlin : Volk und Gesundheit. 1967.

A Modern Pilgrim's Progress with Further Revelations for Diabetics. 2nd edition. By Garfield G. Duncan, M.D., C.M., F.A.C.P. (Pp. 227 + xix ; illustrated. £1 6s. 3d.) London : W. B. Saunders. 1967.

The Human Adrenal Cortex : Its Function Throughout Life. Ciba Foundation Study Group No. 27. Edited by G. E. W. Wolstenholme and Ruth Porter. (Pp. 146. 22s. 6d.) London : J. & A. Churchill. 1967.

Psychiatry for Students. 3rd edition. By David Stafford-Clark, M.D., F.R.C.P., D.P.M. (Pp. 278 illustrated. 21s.) London : Allen & Unwin. 1967.

Middle Articles

GENERAL PRACTICE OBSERVED

Study of the Demand for Urgent Treatment in General Practice

J. A. FORBES,* M.A., M.D.; L. M. M. MUTCH,* M.B., CH.B.; G. T. SMITH,* M.A., B.M., B.CH.;
A. J. TULLOCH,* M.B., CH.B., D.OBST.R.C.O.G.

Brit. med. J., 1967, 3, 856–858

The service that general practitioners give to their patients is based largely on the demands as opposed to the needs of their patients. As a result a disproportionate amount of time may be spent on the trivial and self-limiting, to the detriment of those patients who suffer from serious conditions.

The distribution of disease in general practice has been extensively investigated (College of General Practitioners, 1962, 1965). A more specific approach has been made by Backett *et al.* (1954), Brotherston *et al.* (1959), and Fry and Dillane (1964) by estimating the severity of conditions met with in general practice.

In this study we have looked at the subject from a different viewpoint. An appointment system has been used in this practice for six years. It has proved workable, and acceptable to the majority of patients, but one of the difficulties of such a system is that it needs to be flexible enough to accommodate those patients who come requesting treatment at short notice. If demands of this type are excessive the amount of time which the general practitioner can allot to the supervision of patients suffering from chronic conditions is reduced.

This investigation was initiated to study the nature and extent of this element of urgent demand so that plans could be made to ensure that those patients with serious chronic disease receive the time and care to which they are entitled.

Method

This practice is based on a small market town of some 8,000 inhabitants: 55% of our patients live in the town, and 45% in the surrounding countryside. The survey was confined to surgery attendances. Requests for home visits, antenatal attendances, and attendances at infant welfare clinics were excluded.

Urgent demand was defined as follows: when a patient made contact with the practice and stated that his condition was such that he required medical advice on the same day, he was regarded as having made an urgent demand. The onus for deciding whether treatment was necessary rested with the patient. When such a patient attended the surgery the first part of a form consisting mainly of identification data was completed by the clerical staff. The second part of the form, which included the diagnosis, the reason for the patient's attendance, and the time taken for consultation, was completed by the doctor who treated the patient. The information recorded on the form was coded and transferred to punch-cards. The analyses were carried out by means of business machines under the aegis of the Oxford Record Linkage Study. Information about the age and sex structure of the practice and its geographical distribution during the survey was derived by means of a system of data retrieval described elsewhere (Acheson and Forbes, 1967).

Results

The number of patients at risk midway through the study was 6,850. About one in four who attended the surgery during the nine-week period thought that treatment was necessary the same day (Table I). It would seem, therefore, that about 25% of all surgery appointments should be allotted to patients requiring urgent treatment. It will be seen from Table II, however, that the daily distribution is uneven, suggesting that the number of appointments reserved for urgent cases should vary according to the day of the week.

TABLE I.—*Proportion of Urgent Attendances Demand Compared with Routine Attendances*

No. of urgent attendances	775 (26·7%)
„ „ routine attendances	2,131 (73·3%)
	2,906 (100·0%)

TABLE II.—*Proportions of Urgent Demand Attendances by Week-day*

	No. of Attendances
Monday	255 (32·9%)
Tuesday	132 (17·0%)
Wednesday	115 (14·8%)
Thursday	111 (14·4%)
Friday	93 (12·0%)
Saturday	69 (8·9%)
	775 (100·0%)

Attendance rates by age and sex were computed from the age and sex distribution of the total practice (Table III). Pre-school children made greater demands in relation to their numbers in the practice than the other groups. The middle-aged and elderly made fewer demands relative to their numbers, and attendance rates in young pre-school boys was almost four times that in elderly men.

The practice is divided into five zones—central, north, south, east, and west. The central zone is the town in which the practice premises are situated, and the surrounding country-

TABLE III.—*Urgent Attendance Rates by Age and Sex*

Age Group	Males		Females	
	No. of Attendances	Attendance Rate/1,000	No. of Attendances	Attendance Rate/1,000
Pre-school (0–4 yrs) ..	91	208	68	153
School (5–14 yrs) ..	65	111	72	131
Young adults (15–44 yrs)	139	119	183	118
Middle-aged (45–64 yrs)	71	77	63	99
Elderly (65+ yrs) ..	12	53	11	48
Total	378		397	

---

* General Practitioners, Bicester, Oxfordshire.

side, containing a number of villages, is divided into quadrants. From our knowledge of the number of patients in each zone it was possible to compute attendance rates for each zone during the study (Table IV). We had anticipated that the patient's decision to attend surgery for urgent consultation might be influenced by the distance he lived from the surgery, but this did not appear to be generally true ; for example, in the north zone the female attendance rate exceeded that in all other zones.

Table IV.—*Attendance Rates for Urgent Treatment by Zone*

Zone	Males		Females	
	No. of Attendances	Attendance Rate/1,000	No. of Attendances	Attendance Rate/1,000
Central..	237	121	231	117
North	33	125	64	171
South	50	81	48	105
East	34	123	21	77
West	24	98	33	116
Total	378		397	

A classification of the cases in terms of diagnoses made is shown in Table V. During the study a distinction was made between upper respiratory tract infections ; cardiac and respiratory conditions ; conditions of the ear, nose, and throat ; and eye infections ; it was found, however, that the vast majority of these patients were suffering from acute infections of the upper respiratory tract. In Table V, therefore, all these conditions are grouped under "upper respiratory tract infection." Similarly, a distinction was made between trauma and skeletal conditions—for example, low back pain—but the distinction often proved difficult to make, and consequently all those in these two groups have been classified under the heading of trauma. About 65% of all patients attending for urgent treatment were suffering from upper respiratory tract infections or trauma, a fact which has important implications should a trained nurse be employed. With some experience and judgement it should be possible for her to treat, or at least temporarily reassure, a large proportion of the patients in this group.

Table V.—*Classification of Cases by Diagnosis*

	No. of Attendances
Upper respiratory tract infection, etc.	386 (49·8%)
Trauma	118 (15·2%)
Skin..	78 (10·1%)
Alimentary	74 (9·5%)
Genitourinary	40 (5·2%)
Psychiatric	28 (3·6%)
Obstetric	6 (0·8%)
Cerebrovascular/neurological	4 (0·5%)
Other	41 (5·3%)
	775 (100·0%)

An attempt was made during the study to determine why each patient had decided that treatment was required urgently. It seemed to us that the majority of patients could be placed in one of the following categories: (1) the patient was suffering from a condition which merited urgent treatment ; (2) the patient was suffering from a condition which could not be regarded as urgent, and his primary reason for attendance was to seek reassurance ; and (3) the patient was inconsiderate or frivolous.

We were aware that the placing of patients in one of these categories was arbitrary, and subject to observer variation. What may appear to an overworked doctor to be inconsiderate or frivolous behaviour on the part of a patient may not appear as such to the patient, or indeed to another doctor. In the same way a man of 55 with chest pain of sudden onset is suffering from a condition meriting urgent consultation, but at the same time he is also seeking reassurance. Despite the disadvantages, we felt that an attempt to explore, even superficially, the motivation for seeking urgent medical advice was justified, and the question was included in the study, with the proviso that any results should be treated with reserve (Table VI).

Table VI.—*Reason for Seeking Medical Advice in Total Number of Patients Attending for Urgent Treatment*

	No. of Attendances	
	Males	Females
Condition merited treatment urgently ..	145 (38·4%)	118 (29·7%)
Need for immediate reassurance	142 (37·6%)	174 (43·8%)
Patient was inconsiderate or frivolous ..	71 (18·8%)	90 (22·7%)
Other reasons	20 (5·2%)	15 (3·8%)
Total	378 (100·0%)	397 (100·0%)

During the study it became clear that a number of patients had made more than one demand for urgent treatment during the nine-week period, and this was confirmed when the results were analysed. Eighty-six patients (47 males and 39 females) were responsible for 190 items of urgent demand, constituting 24.5% of all urgent attendances. Our results also showed that 146 family units* created 362 items of urgent demand—that is, 47% of all urgent demand. To put it another way, the representatives of 146 families, composed of some 500 persons (approximately 7% of the total practice) were responsible for almost half of all the demands for urgent treatment during the survey period.

Discussion

Though the immediate aim of this study has been to examine the nature and extent of urgent demand for medical advice and treatment, the long-term objective is to organize our work in such a way that more time is spent where it is most needed. We hold the view that patients who present with an acute illness, whether trivial or serious, are already receiving a first-class service, but that our supervision of those suffering from chronic conditions is of indifferent quality. Our problem, therefore, is to maintain the standard of service given to the acutely ill, and at the same time, with our limited resources, to improve the standard of care given to those suffering from chronic disease.

In an attempt to achieve these long-term objectives we propose taking the following measures.

(1) There appears to be no reason why a trained nurse should not filter a large proportion of urgent demand cases. It has been shown that urgent demand constitutes 25% of surgery attendances, so that if a nurse could advise or treat even half of those patients a considerable saving of doctors' time would be effected.

(2) We propose identifying those patients who feel the need for repeated attendances at a doctor's surgery. Clearly, they need support, advice, and education in the use of the general-practitioner services. With the help of the district nurse, the health visitor, and, if possible, a medical social worker we hope to be able to do this and relieve some of the pressure on the general practitioner. We suggest that a full-scale medical and social investigation of these families would yield valuable information.

(3) During the past few months a chronic disease register has been compiled, consisting of those patients who require regular supervision. It is proposed that these patients should no longer be seen during surgery hours but at special clinics, when more time can be spent with each patient. This will also have the effect of reducing the numbers attending during regular surgery hours.

Summary

Our investigation into the nature and extent of urgent demand in a general practice during a nine-week period showed that 25% of surgery attendances were urgent, the heaviest demand being made early in the week. Attendance rates were

---

* A family unit was defined as a husband and/or wife and/or children living at the same address.

highest in young children. Two out of three patients were suffering from infection of the upper respiratory tract or trauma. It appeared that the distance the patient lived from the surgery played little part in his decision to seek medical advice urgently.

Eighty-six patients were responsible for about a quarter of all attendances, and 146 families for almost half of all urgent demands.

The measures proposed to be taken on the basis of these results are outlined.

We wish to record our thanks to Dr. E. D. Acheson, Director of the Oxford Record Linkage Study, for his helpful advice.

The practice described is associated with the Oxford Record Linkage Study, and one of us (J. A. F.) is in receipt of financial support from the funds allocated by the Nuffield Provincial Hospital Trust to that Study.

References

Acheson, E. D., and Forbes, J. A. (1967). To be published.
Backett, E. M., Heady, J. A., and Evans, J. C. G. (1954). *Brit. med. J.*, 1, 109.
Brotherston, J. H. F., Cartwright, Ann, Cowan, J. L. Baldwin, J. T., Douglas, E. C. K., and Steele, G. A. (1959). Ibid., 2, 1169.
College of General Practitioners (1962). *Studies on Medical and Population Subjects*, No. 14, p. 2. H.M.S.O., London.
—— (1965). *Report on Present State and Future Needs.* London.
Fry, J., and Dillane, J. B. (1964). *Lancet*, 2, 632.

HOSPITAL TOPICS

Neasden Memorandum on Resuscitation

On 16 May 1966 a memorandum on resuscitation after respiratory failure and cardiac arrest was issued by the physician superintendent of Neasden Hospital to all medical officers and senior nursing staff. This stated that

"The following patients are *not* to be resuscitated:

Very elderly, over 65 years.
Malignant disease.
Chronic chest disease.
Chronic renal disease.
Top of yellow treatment card to be marked N.T.B.R. (i.e., not to be resuscitated).

The following people *should* be resuscitated:

Collapse as a result of diagnostic or therapeutic procedure—e.g., needle in pleura (even if over 65 years).
Sudden unexpected collapse under 65 years—i.e., loss of consciousness, cessation of breathing, no carotid pulsation."

The existence of this memorandum was disclosed in the B.B.C. television programme *Tomorrow's World*, which was shown on 20 September. Subsequently it was discussed extensively both on television and in the national press.

Committee of Inquiry

On 22 September a statement was made by a committee set up by the North-west Metropolitan Regional Hospital Board to inquire into the circumstances in which the notice was issued. The members of this committee comprised Miss E. Richards, F.R.C.S. (vice-chairman of the board), Sir Charles Harington, F.R.S. (member of the board), assisted by Dr. F. J. Fowler and Mr. G. H. Weston, respectively senior administrative medical officer and secretary of the board. The statement reads as follows:

"In considering the problem it is important to differentiate between emergency action to combat collapse or a sudden worsening in the condition of the patient which may occur for a variety of possible reasons in the course of an illness and action to remedy 'cardiac arrest' which sometimes occurs in a patient whose life is already in grave jeopardy due to a serious and irreversible complaint but may occur in the course of an illness from which recovery is possible. It should be understood that a patient whose heart stops beating dies unless cardiac action can be started again within at most three minutes, and that the instructions issued were concerned with attempts which must be made within seconds to restore life before the condition becomes irreversible and the patient dies. Action to remedy cardiac arrest can only be appropriately taken in certain cases and each individual case must be a medical decision.

"The Board is assured that no patient who might have benefited by resuscitative treatment during the currency of the notice failed to receive it.

"On the authority of the Vice-chairman of the Board (in the absence of the Chairman abroad) the Board has accepted the report and is acting upon its recommendations. A copy has been sent to the Minister of Health, who has informed the Board that he also accepts the report.

"The findings of fact of members of the Committee of Enquiry are as follows:

"(1) That the idea of issuing instructions on the selection of patients for resuscitation arose from responsible discussion by medical staff in the Central Middlesex Hospital Management Committee Group and their decision that guidance to medical staff and in practice to nursing staff was necessary in the light of experience of wrong use of the resources available.

"(2) That it was also agreed that medical staff in clinical charge of patients should mark case papers of patients who should not be resuscitated.

"(3) That Dr. McMath, the physician superintendent, after seeing a film and hearing a talk on resuscitation given to the staff at Neasden Hospital, prepared the memorandum dated 16 May 1966 and circulated it within the hospital.

"(4) That the Hospital Management Committee and the administrative staff were not involved in the decision to issue such a memorandum, in the composition of the memorandum, nor in the means of disseminating it."

The conclusions of the members of the Committee of Enquiry based on consideration of the evidence they elicited are as follows:

"(*a*) That some guidance to medical staff on selection of patients is necessary to the proper use of resources and for the protection of some patients from distressing and unprofitable procedures.

"(*b*) That age is one of the factors on which the decision on an individual patient may properly be taken, but that any guidance given should in no way imply that a patient should be excluded from consideration for resuscitation merely by reason of age or diagnostic classification.

"(*c*) That the decision on each patient should be taken at the highest medical level available in the particular circumstances and should not be left to nursing staff.

"(*d*) That if it is found necessary to mark case papers to denote whether a patient is considered a suitable subject for resuscitation, the guidance relating to the interpretation of any marking symbol adopted should not be displayed but should be communicated in confidence to staff who need to be aware of it.

"(*e*) That guidance issued relating to the procedure to be adopted by nursing staff for summoning the resuscitation team in cases of cardiac arrest should be given separately from guidance given regarding interpretation of the marking system.

"(*f*) That although Dr. McMath's initiative in attempting to formulate guidance for medical staff on the selection of patients for resuscitation is in itself to be commended we regard the wording of the memorandum issued over his signature as particularly unfortunate and we greatly deplore its distribution in a way which rendered it liable to public view, in which position it remained unchallenged over a considerable period.

"(*g*) That we support the action taken by the Senior Administrative Medical Officer on

Friday, 15 September, following the withdrawal of all copies of the memorandum and agree that the advice which he gave should forthwith be confirmed in writing to all staff concerned at the hospital—namely,

> "'The conditions in which resuscitation measures for cardiac arrest should be applied are under review. Meanwhile, medical staff should know that they are to use their own judgement on individual cases to decide whether resuscitation is to be applied and they are not to be restricted merely by categories of age or diagnostic classification.'

"(*h*) That we welcome action already taken to obtain information as to any procedure adopted in other hospitals in the region.

"(*i*) That we wish to emphasize that in this Enquiry we find grounds for criticism only in relation to the instruction given concerning the application of resuscitation procedures to patients presumed to be suffering from cardiac arrest. These procedures involve mouth-to-mouth breathing, speedy removal of the patient from the bed to the floor, and external cardiac massage, which are initiated by the nursing staff or any doctor available and are continued with the addition of other special procedures by the resuscitation team when it can arrive.

"We are satisfied that although cardiac resuscitation by these special methods will not be appropriate for some patients every treatment appropriate to each patient is given in cases of sudden deterioration within the resources available."

Ministry Statement

On 23 September the Ministry of Health announced that its chief medical officer had written to the chairmen of group medical advisory committees and medical advisory committees of teaching hospitals. This letter stated that the Minister had taken professional advice on this subject as a matter of urgency. This advice was that no patient should be excluded from consideration for resuscitation by reason of age or diagnostic classification alone, and without regard to all individual circumstances. Any form of general instruction was wholly unacceptable. The letter added that, as all doctors concerned knew, only a very small number of patients in hospital were affected by cardiac arrest in circumstances in which it would be possible to take measures which could be effective in reversing the process and restarting the action of the heart. Continuing, the letter stated that the nature of the decision to be taken was no different in principle to that required in other grave circumstances, and a decision to operate on a patient or to refrain from intervention might often be of similar importance. In such a situation the decision to attempt resuscitation must be the decision of the responsible doctor in each individual case. While age was a factor which might properly be taken into account, it was only one of many factors involved, and these must include in any individual case both the nature of the underlying disease and the doctor's assessment of the likelihood that any attempt to resuscitate would be successful.

The letter concluded by pointing out that these views had been formulated in consultation with the Minister's consultant advisers in medicine and his adviser in cardiology.

CONFERENCES AND MEETINGS

Laboratory Screening Procedures

[FROM A SPECIAL CORRESPONDENT]

"Laboratory screening procedures and their clinical implications" was the title of a joint symposium held at the Middlesex Hospital Medical School between the Association of Clinical Pathologists and the Clinical Section of the Royal Society of Medicine on 23 September.

From the chair Professor Sir **MAX ROSENHEIM**, P.R.C.P. (London), asked whether the detection and treatment of all mild hypertensives would prevent cardiovascular complications in later life. This question at once exposed our ignorance of the natural history of disease, the importance of early diagnosis to the clinician, and the problems of manpower and cost of screening programmes. There was need for careful observation and clinical trial of such programmes before it could be decided whether they were worth while.

Professor L. G. **WHITBY** (Edinburgh) was concerned with the screening of well populations—that is, people who were asymptomatic. Much work had been done in the United States, and indeed a Congressional committee had spent three days considering the subject. The Kaiser Permanente Foundation in California had a screening centre operated on production-line principles, which took three hours to perform a multitude of investigations, both biochemical and clinical (including sigmoidoscopy on those over 40), annually on its subscribers at a cost of $30 (£10). The Varmland Health Screening Project was a multiphasic programme offered once only to all those over 25 in the province of Varmland, in Sweden. In the latter, 75% of those invited had taken part; 12% were found to have abnormalities—4% known to the doctor, 5% unsuspected findings of diagnostic value, and 3% abnormalities for which there was no apparent explanation on further investigation, such as proteinuria.

Professor Whitby himself had been concerned with an investigation in Edinburgh, in which 12 biochemical analyses were performed on samples from 1,080 patients attending two general practices. This had allowed the findings to be considered in relation to what the doctors already knew about the patients. The main findings were the detection of some diabetics, some raised blood-urea levels, and some unexplained serum-bilirubin values between 1.1 and 1.7 mg./100 ml. But what had become apparent was that there were difficulties in calibrating the analysers used, and in standardizing the tests with regard to collection and handling of the specimens, and the time of day, venous stasis, diet, posture, and drug intake of the patient. Finally, there was the need to compare the results with previous readings on the same patient. Sophisticated record storage, retrieval systems, and statistical analyses were all essential if full use was to be made of the data derived from well-population screening.

Hospital Studies

Dr. T. P. **WHITEHEAD** (Birmingham) was concerned with the investigations done on patients in hospital. A unit with 550 sq. ft. (49.5 sq. m.) of floor space had been built and equipped to carry out a screening programme of 16 biochemical determinations on about half the intake of inpatients to the Queen Elizabeth Hospital, Birmingham, at a cost of £15,000. The object of the survey was to see whether an initial battery of tests was of more value to the patient, or saved money by reducing bed-occupancy and transport of specimens, than tests done at the discretion of the doctors during the patient's stay in hospital.

A questionary had subsequently been sent to the clinician concerned asking in respect of each test whether it would have been requested—and, if abnormal, whether this would have been expected, whether it had led to a new diagnosis, or whether it had remained unexplained. Of 15,816 tests analysed, 1,203 had been abnormal, 114 had provided a new diagnosis, and 752 had remained unexplained. Data relating to bed-occupancy had not yet been evaluated. It was important, Dr. Whitehead concluded, to avoid seeking figures for figures' sake, and not to produce data on which no action would be taken.

In paediatrics much interest had been aroused by the possibility of screening for genetically determined metabolic disease, Dr. L. I. WOOLF (Oxford) said. Thirty States in the United States had made testing to exclude phenylketonuria a legal requirement. Nevertheless, not all patients with even serious enzyme defects showed clinical signs of disease. But screening to detect cases of phenylketonuria, galactosaemia, maple-syrup urine disease, histidinaemia, and alkaptonuria might be expected to prevent suffering and to save expensive institutional care.

Screening for Phenylketonuria

Valuable lessons were to be learnt from the history of screening for phenylketonuria. It had been thought that simple urine tests which could detect levels of phenylpyruvic acid in the urine above 5 mg./100 ml. were adequately sensitive. But now it was realized that more investigation must be undertaken to determine the rate of the rise in serum phenylalanine and its metabolites after birth, because, on the one hand, the time of testing might be too late for those whose levels had risen rapidly, and, on the other hand, too early for those whose levels were rising slowly. Probably the latter accounted for a substantial percentage of cases which were missed. Dr. Woolf said that now his laboratory employed a chromatographic technique, in which other tests could be done simultaneously, which cost £104 per 10,000 tests for materials. About one million children were born in Britain every year, and one should aim at testing 99% of them.

Mr. G. TEELING-SMITH (Office of Health Economics, London) pointed out that very uneven demands were made by the public on the health services: some resorted to their doctors on very minor indications, and others did not go until they were seriously ill. No method had been devised for telling people when to go or how to recognize the gradual onset or biochemical phase of insidious diseases clinically. It had therefore become necessary to examine people who were unaware of any illness. The factors affecting the cost of such screening were: the cost of doing the test; of contacting the people on whom the test was to be done; of following up those in whom the results were positive; and the frequency with which rescreening was necessary.

The benefits of screening were related to the seriousness of the diseases found; the prevalence of the disease in the community investigated; the sensitivity of the test (whether, for example, there were many false-positive results); whether the disease could be affected by earlier treatment; and whether the treatment itself was acceptable to the patients. In economic terms it would cost, for example, £1½m. to screen the population of Great Britain for diabetes; £300,000 annually to continue the programme; and £2½m. to treat the new cases found. The result would undoubtedly be to increase the cost of the Health Service, and this must be faced. Ultimately there might be a reduction in hospital bed costs, and it might reduce the unnecessary calls made on general practitioners. It would probably contribute little to the national economy because the earning capacity of those treated would be only slightly increased.

In Britain, Mr. Teeling-Smith continued, there was a very cautious attitude to screening programmes. It had been recognized that there was a great lack of knowledge of the natural history of many diseases. Were the patients with raised blood-sugar levels merely a physiological variation from the norm, or suffering from a temporary or a permanent abnormality? He believed that great progress would be made in such differentiation, that much information would come from comparing successive screening results in individuals, and that biomedical engineering would make great strides.

Choice of Tests

Professor HENRY MILLER (Newcastle upon Tyne) thought that laboratory screening should be for hospital patients and that tests should be dictated after a little sifting by the intelligence. In his opinion a lot of chaff was sifted for little grain. Twenty years ago such a discussion would have been unthinkable. A routine battery of tests would have been regarded as depreciating clinical method and grossly extravagant. It was a tribute to the advance in technology that Dr. Whitehead thought that an initial battery of tests would be less extravagant than the series of tests ordered during the inpatient stay on clinical grounds.

Professor Miller would have liked to extend his battery of tests a little beyond the routine now employed to save him from his crasser diagnostic errors. But it was very necessary to establish firmer criteria of normality and to define the scatter of tests used. For example, vitamin-B_{12} levels were far from well defined. Furthermore, computer analysis of screening results might reveal marginal changes in abnormal values of well-investigated diseases, which were not now taken into account for either diagnosis or treatment. This might confirm his belief that many neurological diseases were manifestations of generalized conditions. He concluded that the modern physician should seek help from all sources, and help from autoanalysers was no more humiliating than help from a stethoscope.

Types of Screening

In the discussion Professor W. M. DAVIDSON (London) said that one could not compare screening for tuberculosis with screening for biochemical errors. Professor J. G. SCADDING (London) added that screening to find tuberculosis not only allowed the affected person to be treated but also prevented him from giving the disease to others. In the case of cancer of the lung screening 100,000 people might save 2.5 extra five-year survivors annually. If, on the other hand, the money was spent on campaigns against smoking, in five years' time 25 people a year would not be developing cancer of the lung who otherwise would have done. A veterinary surgeon, who said that his profession was freer to use eugenic methods, asked those whose screening activities were encouraging the wider distribution of mutant genes what they told the owners of such genes to do about future procreative activities.

Other speakers from the floor pointed out that patients were more encouraged to go to screening clinics than to their own general practitioners, and that general practitioners could do annual examinations if they had adequate secretarial and nursing help. The finding of inexplicable abnormalities in a well population produced psychiatric difficulties which outweighed the value of the screening programme, said another speaker. Professor MILLER explained that we were not, unlike the veterinary surgeons, breeding for specific genes, although some genes could probably be wiped out quite easily—for example, those responsible for Huntington's chorea. Personally, he concluded, he did not go either to his general practitioner or to the screening clinic until he had something wrong with him; nor, he was prepared to bet, did the majority of the audience have an annual check-up, which did not cause but catered for hypochondriasis.

Correspondence

Letters to the Editor should not exceed 500 words.

Psychotropic Drugs

SIR,—Some comments on the latest Dunlop Committee's report on psychotropic drugs[1] seems desirable. The Committee is still somewhat lacking in clinicians working whole time at the bedside. Things can too often get out of clinical-treatment perspective when sitting in committee chairs. In psychiatry, for instance, we are getting rid of our administrative hospital medical superintendents only to replace them by administrative professor superintendents, sitting on from 20 to 40 committees apiece. This makes us worse off than ever before when something like the skilled clinical use of psychotropic drugs is under discussion.

Even if there had been 500 deaths instead of a mere 100 in the 43 million prescriptions for psychotropic drugs (around 1 in 500,000 prescriptions) it would still have been well worth while to use them as intensively as necessary. For we have to try to help not only the 30,000 people endeavouring to kill themselves each year but also the quarter to one-third of all patients coming to general practitioners and general consultants with neurotic illnesses. And, using these drugs in large amounts and in many varied combinations in the department of psychological medicine at St. Thomas's and elsewhere in recent years, we can confirm that disasters have been extremely rare. Most can generally be avoided by skilled handling.

Several patients, for instance, have now been on iproniazid for up to five years with none of Professor Sherlock's postulated deaths from liver damage.[2] Supposed "Largactil jaundice" has also almost disappeared despite the ever-increasing use of this drug, probably due to the present decline in cases of infectious hepatitis. The only suggested "Nardil jaundice" death was in a village where there were around 15 other cases of infectious hepatitis in the vicinity.[3] Will the Dunlop Committee now tell us how many cases of clinical jaundice and death were reported among the 43 million prescriptions for psychotropic drugs? They have suddenly become silent on this point. Was the whole thing only another medical professorial scare, as I have repeatedly suggested?

The monoamine oxidase inhibitor group of antidepressant drugs also continue to be safely combined with amitriptyline or trimipramine in large numbers of patients. Fainting may, however, occur with combined imipramine and phenelzine sulphate or isocarboxazid in some patients. None, however, seem anywhere near to dying with "convulsions and hyperpyrexia" unless they have taken an overdosage of one or both drugs; and complications are almost nonexistent when these drugs have been given in definite known amounts to patients under supervision in hospital. We have also given 400 courses of combined narcosis treatment involving the use of up to 1,000 mg. of chlorpromazine a day combined with both groups of antidepressant drugs and E.C.T.—again complications are minimal with skilled clinical handling. There has been one death recently from a cheese reaction—a real and dangerous complication—in a patient taking iproniazid. She continued, despite warnings, to tempt providence once too often by eating cheese, because she had done so several times before without deleterious effects.

About the recommendation that antidepressant drugs should not be used for psychosomatic conditions unless proved to be valuable in controlled clinical trials—how wrong this is. The M.R.C. has already made rather a fool of itself by testing out these drugs *solely* in patients with "Maudsley-Bedlam melancholia" (patients who were ill enough to stay in a mental hospital for months on end being "double blind-sampled"). Many people have been led to believe in consequence that because phenelzine sulphate had little effect on these very depressed and often mad people, which we all knew already, it is also without clinical effect in the sort of cases that constitute a quarter to a third of all patients coming to general physicians at St. Thomas's and elsewhere with psychosomatic disabilities. Here the monoamine oxidase inhibitor drugs, including phenelzine sulphate and isocarboxazid, have proved *clinically* to be some of the best drugs we have for helping psychosomatic states creating prolonged and intense misery and disability. Imipramine hydrochloride and amitriptyline often makes them just so much worse.

Despite these comments I remain aware that the Dunlop Committee is still a paragon of virtue compared with the American Food and Drug Administration, who now "order" doctors what to do rather than "advise" them. Clinicians should be deeply appreciative of the medical liberties we still enjoy in this country, owing to the good sense and restraint of Sir Derrick Dunlop and his colleagues. Suppose we could never do just the opposite to what they advise; how many more patients might kill themselves or remain ill for months or years on end as a result?—I am, etc.,

WILLIAM SARGANT.

Department of Psychological
Medicine,
St. Thomas's Hospital,
London S.E.1.

REFERENCES

[1] *Psychotropic Drugs*, Committee on Safety of Drugs, Adverse Reaction Series, No. 6, September 1967.

[2] Cook, G. C., and Sherlock, S., *Lancet*, 1965, 1, 175.

[3] *Brit. med. J.*, 1965, 2, 1494.

Alcohol and Driving

SIR,—On 9 October it becomes an offence to drive with a blood alcohol level greater than 80 mg./100 ml. This change in the law will come as a relief to many doctors.

Clinical examination of drivers suspected of driving while their ability to do so is impaired by alcohol or drugs is essential to exclude disease or injury, but as a means of testing driving ability it is crude.

Two drivers seen recently by us have been unequivocally normal on thorough examination, yet in each case a charge was brought on the basis of police evidence, and blood alcohol levels were 190 mg./100 ml. or more. Each of these cases was dismissed by a jury, the doctor's favourable examination clearly influencing them in their decision, in spite of his frank admission in court of the shortcomings of the clinical method. In two other comparable cases the drivers chose to be tried summarily and were convicted. This emphasizes the absurdities of the present law.

In future, therefore, we shall reserve the right in any of these cases to decline from passing an opinion, at the time of examination, on fitness to drive on the grounds that the laboratory tests are essential to forming such an opinion.—We are, etc.,

M. E. GLANVILL.
ANTHONY J. FERRIS.

Chard, Somerset.

Cardiac Resuscitation

SIR,—The recent adverse publicity concerning directives issued to the medical staff at Neasden Hospital will no doubt have disturbed many members of the medical profession. Although there may be some doubt about the wisdom of posting notices stating an arbitrary age limit for resuscitation, we feel that there is a good case for limiting this sophisticated procedure to those likely to benefit. There are great differences between hospitals in the National Health Service, both in equipment and in staff. These obviously will reflect the ability of any one hospital to indulge in resuscitation.

It is regrettable that the British Medical Association, which is believed by a large section of the public to represent the profession, conspicuously failed to point out these difficulties, and in particular failed to support the undoubted integrity of Dr. McMath, who has been made something of a scapegoat.—We are, etc.,

M. AMINOFF.
M. ASGHAR.
S. L. BEESTON.
K. D. BHOOLA.
J. A. CHILD.
K. C. CUNNINGHAM.
J. R. GARNHAM.
J. G. RAYMOND JONES.
A. F. KASENALLY.
P. A. KITCHENER.
D. W LITTLEJOHN.
D. LOTFI.
R. L. MACDONALD.
F. J. F. MADDEN.
S. A. MOUSSALLI.
B. MYLES.
D. J. NEWTON.
T. G. PICKERING.
T. PRICE.
R. S. RAWAL.
N. RHYS DAVIES.
M. D. RYAN.
J. SCHLICHT.
A. E. TATTERSFIELD.
A. TOMKINS.
A. TRISCOTT.

Central Middlesex Hospital,
London N.W.10.

Lithotomy Position for Forceps

SIR,—Dr. Margaret J. Watt (26 August, p. 559) is of course absolutely right in stressing the need to avoid Mendelson's syndrome, this potentially fatal complication of obstetric anaesthesia.

In all four of the triennial reports on confidential inquiries into maternal deaths since 1952[1] it is stated with almost monotonous regularity that the commonest cause of death in forceps delivery under general anaesthesia is inhalation of stomach contents. In the third report (1958–61) there are two statements of the utmost significance which sum up the matter:

> (1) "The only safe assumption in any parturient woman is that the stomach is full," and (2) "The lithotomy position with full flexion of the lower limbs is more likely to favour regurgitation than any other posture."

Until some time between 1920 and 1930 the lateral position was used almost exclusively in Britain—indeed, in Australia it was spoken of as "the English position." In those days, though vomiting of course often occurred, inhalation of stomach contents did not, and I have several times been at pains to indict the adoption of the lithotomy position by obstetricians as the cause of this grave and (when it occurs) often fatal complication of labour.[2, 3] I am not of course arguing in any way against regional analgesia in forceps delivery, but if general anaesthesia is employed, as it still is not infrequently, the use of the lithotomy position is just asking for trouble.

The responsibility for these disasters must lie with the obstetricians as long as they continue to use and teach a method of delivery so fraught with danger to the patient. It should be a sobering thought to them that the deaths in forceps delivery under general anaesthesia could certainly be halved by the simple application of common sense and the observance of the simplest law of physics.

As Dr. Watt points out, there is no method of treatment for Mendelson's syndrome which can guarantee 100% safety, but the simplest of preventive methods will ensure a complete freedom from risk never to be attained by any method of treatment of the established condition.—I am, etc.,

London N.W.7. **A. H. MORLEY.**

REFERENCES

[1] *Report on Confidential Enquiries into Maternal Deaths in England and Wales*, 1952-55, 1955-58, 1958-61, and 1961-63, H.M.S.O.

[2] Morley, A. H., *Brit. med. J.*, 1955, **2**, 1351.

[3] Morley, A. H., *London Hospital Gazette*, 1964, **67**, 70.

Safer Dental Anaesthesia

SIR,—Unlike Dr. J. G. Bourne (2 September, p. 616), I do not attribute primary importance to the upright position as the main cause of dental anaesthetic mortality. The upright position was, and is, a common feature in operations on the posterior cranial fossa, anaesthesia for which over several hours must be followed by rapid recovery of consciousness, a desideratum which every neurosurgical anaesthetist is familiar with and competent to provide. Moreover, the dental anaesthetic mortality rate fell substantially while the upright position for induction of anaesthesia was still in general use, as it is indeed to this day, and rightly. This decline in mortality was due to various factors—gradual abandonment of deliberate hypoxia, better drugs, better selection of cases for referral to hospital, increased participation in dental anaesthesia by specialist anaesthetists, and latterly increased avoidance of accidental hypoxia by means of tracheal intubation in the dental surgery.[1] Adequate observation of the patient is indeed an important advantage of intubation which hardly exists without it, for in the latter case the anaesthetist is tethered to the support of the patient's jaw and extremely limited as to what he can observe and do.

Interference with the airway, with or without deliberate hypoxia, is a far commoner primary cause of dental anaesthetic difficulties which may lead to death than depression of the cerebral circulation from the upright position alone. In over 6,000 dental anaesthetics I have seen only one patient develop hypotension from the upright position. The semi-recumbent position, however, which is all that some modern dental chairs will permit at their most upright, must surely be condemned by Dr. Bourne as well as myself, for neither in his view nor in mine can it be considered safe for dental anaesthesia.

In my view, differing again from Dr. Bourne, the security and integrity of the airway of the anaesthetized patient are too important to be left to the divided attention of the dental surgeon who is performing the operation; too important to be left to his unqualified assistant; and in other than short cases too important to be left dependent on the reliability of the aspirator and the dental pack. These makeshifts are employed because the non-specialist cannot intubate the trachea even in emergency let alone in cases of above average duration. No matter how skilfully these makeshifts are applied, they cannot compare in safety or reliability with skilled tracheal intubation.

There is a strong case for insisting that those who administer dental anaesthetics should be trained at least to the level of competence in tracheal intubation, which implies considerably more knowledge of basic sciences and clinical anaesthesia and greater and wider experience than is at present the case.—I am, etc.,

Manchester. **ARNOLD M. DANZIGER.**

REFERENCE

[1] Danziger, A. M., *Brit. dent. J.*, 1962, **113**, 426.

Phenylketonuria: A Reassessment of Screening by Napkin Test

SIR,—Drs. J. B. P. Stephenson and M. S. McBean (2 September, p. 582) rightly draw attention to the unreliability of Phenistix testing. They refer to my contributions to Lyman's book on phenylketonuria,[1] but our knowledge of inborn errors of metabolism in general, and of phenylketonuria in particular, is advancing so rapidly that much of this book must now be considered out of date. I wrote my sections on testing and detection in 1961, when Phenistix and similar tests, using ferric salts, were the only screening techniques in use or at the time possible; later Guthrie[3] published his method, and a paragraph on it was added before the book was printed.

In 1963 I began to come across tragic cases of phenylketonuria undetected by Phenistix testing in the neonatal period.[2] It seemed that "field" tests such as Phenistix would have to be replaced by methods where a specimen of blood or urine is sent to a central laboratory for testing by more sophisticated techniques. Choice of a suitable technique poses problems in basic science, technology, economics, administration, and relations between mother and doctor, health visitor, midwife, or nurse. To ignore any of these aspects is to court disaster. Eight different laboratory techniques are currently in use: the Guthrie method using blood[3]; urine chromatography for *o*-hydroxyphenylacetic acid[2]; spectrophotofluorometry of blood[4, 4a]; the Guthrie method using urine[8]; and chromatography of amino-acids in blood by the methods of Berry,[5] Efron,[6] Scriver,[7] or Mellon.[8] All these methods except spectrophotofluorometry have the great advantage that they test for other inborn errors of metabolism as well as phenylketonuria. Two methods, the Guthrie method using blood[3, 9] and chromatography of urine,[2] have now been used long enough and on a large enough scale for us to say that they meet the criteria of a suitable test. Thanks to the co-operation of the medical officers of health of Buckinghamshire, Cardiff, Oxford, and Oxfordshire, about 25,000 newborn infants have had their urine examined here using chromatography. The advantage of this method is that the mother herself can collect a specimen of her baby's urine on filter-paper and post it.[2]

Dr. Stephenson and Dr. McBean may have been unfortunate in their small sample which gave a failure rate for Phenistix of at least 73%. Data collected from all over Great Britain suggests a lower failure rate, but even if only 10% of phenylketonurics go undetected by use of Phenistix this test should be regarded as unsatisfactory now that we have better ones.—I am, etc.,

Department of the Regius
Professor of Medicine,
Radcliffe Infirmary,
Oxford.

L. I. WOOLF.

REFERENCES

[1] Lyman, F. L., (Ed.), *Phenylketonuria*, 1963. Springfield, Illinois.

[2] Woolf, L. I., in *Proceedings of the Washington Conference on Phenylketonuria*, 1966, ed. K. F. Swaiman and J. A. Anderson. Washington, D. C., in press.

[3] Guthrie, R., and Susi, A., *Pediatrics*, 1963, **32**, 338.

[4] Hill J. B., Summer, G. K., Pender, M. W., and Roszel, N. O., *Clin. Chem.*, 1965, **11**, 541.

[4a] Searle, B., Mijuskovic, M. B., Widelock, D., and Davidow, B., ibid., 1967, **13**, 621.

[5] Berry, H. K., *Amer. J. ment. Defic.*, 1962, **66**, 555.

[6] Efron, M. L., Young, D., Moser, H. W., and MacCready, R. A., *New Engl. J. Med.*, 1964, **270**, 1378.

[7] Scriver, C. R., Davies, E., and Cullen, A. M., *Lancet*, 1964, **2**, 230.

[8] Mellon, J. P., and Stiven, A. G., *J. med. Lab. Tech.*, 1966, **23**, 204.

[9] Guthrie, R., in *Proceedings of the Washington Conference on Phenylketonuria*, 1966, ed. K. F. Swaiman and J. A. Anderson, Washington, D.C., in press.

Respiratory Distress Syndrome

SIR,—We read with interest the paper by Dr. J. M. Abraham and Dr. R. J. K. Brown (9 September, p. 640) comparing the effects of intragastric and intravenous glucose and sodium bicarbonate in the respiratory distress syndrome, and your leading article (9 September, p. 628) on management of the respiratory distress syndrome. We feel that the cases of Abraham and Brown are not truly comparable with those of Hutchison *et al.*,[1] as only 26 cases had positive radiological findings. Forty-three cases were not *x*-rayed, and 10 had negative radiological findings. In contrast with this, Hutchinson's cases all had positive radiological findings.

We have studied 415 infants with respiratory distress since August 1963. Of these, 24 had rarer causes of respiratory distress such as diaphragmatic hernia and pneumothorax, 18 died from other causes, and 59 were not *x*-rayed. Of the remaining 314 cases 150 had radiographs which were normal or showed only localized areas of atelectasis, and the mortality in these cases was only 2%, the three deaths all being in infants of less than 28 weeks' gestation. The good prognosis in these cases shows the necessity of excluding them from studies of the effects on mortality of different methods of treatment.

In your leading article, in discussing treatment of the respiratory distress syndrome with alkalis, you say that "further studies are required to determine the precise effects of these substances and the best way of giving them." We have carried out a study of the effects of intragastric sodium bicarbonate in the respiratory distress syndrome and our findings are to be published.[2] We found a mortality of 58% in 31 cases given intragastric sodium bicarbonate, and 39% in 69 cases given early milk feeds. These mortality figures are higher than those reported by Abraham and Brown, but refer only to cases with positive radiological findings, and are therefore more strictly comparable with the mortality figures quoted by Hutchison *et al*.

We would agree with the view expressed in your leading article that measures directed towards the relief of hypoxia have more effect in lowering mortality in the respiratory distress syndrome than correction of metabolic acidosis alone.—We are, etc.,

MARGARET E. R. STONEMAN.
ROSALIND M. OWENS.

Paediatric Research Unit
and Special Care Baby Unit,
Exeter City Hospital,
Exeter, Devon.

REFERENCES

[1] Hutchison, J. H., *et al.*, *Lancet*, 1962, 2, 465.
[2] Stoneman, M. E. R., and Owens, R. M., *Arch. Dis. Child.*, in press.

SIR,—I was interested to read Dr. J. M. Abraham's and Dr. R. J. K. Brown's article (9 September, p. 640) dealing with bicarbonate administration in the respiratory distress syndrome.

I have two comments to make regarding the treatment of respiratory distress syndrome from my own experience in the special care nursery, Royal Victoria Hospital, Belfast, over the past two or three years. In my experience oral sodium bicarbonate 8.4% may worsen and increase the difficulties in respiration in the very small premature baby, as it causes marked gastric distension with consequent embarrassment of chest expansion, making the infant's labours even more difficult, and for this reason I have not used this method.

Secondly, I have found that the umbilical vein is simple to use and is the least traumatic method for administering intravenous fluids to the small infant, and from my own experience phlebothrombosis has occurred only once during many dozens of catheterizations. Using this route for intravenous fluids the infant is not subjected to repeated trauma of scalp vein infusions that may counteract any good effect obtained from the possible correction of the metabolic acidosis with the bicarbonate. Therefore I feel that this factor may account for the increased mortality in Dr. Abraham's and Dr. Brown's group given intravenous scalp vein fluids.—I am, etc.,

Belfast City Hospital,
Belfast 9.
MARK REID.

Problem of Unused Drugs

SIR,—I was interested to read the article "Collection of Unwanted Drugs from Private Homes" by Dr. W. A. Nicholson (16 September, p. 730). It is extremely difficult for each individual practitioner to gain any control over this mounting problem. However, I think it is worth mentioning an extremely simple technique which gives the doctor a small measure of control in some cases and which I am surprised is not used by many of my colleagues. Quite simply, each patient is asked to bring his supply of medicines with him to each consultation. A great number of patients are willing to co-operate in this way and the prescriber is thus enabled to determine the number of doses required until the next visit.

Using this method, it is surprising how often one meets the patient who says he is taking his tablets regularly but who in fact brings stock bottles which indicate the contrary. This discrepancy can be used as a valuable discussion point about the role which the medicaments are playing in the patient's life and the treatment of his illness. In addition, when he sees all the medicines together, the doctor is reminded of the complex regimen he sometimes asks a patient to undertake and can adjust his prescribing habits accordingly.

I realize that a determined saver of tablets for suicidal purposes will not be influenced by such a system, but I think that quite a number of patients can be spared the risk of having large quantities of dangerous chemicals in their households.—I am, etc.,

Institute of Psychiatry,
London S.E.5.
J. C. GUNN.

SIR,—Being involved as a medical officer of health member of a home safety committee which is currently considering a scheme for the recovery of unwanted drugs, I was particularly interested in the paper by Dr. W. A. Nicholson (16 September, p. 730) on the Hartlepool scheme for this service. However, one aspect which is causing my home safety committee much thought is the method of disposal of the drugs once they are collected. They would normally be brought in to pharmacists, who in turn would be required to devise their own means of disposal or to organize central disposal such as at a hospital. It is generally agreed that neither the refuse collection service nor the public sewers ought to be used. Incineration, either by the pharmacists or by a hospital, could involve some danger.

Would Dr. Nicholson or Dr. Milligan, the medical officer of health, please indicate in your correspondence columns what method of ultimate disposal is used in Hartlepool? This information may be of value to others besides my own committee.—I am, etc.,

Office of the Medical
Officer of Health,
South Wilts County Districts,
Salisbury, Wilts.
JOHN LISHMAN.

Penicillin Encephalopathy

SIR,—Your leading article on this subject (12 August, p. 384) contains the following statement. "And if, as it seems, penicillin G is particularly apt to produce such an encephalopathy, other antibiotics might be considered as first choice in treatment." Since the patients to whom your article refers were all in a state of renal failure, and since the dosage of penicillin G exceeded 25 million units per day, I would like to know what antibiotics you have in mind that can be given more safely, in comparable doses, to uraemic patients The semi-synthetic penicillin and the cephalosporins are not usually less toxic than penicillin G, while most other antibiotics are highly toxic or lethal in such subjects in much lower doses.

The doses mentioned (25–40 million units daily) correspond to amounts of 14 g. per day or more of penicillin G intravenously. At this level plasma concentrations reach 50 mg./100 ml. even in normal subjects, and are much higher in patients with bilateral nephrectomy, azotaemia, and other conditions referred to in the article. The remarkable fact is not that penicillin G causes temporary encephalopathy, but that it can be given at all to such patients in such dosage.

Penicillin G and its simpler semi-synthetic derivatives are among the least toxic of all drugs, being well-tolerated by mammalian tissues in concentrations far exceeding those of many physiological substances. There is evidence,[1] however, that penicillins in solution can polymerize as well as degrade, and it seems possible that some untoward effect might be attributable to these changes, which are minimized if solutions of the purified drugs for injection are used fresh, well within the stated date of expiry.—I am, etc.,

G. T. STEWART.

School of Public Health,
University of North Carolina,
U.S.A.

REFERENCE

[1] Stewart, G. T., *Lancet*, 1967, 1, 1177.

Visual Hallucinations in Cranial Arteritis

SIR,—With reference to the communication of Mr. C. T. Hart (9 September, p. 643) it may be of interest that in my own personal series of some 67 cases of giant-celled arteritis of the aged (which name, despite opposition, I still consider preferable) there have been three in whom formed visual hallucinations were a prominent symptom, and it would seem that this symptom may not be a particularly uncommon characteristic of what is fundamentally an extremely pleomorphic condition.

None of these patients developed signs related to the external visual apparatus, possibly owing to the institution of early treatment. One in particular was most striking, being an 85-year-old retired headmistress in a very good state of mental preservation who was extremely distressed by the continuous appearance of men's faces. These faces were not of people personally known to her but of famous historical figures such as Darwin, Browning, and Thomas Arnold. In yet another case the figure of a rabbit was constantly present. There seems little doubt that these phenomena do arise from an irritative involvement by the arterial process of appropriate cortical areas.

A perhaps significant comment on this particular symptom is that I am aware of at least one case of my own and two others reported by colleagues where the condition occurred in inmates of a mental institution, and the symptomatology had been related to their mental condition rather than to this disease. The importance of this in relation to the prevention of the blindness which may supervene in a third of these cases need not be elaborated.

I would like to question the validity of the very common use of the word "euphoria" in relation to the attitude of these patients to their condition. It would seem to me that this is not really an accurate description of the total unconcern which so many of them display, and one has been seriously tempted to wonder whether this quite remarkable lack of concern may not be explained, in a teleological sense, as a desirable outcome of what at least a considerable number of people would regard as a stress disease *par excellence*.

The importance of this latter feature in relation to the problem of the diagnosis of this condition is well outlined by a patient of my colleague Mr. D. St. Clair Roberts. This was an old lady, who, although patently suffering from giant-celled arteritis of the aged, steadfastly refused to admit to having any pain until the day following commencement of treatment with systemic steroids, when her gratitude at having been relieved of an excruciating headache knew no bounds.—I am, etc.,

Sussex Eye Hospital,
Brighton, Sussex.

M. J. GILKES.

Prophylaxis in Haemophilic Arthropathy

SIR,—Prophylaxis with bank plasma in Christmas disease has not been generally used, and, as severe haemophilic arthropathy is a crippling disease, the favourable results achieved with five years' such treatment are worth reporting.

A 40-year-old male has been a known "bleeder" since childhood and a semi-invalid from the age of 16 years. When well his general physical fitness helped to prevent haemarthroses, but a period of recumbency tended to produce a vicious circle, because muscular flabbiness would lead to more easy recurrence of haemarthrosis as soon as he was ambulant again. General examination was normal except for deformity of the joints, especially the ankles. Christmas disease was diagnosed.

In 1962 it was decided to start him on long-term prophylaxis with bank plasma, and he has received a standard infusion of 2 units (500 ml.) weekly. This has been increased to 3 units (750 ml.) or occasionally 4 units (1,000 ml.) on those occasions when a breakthrough haemarthrosis developed. Altogether there have been eight occasions during the five years when slight to moderate haemarthrosis developed. This usually happened on the sixth or seventh post-infusion day, though on one occasion it occurred on the first postinfusion day. Each time it responded rapidly to an infusion of bank plasma.

He has had urticaria several times which responded satisfactorily to oral promethazine. After three years of treatment (and 80 litres of plasma) he developed acute hepatitis—assumed to be homologous serum jaundice—from which he made an uneventful recovery. This risk is not inconsiderable but is one most patients would accept for the chance to escape the painful round of haemarthrosis and immobility.

Factor IX assays are consistently 0% on the seventh postinfusion day, and he has an average rise of 5% of Factor IX after an infusion of 500 ml. of bank plasma. The half-life of Factor IX is taken to be 24 hours.[1] Assuming an initial concentration of Factor IX of 5%, he should have no more than 0.04% remaining after seven days, and it is remarkable that so little should protect him from further bleeding. Biggs and Macfarlane state that "trivial haemorrhage in Christmas disease may be prevented by as little as 1% of Factor IX," and they refer to one patient whose whole blood-clotting time was still very much shortened three weeks after receiving two litres of plasma.

A recent assay for inhibitors of Factor IX was negative. The danger of inhibitor production seems to be slight in Christmas disease, and a search of the literature has produced reports of only 13 cases.[2-4] Christmas disease is therefore more suitable than classical haemophilia for prophylaxis because of the longer half-life and the more potent effect of low concentrations of the factor, as well as because of the low likelihood of the formation of inhibitors.[1]

At least in this patient bank plasma has proved satisfactory. This plasma is deep-frozen at −18° C. at Groote Schuur Hospital. The average age of a unit was six weeks, with extremes of three weeks to three months. Geratz and Graham[5] have shown that almost normal quantities of Factor IX are present in plasma after six months at this temperature. There has been only one occasion following about 250 infusions when there was evidently insufficient Factor IX in the plasma used, as the patient developed a haemarthrosis on the following day.

This patient has progressed to a nearly normal existence, and the favourable results in his case suggest that the treatment deserves a wider trial.

I would like to thank Dr. R. Sougin-Mibashan for help in the preparation of this paper, and the Medical Superintendent, Groote Schuur Hospital, for permission to publish.

—I am, etc.,

Department of Medicine,
Groote Schuur Hospital,
South Africa.

J. B. KING.

REFERENCES

[1] Biggs, R., and Macfarlane, R. G., *The Treatment of Haemophilia and Other Coagulation Disorders*, 1966, Oxford.
[2] Margolius, A., Jackson, D. P., and Ratnoff, O. D., *Medicine*, 1961, 40, 145.
[3] Roberts, H. R., Gross, G. P., Webster, W. P., Dejanov, I. I., and Penick, G. D., *Amer. J. med. Sci.*, 1966, **251**, 43.
[4] Hardisty, R. M., *Thrombos. Diathes. Haemarrh.*, 1962, 8, 67.
[5] Geratz, J. D., and Graham, J. B., ibid., 1960.

Early Discharge of Maternity Patients

SIR,—The leading article and papers on early discharge of maternity patients (26 August, pp. 508, 517, 520), also the letter by Dr. S. E. Browne (16 September, p. 739) contain no reference to reduction of perinatal mortality that can result from practising early discharge.

More beds being made available, a "noticeable fall in perinatal mortality" resulted from admitting more antenatal cases[1] and by increasing the number of hospital confinements.[2]—I am, etc.,

Mayday Hospital,
Thornton Heath.

ARTHUR CLIFT.

REFERENCES

[1] Theobald, G. W., *Brit. med. J.*, 1959, 2, 1364.
[2] Baird, D., *Lancet*, 1960, 2, 557.

Thrombosis and the "Pill"

SIR,—I was interested to see that the reliability of the Medical Research Council report had come under scrutiny (19 August, p. 493), for, as you know, I have doubted any specific chemical connexion between the pill and blood agglutination ever since the suggestion was first mooted.[1]

As one who spends his entire working day dealing with varicose veins, phlebitis, and deep-vein thrombosis, it does seem to me that one vital piece of information was omitted from the Medical Research Council statistics —namely, did the women on the "pill" who suffered lower limb venous sequelae also have prior varicose veins? As I understand the report, the first study, organized by the Royal College of General Practitioners, compared non-pregnant women of child bearing age who were not taking the "pill" with equivalent women who were taking the "pill" and with women of the same age group who were either pregnant or puerperal, reaching the conclusion that the second and third groups were respectively three and six times more likely to develop phlebitis than their non-pregnant non-"pill"-taking counterparts.

Now it is common knowledge that pregnant women with varicose veins are far more likely to develop pre- or post-gestational phlebitis than those without. It is also known that the commonest cause of phlebitis in men or women at any age is varicose veins. Surely, therefore, the determination of the presence or absence of varices should have been a vital and significant part of the investigation of all three groups, particularly those taking the "pill."

Assuming for the moment, however, that had this information been available it would have demonstrated that the presence of varicose veins was almost a *sine qua non* in those of any group who developed phlebitis, how are we to explain the small but significant increase among those taking the pill? Here again we need look no further than our everyday knowledge of the onset of phlebitis in persons with varicose veins —namely, that the commonest precipitating cause is a diminution in ambulation. We all know the classical example of the active woman whose large varicose veins give her no trouble at all until she retires to bed with influenza or a "disc" and is smitten with phlebitis five days later. But it does not need complete immobilization to lead to phlebitis. Any significant diminution in ambulation can reduce calf-muscle pump action enough to dam back venous return in varicose veins and produce clotting. And for evidence that this can happen we need look no further than your most recent leading article "Which Pill?" (9 September, p. 627), in which you, Sir, state quite categorically that the oestrogenically loaded pill "will produce symptoms such as . . . oedema, tiredness, troublesome varicose veins. . . ."

Summing up, therefore, I would suggest that the connexion between the "pill" and phlebitis, such as it is, is a purely mechanical one, and that the re-examination of the statistical material will show that the women on the "pill" who develop phlebitis are those who have varicose veins and are taking a "pill" with too high an oestrogen content.—I am, etc.,

London N.W.1. STANLEY RIVLIN.

REFERENCE

[1] Rivlin, S., *Brit. med. J.*, 1962, **2**, 547.

SIR,—We would like to record a case of phlebothrombosis and pulmonary embolism occurring in a patient taking an oral contraceptive.

A lady of 30 years was admitted as an emergency to this hospital with a sudden history of shortness of breath for five days. Two days prior to this she had noticed swelling of the ankles, the right side more than the left. She has been on Lyndiol 2.5 (lynoestrenol 2.5 mg. and mestranol 0.075 mg.) over the last nine months and during this period she had put on 28 lb. (13 kg.) in weight. At the time of admission she had definite signs of phlebothrombosis of the right leg, and, although there were no clinical signs on examination of her chest, a chest *x*-ray showed an opacity in the right lower zone with elevation of the right diaphragm and slight prominence of the right pulmonary artery compatible with the diagnosis of pulmonary embolism. An E.C.G. provided contributory evidence, showing an S in lead 1 and a Q with inverted T in lead 3. There was no evidence of any infection, and her Hb, E.S.R., W.B.C., and differential counts were normal. Her S.G.O.T. and S.H.B.D. were normal and the liver-function tests were normal except for a raised S.G.P.T. of 66 units/ml. (normal in our laboratory 4–38 units/ml.). She was treated with anticoagulants and with this the signs of phlebothrombosis cleared up completely and a subsequent chest *x*-ray was within normal limits.

Although a number of cases have been reported of a similar nature in patients on oral contraceptives, this case raises an interesting point because of the great increase in weight starting when the patient was put on oral contraceptives. We are wondering whether this increase in weight played a contributory part in the development of the phlebothrombosis and subsequent pulmonary embolism.

This case also shows slightly abnormal liver-function tests. Similar instances of raised serum enzymes were reported by Stoll *et al.*[1] in menopausal women on Lyndiol even without any frank jaundice. Thulin and Nermark[2] mention a report of abnormal liver-function tests in young women on oral contraceptives, but mostly with only slightly increased value. It is possible that raised S.G.P.T. could be due to Lyndiol.

This case has been reported to the Dunlop Committee.—We are, etc.,

P. GHOSH.
B. A. GWYNNE JENKINS.
F. MANJOORAN.

Tehidy Chest Hospital,
Camborne, Cornwall.

REFERENCES

[1] Stoll, B. A., Andrews, J. T., Motteram, R., and Upfill, J., *Brit. med.*, 1965, **1**, 723.

[2] Thulin, K. E., and Nermark, J., ibid., 1966, **1**, 584.

Human Infection with Porcine Ascaris

SIR,—A male child aged 14 months developed diarrhoea, with green stools during the third and fourth days of the illness, and on the sixth day passed a worm $4\frac{1}{2}$ in. (11 cm.) long, which was identified as an immature female *Ascaris*. The child was treated with a single dose of 7.5 g. Pripsen (piperazine phosphate, *B.P.*, and standardized senna, Westminster Laboratories Ltd.) the same evening, and during the night passed a further eight worms, all of which were identified as immature *Ascaris*. The worms ranged in size from $3\frac{1}{2}$ in. to $5\frac{3}{4}$ in. (9–15 cm.), and all but two were females. The Pripsen treatment was repeated three weeks later, and again nine weeks later, but no more worms were passed.

The child had never been away from his home in the Brentwood area, and had been confined exclusively to the house and garden. During the early spring, pig manure, purchased in bulk from a local supplier, had been spread on the garden. Several weeks later, about six weeks before the worms were passed, the child had been seen in the garden with a small piece of the manure in his mouth. Subsequent microscopic examination of a sample of manure from the same site revealed the presence of fully embryonated *Ascaris* eggs. Some of these eggs were given orally to albino mice. Immature *Ascaris* were found in the livers of each of the mice several days later, which confirmed that the eggs were infective.

It is concluded that there is strong circumstantial evidence that the child became infected by ingesting *Ascaris* eggs from the pig manure. Unfortunately the unequivocal differentiation of human and porcine *Ascaris* species on morphological grounds is very difficult, if not impossible, especially in the case of immature worms. Cameron[1] considered that infection of man with *Ascaris* of porcine origin was undoubtedly possible, and that a study of this problem was far from academic. He also suggested that in an unusual host *Ascaris* larvae might have a greater pathogenicity than in the normal host.

Since *Ascaris suum* Goeze, 1782, is still a common infection in pigs, it is suggested that the use of pig manure in gardens is a potential health hazard, especially to young children.—We are, etc.,

R. F. PHILLIPSON.

Research Laboratories,
May & Baker Ltd.,
Dagenham, Essex.

J. W. RACE.

Brentwood,
Essex.

REFERENCE

[1] Cameron, T. W. M., *Amer. J. med. Sci.*, 1962, **243**, 354.

Chromosomes in Hodgkin's Disease

SIR,—In our paper "Lymphocyte Transformation and Chromosome Studies in Hodgkin's Disease" (16 September, p. 704) we drew attention to the exaggeration of the secondary constrictions in C9 chromosomes observed in some peripheral blood lymphocyte cultures in our patients. Since the paper was submitted it has come to our notice that Nusbacher *et al.*[1] have observed, in addition to a high percentage of chromosome breakage, attenuation of secondary constrictions in cultures of lymphocytes from 1-year-old children with congenital rubella. There is thus evidence that in-vivo viral infection is one of the factors affecting the appearance of secondary constrictions in cultured cells. Nusbacher *et al.* also observed end-to-end association of chromosomes, which was another occasional feature of the metaphase plates of patients in our series. Thus it is possible that the peculiarity of the chromosomes which we observed in Hodgkin's disease could be due to the presence of viral infection in some of the patients.—We are, etc.,

SYLVIA D. LAWLER.
C. R. PENTYCROSS.
B. R. REEVES.

Royal Marsden Hospital
and the Institute of Cancer
Research,
London S.W.3.

REFERENCE

[1] Nusbacher, J., Hirschhorn, K., and Cooper, L. Z., *New Engl. J. Med.*, 1967, **276**, 1409.

Medicine in Burma

SIR,—Lest misunderstanding should arise from Sir George McRobert's admirable letter concerning Burma (9 September, p. 677), I wish to emphasize that in my article I wrote that the Burmese decided "to leave the Commonwealth, and, as a corollary to this, to render themselves ineligible for aid extended to Commonwealth countries." I neither stated nor implied that they rendered themselves ineligible for aid extended to non-Commonwealth countries. Such aid has in fact been small in comparison with that given to Commonwealth countries. Thus, for example, the latest figures available from the statistical department of the Ministry of Overseas Development show that to the following countries total technical aid from Government sources given during 1965–6 amounts to:

Nigeria	£3,069,200
Uganda	£5,203,400
Tanzania	£4,383,400
Kenya	£7,453,200
Burma	£ 250,300

The three East African countries have populations very much smaller than Burma; the populations of Nigeria and Burma are roughly comparable in size; all have received aid 12 to 30 times greater than Burma over this period.

I tried particularly to bring out the point that with limited aid Burma had done much. Figures of this kind emphasize the achievement and the admiration due to them, an achievement which when aid is considered on a per caput basis appears even more spectacular.—I am, etc.,

A. W. WOODRUFF.

London School of
Hygiene and Tropical Medicine,
London W.C.1.

Anxiety State after "Sex Education"

SIR,—A 10-year-old boy known to me for most of his life returned home from his excellent boarding-school, which he would not give up for the best garden railway in the world. The relaxation of his own territory uncovered a distressing condition of general malaise, irritability, nightmares, fears of oncoming traffic, worry about smells, the compulsion to make sexual innuendos, and the awkward behaviour of the very guilty, all pointing to this boy's having been assaulted sexually by an older person probably in authority. Subtle examination—and I have examined children and delinquents since 1941—revealed that no actual assault had taken place, only what this deep-feeling child had interpreted as an assault. He had been submitted, along with his classmates, to a course of instruction from his well-intentioned headmaster on body mechanics, including copulation, "fully illustrated in colour."

This child has always been quick to see the reality behind the symbol and the meaning underlying everything. So now, alerted to the magnitude of the sex act, he found, as it were, that he was armed with a seemingly automatic weapon the control of which was beyond him but for which he would be held responsible. Intercourse with his one permanent and reliable authority (his mother; he has no father) he found impossible, for that act and word had now a sexual connotation. And he found himself party to a sexual experience that was illicit because it was without the knowledge and sanction of his authority. He had therefore three reasons for developing this anxiety state.

This child's very ill condition was recognized and duly treated because of his social connexion with me, a child psychiatrist. Other children's psychiatric states can be passed off as "a phase" which will heal sooner or later with defect, leaving a lasting personal scar. I therefore feel bound to call the attention of my colleagues, especially those concerned with mental health and the health of schoolchildren, to this fresh cause of psychiatric states in the young, the giving of "sex education" (the internal details of the male and female animal, the mechanisms of mating, foetal development, and delivery) to persons in a defenceless position in a class situation before they are sufficiently mature to face these stark, staring realities.—I am, etc.,

LOUISE F. W. EICKHOFF,

Selly Oak Hospital,
Birmingham.

Occupation, Chemicals, and Cancer

SIR,—In a leading article commenting on an excellent article by Dr. Georgiana Bonser (10 June, pp. 649 and 655) you attribute to me a statement which I never made and do not support. You state that I "advocated that evidence of carcinogenic hazard should be clear-cut, and a solution should be available before pressure is put on manufacturers to reduce the exposure of their employees." What in fact I did say was, "Until the data are clear-cut and a solution has been found —i.e., either control of the material or its elimination—*publicity* through newspapers, congressional committees, or other types of *non-scientific* releases can hope to accomplish no useful objective." (My italics.)

Where an adequate occupational health team exists, and this includes both a knowledgeable physician and industrial hygienist, measures can be taken to minimize or eliminate exposures even before a situation is fully understood. In fact in my experience an outmoded plant was once dismantled by a company even before the cause of an occupational cancer was fully understood—obviously eliminating exposure. This was on the recommendation of such an occupational health team. Where such a team does not exist within an industry it can be made available to the industry through Government or consultants. Obviously if an industry, through financial greed, fear of litigation, inertia, or plain laziness, fails to obtain or heed the advice of such consultants, or the Government, additional pressures may have to be brought to bear upon the management, but this can be done through established mechanisms, not through publicity.

Even Dr. Bonser quotes Leitch[1] as follows: "The solution of the problem [of dye-workers' bladder cancer] would be welcome, for until the particular noxious substance or group of substances is known no real measures can be taken to prevent dyeworkers' cancer." Such a solution is arrived at through careful, quiet, competent research, such as has been described by Dr. Bonser, not through raucous publicity in non-scientific channels. I personally have found industrial management easy to convince once the facts are known, but extremely difficult to convince when the facts are unclear or unknown. I personally do not consider this a shortcoming.—I am, etc.,

R. E. ECKARDT.

Linden,
New Jersey, U.S.A.

REFERENCE

[1] Leitch, A., *A.R. Brit. Emp. Cancer Campgn*, 1929, 6, 32.

Second British Academic Conference in Otolaryngology

SIR,—May I be permitted, please, to correct the misunderstanding likely to have arisen from what you printed of your special correspondent's account of the Second British Academic Conference in Otolaryngology under the heading Otolaryngology Conference (26 August, p. 555)? It is true that two half-days of this important four-day meeting were given over to the Sections of Laryngology and Otology of the Royal Society of Medicine for their combined summer meeting and that the presidents of these sections, Mr. T. G. Wilson and Mr. Maxwell Ellis respectively, took the chair at the plenary sessions on the Friday and Thursday mornings, but I cannot believe that Mr. Wilson would wish to pose as "the president of the meeting," which was in fact presided over with characteristic proficiency by the Master, Sir Terence Cawthorne.

I am aware also that your special correspondent was asked to report particularly on the symposia entitled Facial Paralysis, the Catarrhal Child, and the Present Position of Chemotherapy in Head and Neck Cancer. Nevertheless, anyone not there would never guess from the report that these were only three of the forty topics that constituted this part of the scientific programme. There were also an almost continuous display of scientific films, a large area given over to exhibitions, and a very full and varied social programme. The editor of the *Journal of Laryngology and Otology* has generously agreed to make available one-half of the November issue of the journal for an account of this landmark in the history of British otolaryngology, and those of your readers who wish to obtain a correct impression of what took place in Oxford from 30 July to 4 August may care to look out for it.—I am, etc.,

L. F. W. SALMON,
Hon. General Secretary,
The Second British Academic Conference
in Otolaryngology.

Guy's Hospital,
London S.E.1.

Delayed Death in Imipramine Poisoning

SIR,—Dr. C. M. Steel and his colleagues (9 September, p. 663) in their article on imipramine and amitriptyline poisoning in children refer to two noteworthy cases where sudden collapse and death occurred after periods of progressive clinical improvement. The following case, where death occurred after apparent recovery from an overdose of imipramine, may be of interest.

A woman aged 49 was admitted to hospital on 17 March 1967 at 12.10 p.m. She had been taking imipramine intermittently for recurrent depression, and had apparently taken an overdose the night before—two empty bottles were found near the bed after the husband had been unable to rouse her. On admission she was deeply unconscious and unresponsive to painful stimuli. The stomach was washed out and 10 mg. of bemegride given intravenously. During the first hour after admission to the ward the patient had two major epileptic fits, and the level of unconsciousness became deeper. Temperature, pulse, respiratory rate, and blood pressure were within normal limits at this time. Frusemide 40 mg. was given intravenously and 500 ml. of mannitol was transfused during the next two hours. This was followed by 1,000 ml. of normal saline. The patient had five more epileptic fits in the next six hours, and at 8.30 p.m. she started to recover consciousness. At 9.30 p.m. she was reported to be very restless and trying to get out of bed. The intravenous drip was kept running and a further 1,000 ml. of normal saline was transfused.

Throughout the next 96 hours she remained fully conscious, but was confused, restless, and uncooperative most of the time. There were, however, brief periods when the patient was quiet, co-operative, and completely rational. Paraldehyde and chlorpromazine hydrochloride by intramuscular injection seemed to be producing adequate sedation, but on 21 March she became increasingly confused, agitated, and unmanageable. Her speech showed flight of ideas and her mood was somewhat elated, the picture being typical of a state of mania. At 9 p.m. she became semicomatose and her axillary temperature went up to 105° F. At 11 p.m. the level of consciousness deteriorated, the temperature remained elevated, and generalized muscular twitchings were observed. Three hours later the patient had a sudden cardiac arrest.

On post-mortem examination the leptomeninges on the cerebral surfaces were intensely congested and contained haemorrhages. There were numerous petechial haemorrhages on the subpleural surfaces of both lungs, with massive haemorrhages on the subpleural surfaces of the left lower lobe and right middle lobe. On section both lungs showed typical acute bronchopneumonia. The heart was congested, with haemorrhages in the muscle substance and in the visceral and parietal pericardium. The stomach mucosa was congested and contained semi-solid yellowish material but no evidence of tablets or capsules. The pancreas, spleen, and adrenal glands were congested. The kidneys were red and intensely haemorrhagic, and the bladder showed acute cystitis. Imipramine was detected in the following quantities—stomach contents 3.0 mg./100 ml., liver 4.7 mg./100 g., kidneys 2.8 mg./100 g., and blood a trace.

Previously an uninterrupted recovery could confidently have been expected in this type of poisoning once the patient had regained consciousness. This case would suggest that relapse and sudden death may occur in poisoning by tricyclic antidepressant compounds after apparent recovery. The forced diuresis may have kept the patient alive initially and there could be an argument for continuing this treatment in order to wash out the possible second wave of metabolites, which would otherwise contribute to an unexpected relapse.

I should like to thank H.M. Coroner and Dr. A. A. Miller for permission to describe the post-mortem findings, and Dr. C. Maxwell, of Geigy Pharmaceutical Limited, for helpful advice.

—I am, etc.,

A. B. MASTERS.

Whittingham Hospital,
Preston, Lancs.

Oculogyric Crises after Phenothiazines

SIR,—In view of the reports of bizarre neurological disturbances following treatment with perphenazine (Fentazin) from Drs. D. A. Heath and J. M. McGarry (11 February, p. 363) and Dr. J. R. Harries (22 July, p. 241) we should like to summarize briefly our experience with eight similar cases which have been seen in the last year. The patients have mainly been young adults, their ages ranging from 14 to 50 years with an average of 23 years. In four cases reactions have followed a single 5-mg. intramuscular injection given as premedication or postoperatively for vomiting. Symptoms have begun abruptly from 18 to 36 hours after the onset of treatment, and in none of our patients has this type of reaction been seen as a complication of long-term therapy.

Spasms of the head and neck occurred, most commonly with twitching, neck retraction, risus sardonicus, and oculogyric crises. These spasms were associated with curious subjective feelings of stiffness and immobility of the tongue with difficulties in chewing and swallowing, which occasionally preceded the more dramatic spasms by a few hours. Opisthotonos, flexion, and extension spasms of the limbs with a *main d'accoucheur* deformity were seen in the more severely affected. All patients remained completely alert mentally but were unable to modify their movements in any way. The attacks subsided spontaneously or in a few hours, with or without mild sedation. We have not used benztropine (Cogentin), which Ayd[1] has found to give rapid relief.

We feel that, although these neurological complications are not uncommon, they are as yet poorly recognized, and our cases have presented with a wide range of provisional diagnoses, including tetanus, tetany, epilepsy, and hysteria. Our experience confirms the finding of Kinross-Wright[2] that young people are unduly susceptible to these dystonic and dyskinetic reactions and we would advise caution in the use of this drug parenterally in this age group.—We are, etc.,

E. C. B. KEAT.

Royal Sussex County Hospital,
Brighton, Sussex.

P. J. TOGHILL.

King's College Hospital,
London S.E.5.

REFERENCES

[1] Ayd, F. J., jun., *J. Amer. med. Ass.*, 1961, 175, 1054.

[2] Kinross-Wright, V. J., *S. Afr. med. J.*, 1957, 31, 1167.

Case of Diarrhoea and Goitre

SIR,—I was fascinated by the report in the Clinicopathological Conference of the above case (29 July, p. 293), but, as a surgeon, I would like to have seen some remark to the effect that the patient had been offered an operation to remove the thyroid nodule discovered in 1960.

I have recently seen a young woman with a small lump in the neck which I thought might be a carotid body tumour. Three years before she was told by two practitioners in England that the lump was nothing to worry about. I referred her to South Africa, where the lump was found to be a metastasis from a thyroid carcinoma. At subsequent hemithyroidectomy and block dissection involved nodes were found to extend into the superior mediastinum.

We are used to rural Africans refusing operations until their tumours become inoperable, but it is alarming to find doctors not pressing for the histological diagnosis of "innocent" lumps which their patients bring to their notice.—I am, etc.,

IAN KENNEDY.

Princess Marina Hospital,
Gaberones,
Botswana, Africa.

Mercury Perchloride in Surgery

SIR,—In a letter (9 September, p. 679) Mr. H. B. Devlin discussed the use of 1:500 mercuric perchloride solution in large-bowel surgery. He concluded that it was a safe anticancer agent when used as described by Goligher *et al.*[1] There have been no reported cases of mercury poisoning following the use of this solution in this manner. Keynes[2] has suggested that the solution may be too toxic to leave in the peritoneal cavity to prevent intraperitoneal seedlings of tumour, although he used a 1:500 solution for this purpose on one occasion without ill effect. We wish to report the following case to emphasize that mercuric perchloride is too dangerous to use in the peritoneal cavity.

A woman of 68 years with no pre-existing evidence of renal disease underwent an ovarian cystectomy on 2 May 1967 for what was subsequently shown to be a mucous cystadenoma. During the course of the operation, which was otherwise uneventful, the peritoneal cavity was irrigated with 250 ml. of a 1:500 solution of mercuric perchloride. It was not known whether the peritoneal cavity was mopped dry prior to closure. Immediately postoperatively the patient became severely oliguric, and was transferred to the Hammersmith Hospital on 8 May for treatment of an acute renal failure. On admission peritoneal dialysis was commenced, but, as this was unsatisfactory, a Scribner A-V fistula was inserted into the right forearm to facilitate haemodialysis with a Kolff twin-coil artificial kidney machine.

Ureteric obstruction was excluded by cystoscopy and bilateral retrograde pyelography. Intermittent haemodialysis was necessary on 19 occasions during the next two and a half months. After the first month her urine output gradually increased, and since her discharge on a 20-g. protein diet with moderate fluid restriction the blood urea has remained at 90 mg./100 ml. Her daily urine volume is approximately 800 ml., containing 6.5 g. of urea. On this regimen she is now leading an active life at home.

A specimen of urine taken one month after exposure to mercuric perchloride revealed a mercury content of 150 μg./litre. This figure is much lower than that sometimes observed in chronic mercurial poisoning, but it is known that there is no correlation between the urine mercury level and the degree of renal damage sustained. Indeed, the urine mercury concentration falls with the onset of renal tubular damage.

In view of our experience with this case, we advise that mercuric perchloride should not be used as an irrigating agent in the peritoneal cavity.

We are grateful to Mr. H. T. Delves, A.R.I.C., Institute of Child Health, London, for performing the urine assay for mercury.

—We are, etc.,

J. C. GINGELL.
JOHN CLEGG.
M. WALLACE.

Hammersmith Hospital and
Royal Postgraduate Medical School,
London W.12.

REFERENCES

[1] Goligher, J. C., Dukes, C. E., and Bussey, H. J. R., *Brit. J. Surg.*, 1951, 39, 199.

[2] Keynes, W. M., *Ann. Surg.*, 1961, 153, 357.

Diagnostic Paracentesis

SIR,—I have been glad to note the growing interest in diagnostic abdominal paracentesis as evidenced by the articles of Morris[1] and Baker *et al.*[2] I now use it routinely in all abdominal diagnostic problems, including the patient with ascites of uncertain aetiology.[3] A film, cell count, and protein estimation are all simple procedures for a small laboratory and allow treatment or prognosis on a sure basis.

I am surprised that only "80% positive paracentesis can be expected in intraperitoneal haemorrhage."[2] I have found that a No. 1 needle on a 10-ml. or 20-ml. glass syringe, usually only into either lower quadrant, is quite adequate if the patient has been made to lie on the appropriate side, either before or after insertion of the needle. The needle is withdrawn slowly, the plunger under tension. It is often only as it seems the tap has been negative one obtained a small amount of fluid coming from a thin film on the peritoneum.

A negative paracentesis thus performed is now accepted as a contraindication to surgery for suspected ectopic pregnancy, especially when there is an associated sudden fall in Hb level. Two recent cases in this hospital were explored in spite of negative taps. They were found to be normal intrauterine pregnancies but associated with acute haemolytic crisis.—I am, etc.,

T. O. MULLIGAN.

Wesley Guild Hospital,
Ilesha, Nigeria.

REFERENCES

[1] Morris, P. J., *Brit. J. Surg.*, 1966, 53, 707.

[2] Baker, W. N. W., Mackie, D. B., and Newcombe, J. F., *Brit. med. J.*, 1967, 3, 146.

[3] Nwokolo, C., ibid., 1967, 1, 33.

Headlight Glare

SIR,—Dazzling headlight glare we know is the cause of some of our road accidents at night. Dipped headlights are not 100% effective even if properly adjusted. The following solution is therefore offered for your consideration and comment.

Let us suppose that it was made compulsory to polarize headlights at 45° from the vertical, then if windscreens or sun visors or goggles or glasses were similarly polarized to 45° in the same plane one would not interfere with one's own headlight field, but light from on-coming cars would be cut out, since there would be a 90° rotation. Awareness of on-coming traffic may be achieved by using a polaroid material of suitable density and efficiency so that not all light is stopped. Fog light would be exempt.

If headlight adaptation is made compulsory it leaves the choice of selecting the method of cut-out to the individual driver, should he so desire. The most convenient but expensive way would be by incorporating the material between the layers of the windscreen during manufacture, but the alternatives mentioned above would be simpler and cheaper. Headlights may be adapted by using clip-on polaroid screens or by inserting them on the inside of the glass during assembly.—I am, etc.,

S. J. LINES.

Peterborough Memorial Hospital,
Peterborough, Northants.

where mutual confidence and responsibility do not exist, situations where no credit is to be found will arise.

The answer is, I maintain, in our own hands.—I am, etc.,

NOEL CASH,
Hon. Secretary, Kettering Division B.M.A.
Desborough,
Northants.

Doctoring the Unattractive Areas

SIR,—An unattractive area is one where the number of applicants for a practice vacancy is consistently low. The reasons for this state of affairs are varied, and include high morbidity, above-average number of items of service per patient, educational and recreational deficiencies of the area, poor accessibility to London or other cities, a reduced number of general practitioners in the area, their above-average age, and high average list size.

The defining of an area is frequently done by the young general practitioner's wife, and was not so acute when doctors married after starting in practice. The problem has to be solved and the obvious methods are by attraction or direction. We despise the one and fear the other. If there were too many general practitioners chasing too few jobs there would be no problem, but it is pretty certain that any increase in numbers of available general practitioners would lead to the advocating of reduced lists in attractive areas and not to the manning of unattractive areas. We are duty-bound to help our fellow practitioners and should not stand by merely watching the increasing work load and incidence of coronary disease among our colleagues.

A possible solution to the problem is that service in unattractive areas would count as time and a half for superannuation purposes. Capitation fees could be raised according to morbidity and "doctor demand" rate. It is no fault of today's doctor if the patients were spoilt yesterday. Health centres could be built with living accommodation for the duty doctor. By grouping practices the general practitioner could be on duty only one week-end a month and not more than two nights a week. He should be allowed to live up to seven miles from his practice, and in winter months use the health centre flat when "on call." There should be ample clinical-assistant posts and a brake put on the closure of the local hospitals in such areas. The Ministry could inaugurate a scholarship fund for the education of doctors' children from unattractive areas.

We as custodians of the nation's health must not evade our responsibility. There is a solution and we must implement it. If we cannot alter the geography of the difficult areas the Ministry could set the medical scene, arrange the conditions and remuneration, and then advertise the vacancies.—I am, etc,

Caerphilly,
Glam.

G. MURRAY JONES.

Financing the Health Service

SIR,—£17,000,000 is a lot of money, yet it is the amount by which doctors' families are subsidizing the Health Service, I believe. It may not be understood how this is done.

> I am single-handed, in general practice, and employ, on contract through an agency, a dependant relative, for whom I pay £1,200 per annum. My accountant has recently agreed my last year's accounts, which include this figure, with the Revenue. Now, if 5,000 single-handed practices employ such relatives full time (secretary and receptionist, nights and week-ends as well) at, say, £1,000 per annum each, this would represent £5,000,000. Say 10,000 doctors employ dependant relatives part time (nights and week-ends only) at £500; this represents another £5,000,000. Add on to this another 5,000 doctors whose related staff are working on an occasional basis—odd nights and holidays, at £250 per annum, say; then one has £1,250,000, making an approximate total of nearly £12m., on which tax has in effect been "paid"; which at 8s. in the £ would add on something like £4,800,000 to make a grand total of from £16m. to £17m.

This all sounds very nice, but has anyone any evidence to support this proposition? Especially just now when our B.M.A. is about to present further ideas to the Review Body?—I am, etc.,

Bebington,
Cheshire.

ANTHONY YOUATT.

Consultants' Views of General Practitioners

SIR,—Mr. W. B. S. Crawford in his letter (16 September, p. 735) has pinpointed the essence of this problem, which is that generalizations by any section of the profession are tendentious in the extreme. That problems exist is not in doubt; the answer lies in understanding why they exist and in trying to rectify them.

In this area, for example, the relationship between consultants, junior hospital staff, and their general-practitioner colleagues is excellent. The reasons for this are not hard to find. The local hospital has grown out of a general-practitioner hospital, and many of the original staff are still in local practice. The consultants have been painstaking to leave intact the special relationship which has always existed between general practitioners and the hospital, and have built up a rapport, based on personal contact, which can be second to none. Furthermore, the weekly seminar, attended by senior and junior hospital staff and by a large number of general practitioners, is outstanding not only for its postgraduate benefits but because it is preceded by a luncheon at which a close social and clinical intercourse is established at all levels.

The local medical society acts in a similar fashion, encouraging this essential contact. A new Division of the B.M.A. has started promisingly, based on the hospital, and care has been taken to ensure a balance between hospital and general-practice appointment to the various offices. The domiciliary consultation is properly and extensively used—no small factor in the proper understanding of each other's problems. Last, but not least, the fact that general practitioners have full access to all the facilities for investigation ensures that a satisfactory clinical basis exists on which the general practitioners can build their standard of practice to a level at which, I believe, the local consultants do not feel that unnecessary work is "being dumped on the hospital service." With these points kept in mind it is difficult to see how, apart from sheer bigotry, a correct and mutually respecting relationship cannot be built up.

On the other hand, it is easy to see how, in an area where the general practitioners do not have full access to hospital facilities, where their lists are oversubscribed owing to the shortage of general practitioners, where contact with the hospital is not encouraged, where some members of the senior hospital staff are suffering from a combination of egotism and an overt sense of clinical superiority (however well founded), in areas

Sales Promotion

SIR,—As a medical representative for the past 23 years and now retired, I am well aware of the comments of Dr. J. R. Caldwell regarding the frequency of representatives' visits to general practitioners (16 September, p. 741). Personally I was never accused of calling too frequently.

Most pharmaceutical companies respect the recommendations of the A.B.P.I.—namely, that three or four visits during 12 months are adequate.

The representative is not entirely to blame, he is carrying out company policy. There is no reason for doctors to see representatives more frequently than they wish.

The remedy is simple: advise the representative of the call frequency acceptable to him and if this is exceeded refuse to interview, and advise the company that he has done this. It is only by so doing that the people responsible for sales promotion in the pharmaceutical industry will realize that the wishes of the medical profession must be respected.

In respect of mailings, a doctor can quite easily request his name to be erased from a specific company's list, or, further, from all pharmaceutical company lists.—I am, etc.,

Nottingham.

WILLIAM H. SIMS.

Obituary Notices

F. J. BENTLEY, M.D., F.R.C.P., D.P.H.

Dr. F. J. Bentley, a former senior medical officer to London County Council, died suddenly on 10 September. He was 67.

[Antonio Chacon

Francis Joseph Bentley was born in Middlesbrough, Yorkshire, on 28 December 1899. He was educated at Middlesbrough High School and Durham University, graduating M.B., B.S. in 1922, and taking the Conjoint diploma in the same year. He held early appointments as house-surgeon to Grey Turner and house-physician to Alfred Parkin at Royal Victoria Infirmary, Newcastle upon Tyne, after which he came to London and was appointed house-physician to Sir Robert Hutchison, Sir George Frederick Still, and Sir Hugh Thursfield, at the Hospital for Sick Children, Great Ormond Street. Subsequently, under Still's guidance, he worked for the Medical Research Council on acute rheumatism in childhood. In 1924 he proceeded M.D. and took the M.R.C.P. in 1925 while still working for the Medical Research Council. He then entered the tuberculosis service of the Metropolitan Asylums Board, and was appointed senior assistant medical officer at Grove Park Hospital. After taking the D.P.H. in 1928 he joined the public health service as an assistant county medical officer of health for Surrey. In 1920 he was appointed divisional medical officer at London County Council in the tuberculosis service. He did much work to improve this service in many ways, and during this period he made a critical assessment of the value of artificial pneumothorax therapy. His results were published by the Medical Research Council. This work provided both a necessary corrective to the use of the method in unsuitable cases and a plea for the wider employment of thoracic surgery. Shortly afterwards he was elected F.R.C.P. in 1937. During the second world war he continued his work at the County Hall, but inevitably with much widened duties. He was promoted to principal assistant medical officer, and then to senior medical officer.

In 1948 he was appointed physician superintendent at Highwood Hospital for Children, Brentwood, later becoming senior physician. Then began the most rewarding period of his career. Much research on pulmonary tuberculosis in childhood was carried out at Highwood. Together with his colleagues, S. Grzybowski and B. Benjamin, he produced his major work, *Tuberculosis in Childhood and Adolescence,* in 1954, which achieved a world-wide reputation.

The amount of time he devoted to his research did not deter him from maintaining an interest in clinical problems and undertaking regular teaching of postgraduates from the Institute of Diseases of the Chest and Great Ormond Street Hospital and undergraduates from the London Hospital and Guy's Hospital. Visitors came from many parts of the world to consult him, and many were internationally recognized as experts in this field. Dr. Bentley was a keen gardener, an excellent photographer, and an enthusiastic traveller abroad; and in his later years, in spite of poor health, he enjoyed croquet at Hurlingham. He loved the theatre, good books, and the company of his friends and family. By his death we have lost an eminent worker in the field of tuberculosis. He will, however, be remembered for his work particularly on tuberculosis in childhood.

We extend our sympathy to his widow and two daughters.—M. A. B.

K. F. D. WATERS, M.A., M.B., B.CH. F.R.C.S.ED.

Mr. K. F. D. Waters, a former consulting surgeon to the Chelsea group of hospitals, London, died on 12 September in St. Stephen's Hospital, Chelsea, after a series of illnesses which he had borne with much fortitude. He was 75.

Kenneth Fraser Darrell Waters was born on 2 July 1892, and obtained a first-class honours degree in physiology at Oxford in 1915. He undertook his clinical studies at St. Bartholomew's Hospital, graduating M.B., B.Ch. in 1918. After early house appointments at St. Bartholomew's Hospital and at the Radcliffe Infirmary, Oxford, in 1922 he came to the hospital, then known as the St. George's Union Infirmary, where he was to stay for so long and help to build it into a modern general hospital. In addition, he was involved in giving the hospital its present name—St. Stephen's. From his appointment until the second world war Mr. Waters was the only resident surgeon for a busy general hospital of 600 beds. Although there were a number of visiting surgeons, the main brunt of the surgical work during this period fell on him, and he became well known for his long operating lists, which were endured good-humouredly by the theatre staff because of his well-remembered "winning" smile. During this period Waters obtained his F.R.C.S.Ed. in 1931. In addition to coping with most of the general surgery, he also had to tackle gynaecological problems. During the war, although he had periods of ill-health himself, Mr. Waters played an extremely active part in keeping the hospital functioning normally. He was a patient during one of the bombing attacks that hit the hospital, and staff still remember his efforts to help the injured after a bomb had fallen on one of the ward blocks, killing a number of patients and staff.

After the war Darrell Waters continued to devote his considerable energies to developing the practice of surgery in the hospital, and pressed strongly for a new theatre suite. His efforts bore fruit when a complete twin operating-theatre suite was opened in 1952. He had been closely involved in the design, and the new facilities ranked among the best in London. Fifteen years afterwards the theatre suite continues to give excellent service, and is a testimony to the success of Darrell Waters in developing the sound surgical practice of the hospital. His skill in diagnosing children's conditions was especially well known, and his second marriage to the writer of children's stories, Miss Enid Blyton, was a happy union for the hospital, as Mr. and Mrs. Waters took a great interest in the children's ward, and arranged for murals of the characters from her books to be displayed there.

Mr. Waters retired from active practice in 1957. His energy and devotion in developing surgery at St. Stephen's are still well remembered, and he was a much-loved and respected patient at the hospital in recent years. Sympathy is extended to his widow, two daughters, and the rest of the family. —M. G. R.

I. GLUCK, M.D., D.P.M.

Dr. I Gluck, consulting psychiatrist at the Portman Clinic, London, died suddenly on 10 July. He was 52.

Imrich Gluck was born in Budapest on 12 December 1914. In his late adolescence he moved to Czechoslovakia, where he took up the study of medicine. However, he was forced to interrupt his studies in 1938, and shortly after the outbreak of the second world war he succeeded in escaping to France, where he joined the Czech forces and was eventually evacuated to England. He was enabled to complete his medical studies at Manchester, graduating M.D. in 1942, shortly afterwards joining the R.A.M.C. During the latter part of the war Dr. Gluck served in the front line in Belgium and Germany, and he was with the first British troops to enter Belsen. Meanwhile all the members of his family had lost their lives in Nazi-occupied Europe. Returning to England on demobilization in 1946, he turned to psychiatric work and psychoanalytic training, taking the D.P.M. in 1948. He became a full member of the British Psychoanalytical Society in 1955. After working in the department of psychiatry of Leeds Medical School, and at Shenley Hospital, Dr. Gluck joined the staff of the Cassel Hospital, Richmond. His creative mind led him to explore new problems and new methods of treatment. He realized the importance of helping mothers who had disturbed relations with their small children, and that the setting of the Cassel Hospital would allow treatment to be carried out without separating mother and child. The results of this work were published in a clinical paper, and illustrated in a film which aroused much interest. The last years of his life were devoted to private psychoanalytic practice and psychotherapeutic work at the Portman Clinic, London. The depth of his understanding, and his human sympathy, were greatly appreciated by his patients. His colleagues remember his readiness to help in difficult tasks, his keen sense of humour, and the warmth of his personality.

Dr. Gluck had a profound knowledge of music, and was a competent violinist. He could have reached a very high level in this field had he not chosen medicine as his first calling.

He married in 1960 Evelyn, daughter of Sir Edward Beddington-Behrens, who survives him with their daughter.—L. H. R.

F. S. BONUGLI, M.D., D.R.C.O.G.

Dr. F. S. Bonugli, consultant venereologist to the Northern Ireland Hospitals Authority, died suddenly on 28 August. After attending his clinic in Coleraine, County Londonderry, he was taken ill in his car, and died in Ballymoney Hospital. He was 54.

Frederick Silvester Bonugli was born in Larne on 28 June 1913. He was educated at the Methodist College, Belfast, where he played rugby for the school's first XV. He received his medical education at the Queen's University of Belfast, graduating M.B., B.Ch., B.A.O. in 1937. In 1939 he gained the diploma of the Royal College of Obstetricians and Gynaecologists after working in the Royal Maternity Hospital and the gynaecological wards of the Royal Victoria Hospital, Belfast. He served in the R.A.M.C. in the second world war, and after demobilization he proceeded to the degree of M.D. at Queen's University, Belfast, in 1946. In the meantime he had decided to specialize in the field of venereology. He was appointed to the venereal diseases department of the Royal Victoria Hospital in 1946, and in 1951 became a consultant venereologist to the Northern Ireland Hospitals Authority, with his main clinics at the Royal Victoria Hospital, Belfast, and Coleraine Hospital, County Londonderry, an appointment which he held at the time of his death. He was a clinical teacher in venereal diseases and a lecturer in venereal diseases in social and preventive medicine to the Queen's University medical school.

For many years he was a member of the Medical Society for the Study of Venereal Diseases, and a correspondent member of the American Venereal Diseases Association.

He is survived by his widow and two daughters, to whom we extend our sympathy. —J. S. McC.

P. T. HARPER, M.R.C.S., L.R.C.P.

Dr. P. T. Harper, formerly of the Fiji Medical Service, died on 21 August at his home in Chertsey, Surrey. He was 83.

Philip Thomas Harper, eleventh of the thirteen children of Dr. Joseph Harper, of Barnstaple, Devon, was born on 2 February 1884. He was educated at Blundell's School, Tiverton, and St. Thomas's Hospital, London, qualifying with the Conjoint diploma in 1908. He held the appointment of senior obstetric house-physician at St. Thomas's Hospital before going out to Fiji in 1910, when he began a distinguished career in the Fiji Medical Service. He was appointed district medical officer at Ra and at Nadi, and in 1911 became resident medical officer at the Colonial Hospital, Suva. During the same year he married Miss Winifred Coster, a qualified nurse and midwife in the service of the Fiji Government. During the first world war he was commissioned as a captain in the New Zealand Medical Corps.

After demobilization he resumed his work in Fiji, and in 1920 became medical superintendent at the Leper Station, Makogai, playing an important part in advances in the treatment and management of this disease. During this period of three years he lived with his wife and small children at the station. He became medical superintendent of the new Colonial War Memorial Hospital at Suva, taking an active part in medical education and in the development of the hospital and medical services in Fiji until his retirement in 1938, when he returned to England. When the second world war broke out he volunteered again, and served in Egypt and later at Millbank Hospital, London.

He is survived by his widow and three daughters; his only son was killed in action with the R.A.F. in 1940.—R. H.

L. MURIEL RHODES-CLOONEY
M.B., B.S., D.A.

Dr. L. Muriel Rhodes-Clooney, a medical practitioner at Bexhill-on-Sea, died on 3 September. She was 67.

Laura Muriel Rhodes-Clooney, the youngest daughter of the late Canon A. H. Rhodes, of Cheltenham, was born on 24 September 1899, and was educated at Wycombe Abbey School, where she obtained one of the first medical scholarships. She received her medical training at the Royal Free Hospital and St. Mary's Hospital, London, qualifying with the Conjoint diploma in 1924, and graduating M.B., B.S. the following year. She held house appointments at St. Mary's Hospital, and afterwards became the first woman doctor to practise in Bexhill. She was also appointed medical officer to the infant welfare clinic in 1928, where she continued until April of this year. She did much pioneer work in the Bexhill maternity and child welfare clinics in the early days of their inception. Dr. Rhodes-Clooney was lecturer to the Bexhill Red Cross until after the second world war, and during the war was appointed to the Emergency Medical Service as anaesthetist in Bexhill and Hastings. She took the diploma in anaesthetics in 1944, and in 1948, when the National Health Service was formed, became part-time anaesthetist to the Hastings hospital group. In 1958–9 she was chairman of the Hastings Division of the British Medical Association. She retired from general practice in the National Health Service in October of last year, but continued in private practice until her death.

A keen sportswoman, Muriel Rhodes-Clooney played lacrosse for the University of London and county of Middlesex in her younger years, and was an active member of the Highwoods golf club up to the time of her death. She will be very much missed in Bexhill, and there are many who will look back in gratitude for all that she did.—T. K. B.

S. PORTERFIELD, B.A., M.B., CH.B.
B.A.O.

Dr. S. Porterfield, a general practitioner in Widnes for over 30 years, died at his home in Portstewart on 31 August. He was 87.

Samuel Porterfield, who came from Ballylennon, Co. Donegal, was born on 12 May 1880, and was one of a talented band of medical students who came north from Queen's College, Galway, to Queen's College, Belfast, for the last two years of their course. He graduated B.A., and M.B., Ch.B., B.A.O. in 1905 at the old Royal University of Ireland. For a time he was demonstrator of anatomy at Galway. Most of his career, after assistantships in Maesteg and South Emsall, was spent in Widnes, near Liverpool, a Lancashire town in those days famed for smoke and fumes. In 1914 he married Lilian Gourley, from Carnshanna, and joined her uncle, Dr. McCausland, in Widnes. He worked single-handed in the large practice during the first world war and gave enthusiastic support to the St. John Ambulance Brigade as a lecturer and examiner. Dr. Porterfield was one of the old school of "family doctors," much appreciated by his patients and colleagues—a type now said to be almost extinct except in remote areas.

With his partners he conducted a busy practice until his retirement, when he went to live at Portstewart, Co. Derry. Our deep sympathy is extended to his widow, his two sons, and four daughters.—A. P.

C. B. WAINWRIGHT, B.A., M.B.
B.CHIR.

Dr. C. B. Wainwright, formerly in practice in Bermuda, died there on 16 June. He was 82.

Charles Barron Wainwright was born in Bermuda on 12 June 1885, and was educated at the University of Cambridge, graduating B.A. in 1908. For his clinical studies he went to St. Thomas's Hospital, London, qualifying with the Conjoint diploma in 1911, and graduating M.B., B.Chir. the following year. After early house appointments at Guy's Hospital, London, he went out to British Columbia and on the outbreak of the first world war immediately joined the Forces, serving for a time in a submarine, and he also arranged the fitting out of a hospital ship in British Columbia. Shortly after this he came to England, joining the R.A.M.C. and serving for the remainder of the war. After demobilization in 1919 with the rank of captain, he returned to Bermuda and settled in general practice. In addition to carrying on a large practice, he was for many years chairman of the local medical board, and held the appointment of surgeon to the King Edward VII Hospital in Bermuda, where he also supervised the *x*-ray department. He was instrumental in organizing the Bermuda war veterans' association in 1919. For many years he was senior medical officer to the Bermuda Volunteer

Rifle Corps, in which he held the rank of major. He was honorary secretary of the Bermuda Branch of the British Medical Association from 1921 to 1953, and president of the Branch from 1953 to 1963.

Despite his many activities, Dr. Wainwright found time for relaxation and recreation. He was an excellent fisherman and a keen golfer, but his favourite pastime was sailing, and he had held all three ranks as flag officer of the Royal Bermuda Yacht Club. He leaves a widow and a daughter.

P. G. TRAFFORD, M.R.C.S., L.R.C.P. L.D.S.

Dr. P. G. Trafford, who practised in Scunthorpe, Lincolnshire, for nearly forty years, died suddenly on 2 August. He was 68.

Philip George Trafford was born at Ruskington, Lincolnshire, on 20 July 1899, and qualified as a dental surgeon in 1922. Shortly afterwards he entered Guy's Hospital, London, taking the Conjoint diploma in 1925. He held the appointment of honorary dental surgeon to the War Memorial Hospital at Scunthorpe for over thirty years, and during the second world war also carried out the duties of anaesthetist with the Emergency Medical Service. Although practising as a dental surgeon, Philip Trafford retained his medical knowledge, and kept well up to date to a considerable degree. His skill as a diagnostician was revealed on many occasions.

Philip was a man of absolute integrity and transparent honesty, and these qualities made him one of the most respected members of the profession. He was very happily married, and, although not blessed with children, he had quite a number of godchildren. They not only loved him but also went to him not infrequently with their troubles, and they were always received in a very friendly and sympathetic manner. "P.G.," as he was not infrequently known to his friends, enjoyed a game of golf, and was an expert fly fisherman.

We extend to his wife, who was always a wonderful partner, our heartfelt sympathy.—W. H. B.

A. SIMONS, L.R.C.P.&S.ED. L.R.F.P.S.GLASG., D.OBST.R.C.O.G.

Dr. A. Simons, a general practitioner in Glasgow, died suddenly at his home on 1 September. He was 50.

Aaron Simons was born in Glasgow on 16 October 1916, and received his early education at Queen's Park Secondary School. He left school to work in the family business, but in a few years realized that this did not provide the challenge he wanted. He studied privately, passed the university preliminary examinations, and entered Anderson's College of Medicine in Glasgow at the age of 21, taking the triple qualification in 1943. During his student life he took part in many activities, and was president of the Glasgow Jewish Students Society. He was house-surgeon at the Royal Maternity Hospital, Glasgow, and during the second world war was house-physician at Lennox Castle Hospital, under the Emergency Medical Service, before serving in the R.A.M.C. in the United Kingdom, Italy, and India. After demobilization with the rank of captain, he took the D.Obst.R.C.O.G. in 1948, and entered general practice.

Aaron Simons had a profound understanding of human nature and a respect for learning, and these qualities, together with his warm-heartedness, made him an excellent general practitioner who was loved by his patients. He lost no opportunity in attending postgraduate lectures and courses, and was a member of the College of General Practitioners and the Psychosomatic Society. By nature he was gay and relaxed and delighted in the theatre, music, and literature. He was a proficient violinist, and even took his violin with him abroad when he was in the Army. He married his wife, Rose, in 1952, and they were ideally happy with their three children, and we all gained strength and comfort from association with a man of noble character. For several years before his sudden death his youthful bounding energy was diminished, but he maintained a courageous face to the world and never complained.—A. G.

J. M. KNIGHT, M.R.C.S., L.R.C.P.

Dr. J. M. Knight, a former assistant geriatrician to the Wigan and Leigh Hospital Group, died suddenly on 21 August. He was 58.

James Manson Knight was born on 21 June 1909, and received his medical education at Leeds University, qualifying with the Conjoint diploma in 1940. He then joined the R.A.M.C., and spent four years as a prisoner of war. On his return he served as a medical officer at the sanatorium, Bridge of Weir, and at Scotton Banks Hospital, Knaresborough. He later moved to Lancashire, and became assistant geriatrician at Billinge Hospital, near Wigan.

J. K. H. writes: Until shortly before his death Dr. Knight had been a devoted worker in the geriatric department of Billinge Hospital. He was a man with an active brain and many gifts, but one whose life had had more than its share of tragedy. At an early age he lost his father—a medical officer of health for Scarborough. After his four years as a prisoner of war his first wife died in childbirth. Later he developed tuberculosis, for which he required extensive operative surgery. On recovery he worked in tuberculosis sanatoria for several years. He married a nursing sister, who died just over a year ago after a prolonged illness. So has passed a sympathetic doctor, a forthright and honest man, and a firm friend.

J. A. HADFIELD, M.A., M.B., CH.B.

G. N. and G. A. write: Many years ago, when we first became interested in the uses of hypnosis in medicine, we naturally came across the name of J. A. Hadfield (obituary, 16 September, p. 742). Even then his name was almost a legendary one because of his work in restoring to health many of the victims of "shell-shock" during the first world war. His recent death at an advanced age has thus severed the last remaining link between those earliest psychiatrists working on hypnosis and the present generation. It is to him that we owe the development of the technique of hypnoanalysis in psychotherapy, and it was from studying his pioneer work with this method of abreaction and psychocatharsis that most of us have obtained our results. Many have followed the lead which he gave as a result of his own wartime experiences of 50 years ago. He had a far-reaching and inquiring mind which ranged over the whole of medicine, and if he had not chosen psychopathology as his specialty he would have undoubtedly become a great general physician. His own *Psychology and Morals*, which has been reprinted in many editions since 1920, bears witness to his literary skill as well as to his penetrating insight into human nature.

As to Hadfield's personal charm, and his attitude of benign love and affection, others have written elsewhere. His death has meant a great loss to our profession and to psychiatry in particular.

L. MORRIS, M.D., F.R.C.S.

S. R. writes: Having had the privilege of close association with the late Mr. Leslie Morris (obituary, 9 September, p. 685) for more than 20 years, I would like to pay tribute to this very remarkable, able, and kindly man. Two aspects of his personality made a very profound impression. One was his amazing degree of intelligence—often hidden under a cloak of genuine modesty—and the high intellectual level at which he studied and enjoyed those cultural pursuits which afforded him so much deep pleasure. The other was his innate kindness, generosity, and compassion, qualities which he was shy of emphasizing, but which he exercised in his quiet retiring way whenever the opportunity occurred. Many patients unknowingly benefited from his practical help, when Morris ruthlessly cut through red tape in order to speed succour to the handicapped.

The pursuit of his hobbies afforded him a wealth of happiness. He became extremely knowledgeable about ballet and opera—especially Wagner—and whenever possible he would travel to Covent Garden, to become immersed in the music of *The Ring*, or to pick out infallibly the talented and rising ballerinas. He was a discriminating collector of old English silver, being satisfied only with the genuine and artistically designed pieces. Persian carpets and water colours by the masters of this kind of painting attracted him strongly, while on old English porcelain he had an unrivalled expertise.

In the social field Morris was a delightful host, ever thoughtful for the comfort and contentment of his guests, never at a loss for light or enlightened conversation. During his latter years the domestic scene was enlivened by the happy marriages of his daughters, and by the arrival of grandchildren. His wife, always steadfast and ready to join in with anything that gave him pleasure, was a source of great comfort, especially in the period of his illness shortly before retirement. With her, and all his family, his many friends will feel the utmost sympathy at his passing.

News and Notes

EPIDEMIOLOGY

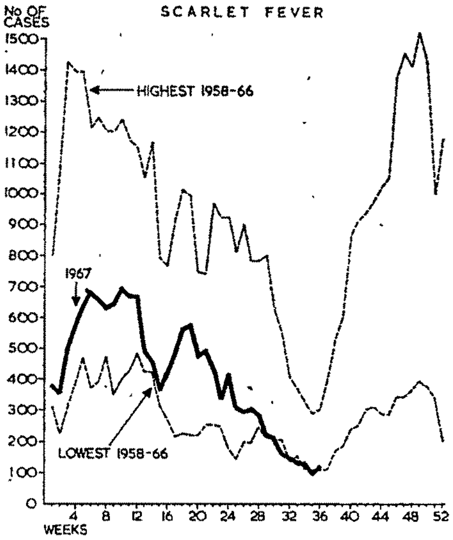
Infectious Diseases

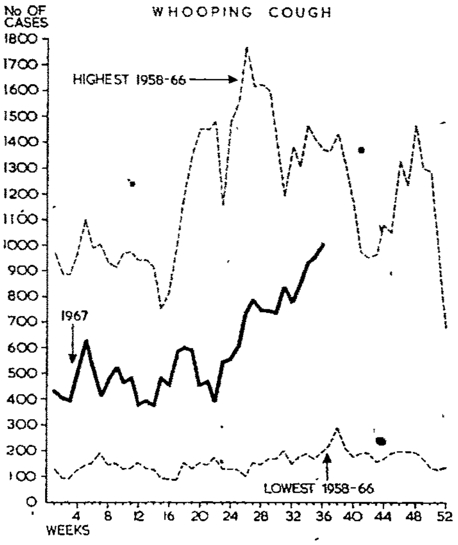
Areas where numbers of notifications were high in the latest two weeks for which figures are available.

Dysentery	Week Ending 8 Sept.	Week Ending 15 Sept.
Greater London	34	**26**
Lancashire	50	**43**
Surrey	4	**22**
• Reigate M.B.	0	**22**
Warwickshire	13	**20**
Birmingham C.B. ...	9	**17**
Yorkshire West Riding ...	36	**54**
Bradford C.B.	10	**14**
Leeds C.B.	16	**19**
Hemsworth R.D. ...	1	**15**
Glasgow	33	**46**
Edinburgh	18	**14**
East Lothian County ...	4	**15**

Graphs of Infectious Diseases

The graphs below show the uncorrected numbers of cases of scarlet fever and whooping-cough in England and Wales. Figures for 1967 are compared with the highest and lowest figures for each week in the previous years shown.





INFECTIOUS DISEASES AND VITAL STATISTICS

Summary for British Isles for week ending **9 September** (No. 36) and corresponding week 1966.

Figures of *cases* are for the countries shown and for Greater London. Figures of *deaths* and *births* are for the whole of England and Wales (London included), Greater London, the 17 principal towns in Scotland, the 10 principal towns in Northern Ireland, and the 14 principal towns in Eire.

A blank space denotes disease not notifiable or no return available.

The table is based on information supplied by the Registrars General of England and Wales, Scotland, N. Ireland, and Eire, the Ministry of Health and Local Government of N. Ireland, and the Department of Health of Eire.

CASES	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0	0	1	0		0	0	0	0	
Dysentery ..	216	34	67	0	7	261	39	120	16	3
Encephalitis, acute ..	1	0		0		4	0		0	
Enteric fever: Typhoid ..	5	1	0	0		4	2	0	1	
Paratyphoid	1	0	0	0		5	2	0	0	
Food-poisoning	160	41	12	3		152	46	2	2	
Infective enteritis or diarrhoea under 2 years				22	56				13	46
Measles* ...	1,055	75	4	23	27	3,321	401	45	38	79
Meningococcal infection ..	2	0	2	0		4	1	4	0	
Ophthalmia neonatorum	14	0	0	0		11	2	1	0	
Pneumonia† ..	68	5	39	2		57	3	62	3	
Poliomyelitis, acute: Paralytic ..	1	0	0	0		0	0	0	0	
Non-paralytic	0	0	0			0	0	0		
Puerperal fever§	73	22	2	0		82	44	8	0	
Scarlet fever ..	119	20	14	5	5	169	17	19	2	5
Tuberculosis: Respiratory ..	177	37	32	5		200	54	37	7	
Non-respiratory ...	45	8	5	1		48	9	10	2	
Whooping-cough	1,008	166	75	10	20	570	70	91	9	17

DEATHS	1967					1966				
	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire	Eng. & Wales	Gtr. Lnd	Scot.	N. Ire.	Eire
Diphtheria ..	0		0		0	0		0	0	0
Dysentery ..	2	0				1	0		0	
Encephalitis, acute ..					0					0
Enteric fever ..	0	0	0			0	0	0	0	
Infective enteritis or diarrhoea under 2 years	3	0	1		2	5	0	0	0	2
Influenza ..	1	1	0		0	2	0	0	0	0
Measles ..	0		1		0	0		0	0	0
Meningococcal infection. ..			0					0		
Pneumonia ..	480	61	18		4	496	86	14	9	6
Poliomyelitis, acute ..	0	0			0	0	0		0	0
Scarlet fever ..	0		0		0	0		0	0	0
Tuberculosis: Respiratory	31	8	6		0	44	9	1	0	1
Non-respiratory ..					1				0	1
Whooping-cough	0	0	0		0	0	0	0	0	0
Deaths 0-1 year	241	37	12		5	286	42	28	10	11
Deaths (excluding stillbirths)	8,805	1280	514		138	8,861	1436	519	107	137
LIVE BIRTHS	16,153	2717	777		381	16,988	2883	934	279	456
STILLBIRTHS	232	28	19			249	40	20		

* Measles not notifiable in Scotland, whence returns are approximate. † Includes primary and influenzal pneumonia. § Includes puerperal pyrexia.

MEDICAL NEWS

Clinical Pharmacology

The need to increase facilities for clinical pharmacology in Britain is urged by Dr. D. A. LONG, Chief Medical Adviser and Deputy Research Director of the Wellcome Foundation Limited. In a report to the Association of the British Pharmaceutical Industry he suggests that a committee representing industrial and academic medicine should be set up to advise on this. Other suggestions include setting up a chair of clinical pharmacology in every teaching school in Britain; establishing training fellowships in clinical pharmacology; and the creation of an institute of therapeutics to arrange clinical pharmacological studies and to investigate special problems, such as the toxicity of phenacetin. The report is obtainable free of charge from the Information Services Department of the A.B.P.I.

Head of John Curtin School of Medical Research

Professor FRANK FENNER has been appointed Head of the John Curtin School of Medical Research in the Institute of Advanced Studies of the Australian National University at Canberra. Professor Fenner graduated in medicine at the University of Adelaide in 1938. From 1940 to 1946 he served in the Second Australian Imperial Force in the Middle East and South-west Pacific Areas, and in 1946 joined Sir Macfarlane Burnet, F.R.S., at the Walter and Eliza Hall Institute in Melbourne. After a year (1948–9) at the Rockefeller Institute in New York he was appointed to the foundation Chair of Microbiology in the John Curtin School of Medical Research, where he developed a group working on animal virology. He was elected Fellow of the Australian Academy of Science in 1954, F.R.S. in 1958, and F.R.C.P. in 1967. His predecessor, Sir Hugh Ennor, was appointed to the position of Secretary to the Department of Science and Education of the Commonwealth of Australia in February this year.

[Australian News and Information

Professor of Ophthalmology at Enugu

Professor H. C. KODILINYE, professor of ophthalmology at the University of Ibadan, has been appointed Dean of the Medical School of the University of Biafra, Enugu, and also to the Chair of Ophthalmology in the University.

Professor Kodilinye, who graduated at the University of Glasgow in 1935, trained in ophthalmology at Newcastle upon Tyne, Oxford, and London, and was for over 12 years consultant ophthalmic surgeon to the Manchester Regional Hospital Board prior to accepting in 1961 the appointment of senior lecturer in ophthalmology at the University of Ibadan. There he built up a department of ophthalmology and was in 1963 appointed to the first Chair of Ophthalmology in tropical Africa.

Professor Kodilinye is a member of the Faculty of Ophthalmologists, the Ophthalmological Society of the United Kingdom, and the West African Association of Surgeons. He has published many papers on his own subject.

Indomethacin: Unidentified Drug

The Minister of Health has received the following letter from the Committee on Safety of Drugs:

> "It has come to the attention of the Committee that two varieties of capsules of an unidentified drug described as 'indomethacin' have been distributed at a number of pharmacies in the London area. Indomethacin is a patented drug, and capsules supplied by its manufacturers in this country are coloured yellow and bear the inscription 'MSD 25' in pale bluish-grey. The unidentified capsules are either yellow with a reddish tinge but unmarked, or yellow with the inscription in black 'MRC 25.'
>
> "Indomethacin is a valuable and potent drug, but one whose known side-effects call for care in its use by the physician. It is a matter of especial concern, therefore, to the Committee that it has received no submission from manufacturers or importers of the unidentified drug.
>
> "The Committee accordingly recommends to the Ministers that doctors and pharmacists should be advised that, since the unidentified preparations described have not been submitted for its scrutiny, the Committee is unable to pass any opinion on their safety in use."

The Ministry states that further inquiries are being made about this drug, but in the meantime pharmacists, dispensing doctors, and hospitals are advised not to use the unidentified capsules described in dispensing prescriptions.

Plight of the Disabled

In Britain too little effort has been made to assess the effects of disability on function. This claim is made by Professor PETER TOWNSEND, of the Department of Sociology at the University of Essex, in a lecture to the Royal College of Surgeons in May 1967 which has recently been reprinted as a pamphlet. If a functional assessment was used he considers that between 3% and 6% of people under pensionable age would be classed as physically or mentally handicapped. A survey by his Department showed that there were four major problems: poor housing; inadequate community care services; finding paid employment: and inadequate total income. Professor Townsend lists the priorities for improving this situation as more good housing, better community services, and more generous motorized transport. Other proposals are that various forms of subsidy and encouragement to employers might be tried, and that a generous pension based on the degree of limitation of capacity should be introduced for both men and women. The pamphlet, entitled *The Disabled in Society*, is obtainable from the Greater London Association for the Disabled, 183 Queensway, London W.2, price 3s.

National Nursing Staff Committee

A National Nursing Staff Committee has been set up by the Minister of Health, with Mrs. I. GRAHAM BRYCE as Chairman, following the recommendations of the Salmon Committee on Senior Nursing Staff Structure (see *B.M.J.*, 1966, **1** 1375). Its members include Dr. D. MACMILLAN, of the University of Leeds, and Dr. A. B. TAYLOR, of the United Birmingham Hospitals.

Interview Board for North America

The Interview Board sponsored by the Ministry of Health (see *B.M.J.*, 15 July, p. 128) will leave London on 30 September to meet British doctors in North America. The Board consists of Dr. R. H. BARRETT, Dr. A. TALBOT ROGERS, and Mr. A. J. COLLINS—all from the Ministry; and Dr. CHRISTIE W. GORDON, Dr. STEPHEN R. S. WHITTAKER, and Professor A. G. W. WHITFIELD. The Ministry state that the response to the creation of this Board has been so good that its tour has been extended. Interviews have been arranged in Washington, Chicago, San Francisco, Vancouver, Calgary, Winnipeg, Toronto, and New York. The purpose of the interviews is to give British doctors the latest information on opportunities in the hospital and general-practitioner services and to ascertain their views about medical emigration. Hospital boards and executive councils have told the Interview Board about current vacancies in posts which might interest doctors wishing to return to Britain.

Research in Otology

Applications are invited by the Royal Society of Medicine for the Norman Gamble Research Prize of £50, and for grants from the Norman Gamble Research Fund. Further details may be obtained from the Assistant Secretary, Royal Society of Medicine, 1 Wimpole Street, London W.1.

Order of St. John of Jerusalem

We regret that the list of appointments and promotions to the Most Venerable Order of the Hospital of St. John of Jerusalem (23 September, p. 807) omitted the name of Colonel ROBERT G. W. OLLERENSHAW, E.R.D., T.D., who has been promoted from Commander (Brother) to Knight. Colonel Ollerenshaw has also recently been appointed a Deputy Lieutenant for the County Palatine of Lancashire.

People in the News

▶ PROFESSOR W. J. H. BUTTERFIELD, professor of medicine at Guy's Hospital Medical School, and a member of the World Health Organization Expert Committee on Diabetes Mellitus, has been elected chairman of the British Diabetic Association executive council.

▶ Dr. R. A. KEMP HARPER has been appointed as civilian consultant in radiology to the Royal Navy.

▶ Dr. K. B. ROBERTS, at present Reader in Physiology at the London Hospital Medical College, has been appointed Associate Dean of Medicine and head of the department of physiology at the Memorial University, St. John's, Newfoundland.

▶ Professor IAIN MACINTYRE of the Royal Postgraduate Medical School, London, is to share with Professor D. H. COPP, of Vancouver, a $5,000 annual award by the Gairdner Foundation of Canada for his demonstration that thyrocalcitonin is produced by the thyroid gland.

Coming Events

Middlesex Hospital Medical School.—Annual refresher course for former students, 29 September to 1 October.

Westminster Hospital and Medical School Old Students.—Annual dinner, 5 October, 7.15 p.m., Quaglino's Restaurant. The chairman will be Dr. S. P. MEADOWS.

Institute of Hospital Administrators.—Conference, "The Future Pattern of Hospital Management," 19 October, 10.30 a.m., Queen Mary Hall, Y.W.C.A. Central Club, Great Russell Street, London W.C.1. Fee £1 (10s. to members of I.H.A.). Applications for tickets, accompanied by remittance, should be sent to Secretary, Institute of Hospital Administrators, 75 Portland Place, London W.1.

Biological Engineering Society.—Demonstrations in biomedical engineering, and scientific meeting, 20–21 October, London W.C.1. Details from Mr. W. J. Perkins, National Institute for Medical Research, Mill Hill, London N.W.7.

Societies and Lectures

For attending lectures marked ⊕ a fee is charged or a ticket is required. Applications should be made first to the institution concerned.

Friday, 29 September

ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS.—4 p.m., William Meredith Fletcher Shaw memorial lecture by Dr. E. A. Gerrard: The Patient as an Individual.⊕

Monday, 2 October

BLAIR BELL RESEARCH SOCIETY.—At Nuffield Hall, Royal College of Obstetricians and Gynaecologists, 5.30 p.m., papers by Professor A. C. Turnbull, Dr. R W. Beard, and Dr. S. M. M. Karim.

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 5.30 p.m., clinical meeting.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—5.30 p.m , Professor I. Friedmann, Dr. D. A. Osborn, Dr. M. I. Wright: clinicopathological conference.

ROYAL COLLEGE OF PHYSICIANS AND SURGEONS OF GLASGOW.—At Maurice Bloch Lecture Theatre, 5.30 p.m., Blackham lecture by Professor C. C. Booth: Cellular Responses in the Small Intestine.

SOCIETY FOR MEDICAL AND DENTAL HYPNOSIS.—At Royal Society of Medicine, 8 p.m., presidential address by Dr. J. Hartland: Hypnosis in the Development of Modern Psychological Medicine.

Tuesday, 3 October

KENT POSTGRADUATE MEDICAL CENTRE AT CANTERBURY.—At Kent and Canterbury Hospital, 8.30 p.m., Dr. W. W. Brigden: General Principles of Electrocardiography.⊕

NEATH POSTGRADUATE MEDICAL CENTRE.—At Neath General Hospital, 4 p.m., Professor A. J. Dhruva (Bombay): Our Experiences with Prolonged Perfusion.

ROYAL ARMY MEDICAL COLLEGE.—5 p.m., Sir Graham Wilson: Prophylaxis of Tetanus.

ST. CHARLES'S HOSPITAL MEDICAL CENTRE.—8 45 p.m., Mr. L. A. Ives: The Acute Abdomen.

WHIPPS CROSS HOSPITAL.—At Medical Education Centre, 1 p.m., clinical meeting.

Wednesday, 4 October

BROOK GENERAL HOSPITAL.—At Postgraduate Medical Centre, 8 15 p.m., Mr. D. W. C. Northfield: Differential Diagnoses of Intracranial Tumours in the Adult.

CHELMSFORD MEDICAL EDUCATION AND RESEARCH TRUST.—At Chelmsford Medical Academic Unit, London Road (grounds of Chelmsford and Essex Hospital), 12 noon, surgical meeting.

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. F. P. Lee Lander: Bronchial Suppuration.

ROYAL FREE HOSPITAL.—5.15 p.m., Dr. D. Zimmon (New York): Hepatic Coma.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—2 p.m., Professor G. M. Bull: Place of Chemical Pathology in Modern Medicine.

STOKE MANDEVILLE HOSPITAL.—(1) 12.15 p.m., Dr. H. L. Frankel: Assisted Respiration. (2) 6 p.m., Dr. C. S. Pitcher: Megaloblastic Anaemias—I.

WHIPPS CROSS HOSPITAL.—At Medical Education Centre, course for general practitioners, 2 p.m., Dr. J. T. Wright: The Wind ; 3 p.m., Dr. R. S. Francis: The Respiratory Cripple.

Thursday, 5 October

LONDON UNIVERSITY.—At Anatomy Theatre, University College, 5.30 p.m., special university lecture in human anatomy and morphology by Professor J. E. Rose (Wisconsin): The Tonotopical Organization of the Cochlear Nuclear Complex and On Some Input Signals Reaching It.

ROYAL PHOTOGRAPHIC SOCIETY: MEDICAL GROUP.—At Commonwealth Building, Hammersmith Hospital, 6.30 p.m., visit to new department of medical illustration of Royal Postgraduate Medical School.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—4 p.m., Mr. J. I. Burn: Cancer Chemotherapy and the Surgeon.

ST. MARY'S HOSPITAL MEDICAL SCHOOL.—At Wright-Fleming Institute Theatre, 5 p.m., Aleck Bourne lecture by Mr. E. A. Williams: Congenital Absence of the Vagina.

WHIPPS CROSS HOSPITAL.—At Medical Education Centre, 5 p.m., clinicopathological conference.

Friday, 6 October

INSTITUTE OF DISEASES OF THE CHEST.—5 p.m., Dr. N. C. Oswald: clinical demonstrations.

INSTITUTE OF LARYNGOLOGY AND OTOLOGY.—4.30 p.m., annual address by Dr. P. J. Lawther: Air Pollution and Disease. (At home to medical visitors from 2.30 p.m.)

NEATH POSTGRADUATE MEDICAL CENTRE.—At Neath General Hospital, 8.15 p.m., Professor A. C. Turnbull: Advances in Obstetrics.

ROYAL POSTGRADUATE MEDICAL SCHOOL.—(1) 10.15 a.m., Mr. T. Gibson: Bio-engineering Studies of Skin and other Human Tissues ; (2) 11.30 a.m., Mr. J. S. Calnan: clinicopathological conference (plastic) ; (3) 4 p.m., Professor W. I. Card: Clinical Medicine in the Computer Age.

SCOTTISH PSYCHIATRIC RESEARCH SOCIETY.—At Recreation Hall, Royal Dundee Liff Hospital, 11 a.m., all-day scientific meeting.⊕

WHIPPPS CROSS HOSPITAL.—At Medical Education Centre, 8.30 p.m., clinical meeting.

Saturday, 7 October

ROYAL COLLEGE OF GENERAL PRACTITIONERS: MERSEYSIDE AND NORTH WALES FACULTY.—At Liverpool Medical Institution, 3.15 p.m., Dr. T. S. Eimerl: A Look at General Practice in Australia and New Zealand.

ROYAL COLLEGE OF SURGEONS OF ENGLAND: FACULTY OF RADIOLOGISTS.—At Large Lecture Theatre, Medical School, Foresterhill, Aberdeen, 9.30 a.m., joint meeting of Diagnosis and Therapy Sections devoted to Radioisotope Scanning.⊕

Sunday, 8 October

BRITISH DIABETIC ASSOCIATION: MEDICAL AND SCIENTIFIC SECTION.—At School of Nursing Lecture Theatre, King's College Hospital, London S.E., 11 a.m., symposium for general practitioners: Clinical Diabetes.

ROYAL COLLEGE OF GENERAL PRACTITIONERS: MERSEYSIDE AND NORTH WALES FACULTY.—At New Medical Lecture Theatre, Liverpool, 10.30 a.m., symposium: Recent Advances in General Practice. Speakers, Dr. E. V. Kuenssberg, Dr. J. M. G. Wilson, Dr. P. S. Byrne, Dr. G. W. Roberts. (Details from Dr. A. E. Elliott, 1 Sandown Terrace, Chester.)

Universities and Colleges

LONDON

The title of reader in neurophysiology has been conferred on Dr. G. B. Arden in respect of his post at the Institute of Ophthalmology.

BIRMINGHAM

Appointments.—Dr. D. S. Rowe (reader in experimental pathology) ; Dr. P. Eckstein (reader in endocrinology).

ROYAL AUSTRALASIAN COLLEGE OF PHYSICIANS

The following candidates, who were successful at an examination held in Australia and Singapore, were admitted to Membership of the College on 14 September 1967: R. A. V. Benn, J. P. Chalmers, D. Curran, J. D. Gillies, W. Harvey-Smith, K. J. Hourigan, S. N. Hunyor, A. T. Lammi, R. A. Ouvrier, J. G. Polgar, L. P. Roy, S. K. Sinha, O. T. Stanley, D. J. Tiller, A. G. Walker, M. H. Williams, R. C. Wright, W. E. Woods, and J. S. Yu, of New South Wales ; T. C. Y. Choy, A. Ebringer, A. S. Gallus, J. Igra, G. C. McKay, D. C. Mauger, J. H. McDonald, C. R. F. Richardson, and A. P. Yung, of Victoria ; M. H. Alp, C. W. Bryan, W. Mirosch, and T. J. Myers, of Queensland ; A. B. Black, A. J. S. Corbet, and H. M. Dean, of South Australia ; J. W. Freeman, of Tasmania ; G. N. Cumpston, of Western Australia ; P. M. P. Choy, of Hong Kong ; K. C. Koh, of Singapore.

The following physicians were admitted to Membership of the College without examination under the special provisions of Article 37 on 5 May 1967: J. G. MacKenzie, of Victoria ; D. S. Nelson, of New South Wales.

The following physicians were admitted to Membership of the College without examination under the special provisions of Article 37A on 14 September 1967: D. G. Abrahams and G. C. Smith of New South Wales ; J. A. Forbes, of Victoria ; G. M. Maxwell and T. G. Paxon, of South Australia ; G. Howells, of A.C.T.

New Issues of Specialist Journals

Obtainable from the Publishing Manager, B.M.A. House, Tavistock Square, London W.C.1.

BRITISH JOURNAL OF OPHTHALMOLOGY

Contents of the October issue are as follows :

Xerophthalmia and Protein Malnutrition in Bantu Children. B. S. Kuming and W. M. Politzer.
The Chevalier Taylor and His Strabismus Operation. Fredrik Berg.
Mucocele of the Sphenoid Sinus : A Benign Imitator. A. L. Waldman, R. Merrell, R. B. Daroff, and A. Geltzer.
Primary Tuberculosis of the Conjunctiva. Desmond Archer and Alan Bird.
Primary Conjunctival Tuberculosis. A. W. Sollom.
Retinal Arteriolar Collaterals in Man. C. J. Ball and P. Henkind.
Influence of Menstruation on Glaucoma. Katherina Dalton.
Ocular Manifestations of Polyarteritis Nodosa. M. R. Nanjiani.
Chronic Retrobulbar and Chiasmal Neuritis. Bryan Ashworth.
Optic Nerve Glioma. John R. Condon and F. Clifford Rose.
Multiple Malignant Melanomata of the Uveal Tract in One Eye. R. A. Condon and Joan Mullaney.
Pyrrolidinomethyltetracycline in Cavernous Sinus Thrombosis. B. B. Khare.
Ophthalmological Synopses.
Simple Corneal Lamellotome for Keratoplasty. J. G. Louw, P. L. M. Le Roux, and E. F. Rhategan.
Reviews. Notes.

Volume 51, No. 10. Yearly subscription (12 numbers) inland £8 8s., overseas £9. With *Ophthalmic Literature* and Index (7 numbers) inland £15, overseas £16.

All communications with regard to editorial business should be addressed to THE EDITOR, BRITISH MEDICAL JOURNAL, B.M.A. HOUSE, TAVISTOCK SQUARE, LONDON W.C.1. TELEPHONE: 01-387 4499. TELEGRAMS: *Aitiology, London W.C.1.*
ORIGINAL ARTICLES AND LETTERS forwarded for publication are understood to be offered to the *British Medical Journal* alone unless the contrary be stated.
Authors desiring REPRINTS should communicate with the Publishing Manager, B.M.A. House, Tavistock Square, W.C.1, on receipt of proofs.
ADVERTISEMENT AND SUBSCRIPTION ORDERS should be addressed to The Manager at B.M.A. House, London, or at 415 Bourke Street, Melbourne, Victoria, Australia.
MEMBERS' SUBSCRIPTIONS should be sent to the SECRETARY of the British Medical Association, B.M.A. House, London, or to the Scottish Secretary, B.M.A Scottish Office, Drumsheugh Gardens, Edinburgh

British Medical Journal Supplement

LONDON SATURDAY 1 JULY 1967

CONTENTS

Annual Conference of Representatives of Local Medical Committees - 1
Removal Expenses - 12
Supplementary Annual Report of Council - 13
Annual Representative Meeting Supplementary Agenda - 13
Association Notices - 14

Annual Conference of Representatives of Local Medical Committees

Second Day's Proceedings

The Annual Conference of Representatives of Local Medical Committees met in the Great Hall of B.M.A. House, London, on 14 and 15 June. Dr. R. B. L. Ridge was in the chair. A report of the first day's proceedings was printed last week (Supplement, *24 June, p. 177). A report of the proceedings on the second day appears below.*

Payments for Special Experience and Service (Resumed Debate)

The Conference resumed at 10 a.m. on 15 June, with Dr. R. B. L. RIDGE in the chair.

Dr. W. B. WHOWELL (Leicestershire and Rutland) moved:

"That this Conference rejects the concept of merit awards as proposed by the B.M.A. working party but it is in favour of the principle of advancement of general practice, and believes that this can best be served by the setting up of a fund to which any general practitioner could apply for the reimbursement of expenses incurred in approved research projects and in approved courses of study of unusual duration."

Dr. Whowell said it was a general motion that should appeal to the Chairman of the General Medical Services Committee, since it did not tie his hands. He realized that the Review Body had stated that the money could be used for no other purpose than for merit awards, but there was a large sum of money available. If the Ministry showed its good faith in its desire to advance general practice and if the Review Body endorsed it the money could be made available for the advancement of general practice. The motion asked for nothing specific and it left the negotiators to obtain what terms they could.

Dr. J. C. CAMERON, Chairman of the G.M.S. Committee, said that, in view of the Conference's decision on the previous day, he was willing to try to carry out the terms of the motion, but it was not going to be easy. It was not a matter for negotiation but of trying to enlist the sympathy of the Minister of Health. Provided that he was allowed a broad interpretation, he was willing to accept the motion.

The motion was carried.

Dr. A. LASK (Middlesex) moved: "That this Conference affirms that it has the future well-being of general medical practice at heart, denies Luddite tendencies, and calls upon the Government to show its sincerity as follows: to use the money allotted for advancement allowances prospectively not retrospectively as awards not rewards; as grants and not part of the pay structure—e.g., experimental and research projects—for sabbaticals, for study leave, and other appropriate schemes."

Dr. Lask said that those in the "highest circles" had strange ideas about general practitioners. They said general practitioners were obstinate, that they were reactionaries on the medical scene, that they had no vision, that they were "Luddites thwarting the progress of medicine." Because general practitioners saw people in their houses, flats, and cottages general practice was called a cottage industry. General practitioners were called mercenary. He hoped the Minister would listen to the wisdom and the experience of general practitioners, and use the money for specific grants and allowances. The Minister should be forward-looking.

Dr. G. R. OUTWIN (Doncaster) said that the profession had unequivocally rejected merit awards. Neither the Ministry nor the Establishment could be in any doubt about the views of the profession. It should retain its dignity. It would be graceless for it to go back and say, "We don't want the money in this way, but we would like to have it in another way."

The motion was lost.

Other Schemes

Dr. A. SPEAKMAN (Liverpool) moved: "That the G.M.S. Committee is requested to prepare schemes for the financing of projects, scholarships, exhibitions, etc., for which general practitioners could apply; also a scheme for the reimbursement of time spent in committee work in the service of general practice as a whole."

The motion was lost.

Dr. A. POLLACCHI (Dunbartonshire) moved: "That, since the Government appears to have £2¼ million to spend on the special payments but is unwilling to allow it to be spent in any other way connected with doctors' remuneration, this Conference suggests that this money be devoted to cancer research."

Dr. SPEAKMAN (Liverpool) moved as an amendment: "That the sentence be altered to read 'This Conference suggests that this money be devoted to cancer and other research in general practice.'"

The amendment was carried.

The motion as amended was lost.

Dr. F. R. B. H. KENNEDY (Isle of Wight) moved: "That this Conference suggests that the £2¼ million be used for the establishment of chairs of general practice."

He said that neither the Minister nor the Review Body were likely to allow this money to go into the pockets of general practitioners, but the motion was a reasonable suggestion for improving general practice. A speaker the previous day had asked for departments of general practice—a department needed a professor and vice versa.

Dr. A. C. ALLEN (Inner London) moved as an amendment: "That the words after 'establishment' be deleted and the following substituted: 'of departments of general practice in teaching and district hospitals staffed by general practitioners.'"

He said that the G.M.S. Committee should be given more direction. The amendment would show general practitioners in this country that the Conference was interested in them.

Dr. G. S. R. LITTLE (Inner London) said the idea of the amendment was to extend the motion. The professorial, academic mind might not always be in touch with the day-to-day affairs of general practice. The motion amended in this way would give a better return.

The amendment was lost.

A motion to pass to the next business was carried.

Direct Charges to Patients

Dr. P. SPENCE (Cheshire) moved: "That the General Medical Services Committee should continue to make representations to the Minister that a doctor be permitted to make a charge to N.H.S. patients for arranging private hospital treatment or private consultation."

He said that when a general practitioner met a consultant at a domiciliary consultation much time was consumed. A consultant often suggested a time for the consultation after surgery hours, perhaps at a weekend. So much depended on the general practitioner's knowledge of the medical history of the case that his place at the consultation could not be taken by a partner or deputy. Surely doctors should be allowed to charge a modest fee for this extra work which the patient in most cases would be only too willing to pay.

Dr. D. NUTTALL (Leeds) supported the motion. He said that if it was accepted it would not bring any hardship on any patient. Dr. F. J. DAVIES (Dudley) said it was a mean motion based on the principle, "If I can't have it, why should the consultant?"

Dr. B. J. KENDRICK (Nottingham County and City) was against the motion on principle. It was wrong that a patient could decide to be a private patient on some occasions and a National Health Service on others.

Dr. CAMERON said that it was not quite so simple as the last speaker had made out. There were many people who insured for hospital and consultant treatment and yet remained on a doctor's N.H.S. list. General practitioners were not unwilling to help their patients to have their treatment in whatever form they wished it, but there was much to be said for the doctor being recompensed for the time spent in making the arrangements for his N.H.S. patients to have specialist treatment privately. During the negotiations the Minister had been sympathetic on this matter, but in the end he had come down against the idea, because, as he had often put it, while he did not want to do anything to discourage private practice, he was not prepared to do anything which might encourage it. Dr. Cameron did not think any further progress would be made on this subject in the present political climate, but at an opportune moment further efforts might be made to open discussions again.

The motion was carried.

Prescribing Oral Contraceptives

A motion by Warwickshire and Solihull and one by Inner London were, by leave, withdrawn, and substituted by the following composite motion:

"That the recommended fee of 10s. 6d. for a private prescription for oral contraceptives is entirely inadequate and unrealistic, and there should be a revision of paragraph 10(1)(G) of the terms of service so that a proper fee can be agreed for the examination of and the advice given to a patient when the work is done solely as a result of her request for contraception and is not indicated by any of the signs or symptoms of medical or physical disease."

Dr. T. A. W. PARKES (Warwickshire and Solihull) said that the motion called for a review of the paragraph of the terms of service which stated that no fee should be demanded or accepted for examining or advising patients in connexion with contraception, though a fee could be claimed for writing a prescription for contraceptive pills or appliances. Dr. Parkes said that in his area there was a great demand for oral contraceptives, and that meant far more than writing a prescription. It was necessary to take a careful history and make a detailed examination followed by advice and instruction and a follow-up at intervals. Most of the requests were on purely social grounds and could not be regarded as treatment. It was a time-consuming procedure for which the doctor should be paid a proper fee.

Dr. M. L. HUDSON EVANS (Inner London) supported the motion, and hoped that its scope would be widened. Dr. H. S. SAMUEL (Berkshire) opposed the motion. The provision of contraceptives should be, and always was, accompanied by the necessary examination, and it was important to the patient's mental and physical health as well as to that of her husband. It was impossible to draw the line between what was mental and physical health and what was not. This was essentially part of medical services, and it was derogatory to the profession to demand an extra fee.

Social and Medical Indications

Dr. JOAN CHAPPELL (G.M.S. Committee) said that the subject was much more complicated than it appeared at first sight. Family doctors could not escape their responsibility for giving contraceptive advice. To distinguish between the medical and social indications for contraception was unrealistic. A doctor's first concern was with his duty to his patients. Legal opinion had been taken and she believed that an amendment to this section of the terms of service was already in hand.

Dr. CAMERON said that progress was being made, but negotiations had broken down because of the difficulty in separating medical from social grounds. He hoped that the Conference would allow the matter to rest for the moment.

Dr. SHERLOCK (East Suffolk) reminded the meeting that before the National Health Service doctors charged their patients what they thought was reasonable in the circumstances, in some cases nothing. Today a fee of half a guinea was worth little. The advice would be cheap at double or treble the amount.

The motion was lost.

Bolton, by leave, withdrew a motion "That this Conference registers its protest at the delay in settlement of the Pool payments for the years 1964–5 and 1965–6, and urges the Minister of Health to expedite an early settlement of these payments."

Payment by Salary

Dr. ALLEN (Inner London) moved:

"That this Conference instructs the General Medical Services Committee to cease all negotiations on a salaried service for those who desire it until the Minister of Health agrees that provision for payment by item of service, envisaged in the Charter, should also be made available for those who wish to be remunerated in this way."

He said that, despite his promise, the Minister had refused to consider payment by item of service. General practitioners must face the Minister's intransigence with determination. So long as he refused to discuss what doctors wanted they should refuse to discuss what he wanted.

Dr. D. DEENY (Armagh) said he did not believe that the item-of-service method of payment was contrary to socialist ideas. If there was such a method of payment it would show that doctors were now being poorly paid. The existing method of payment was only indirectly related to the amount of work done. Item-of-service payment was part of the Charter. It was the method by which their dentists were paid, and it was the method in use in many countries.

Dr. R. W. SMITH (North-east London) said that he did not find the existing method of payment particularly distasteful, and any scheme for payment by salary would need to have very definite advantages before he would be prepared to consider it. Nothing acceptable had so far emerged in the discussions with the Ministry, but that was no reason for not exploring the matter further. That was what any trade union would do—explore all the possibilities. Doctors could learn from the flexibility of approach of their Continental colleagues.

Dr. G. MURRAY JONES (G.M.S. Committee) said that a salaried service meant being paid on a sessional basis, as were consultants. No form of payment should be thrust on the medical profession. There must be trial schemes.

Dr. J. S. NOBLE (G.M.S. Committee) asked the Conference to read the motion carefully. It said nothing about exploring the possibilities: it said "cease all negotiations." He hoped the motion would be passed. The doctor had an individual responsibility to his patient and the patient had a loyalty to his doctor. The personal relationship was being eroded, and there must be a return to the individual element rather than the salary element in the payment of doctors. This could be done by negotiating an item-of-service basis of payment.

Dr. C. J. SWANSON (G.M.S. Committee) spoke against the motion. He had in mind doctors who worked in remote places. Many of them would prefer a salary, and he did not want to have to go back to them and say, "You cannot possibly have a salary until Inner London doctors are paid by item of service."

Dr. KENDRICK (Nottingham County and City) said that what the profession had in mind was payment on a sessional basis, but when the Minister talked about salaried service he meant a service like the Army or the police. The profession should be prepared to talk to the Minister about sessional payments, but it was stupid to negotiate a salaried service when nobody wanted it.

Breach of Faith

Dr. I. M. JONES (G.M.S. Committee) supported the motion. The Charter for the Family Doctor Service had had a wider measure of support than any other recent proposals for general practice. The Charter had stated that a doctor should have the option of payment by capitation, by item of service, or by salary. The Minister of Health had accepted the Charter as a basis for negotiation. Since then he had been prepared to discuss ways of implementing the salaried option but unprepared to discuss the implementation of the item-of-service option. That was a breach of faith. The Conference should meet the Minister's obduracy with obduracy, and state that it would discuss the Charter in full as originally agreed.

Dr. E. V. KUENSSBERG (G.M.S. Committee) said that the motion was telling Dr. Cameron how to conduct the negotiations. It was wrong to tell somebody so experienced in negotiations how and when to play his trump card.

Dr. CAMERON said that to pass the motion would be doing an injustice to those doctors, however few, who wanted a salaried method of payment. The G.M.S. Committee had been asked to devise some method of salaried payment for a limited number of doctors in selected areas, perhaps in group practices. Mention had been made of sessional payments. The Ministry's proposals had been merely a salaried method of payment. The G.M.S. Committee intended to discuss the matter again with the Ministry. If this motion was passed it would be the end of the discussions. That would not worry him personally, but it would be an injustice to those doctors who had supported the Charter and who wished for an experiment in payment by salary.

Dr. ALLEN, replying to the debate, said, "We are weakening, in the same way as we did last year on merit awards. This is . . . where the chink in the armour will occur if we fail to show the Minister that we mean what we say. He will know that the same weaknesses as occurred over merit awards will occur again and again, and he can do what he likes. I beg you to pass this motion."

The motion was carried.

Government's Failure

Dr. M. D. MANSON (Denbigh and Flint) moved: "That the G.M.S. Committee shall not agree to any form of salaried employment for general medical services until the detailed terms and conditions have been approved by the Conference."

He said that a choice of salaried service was part of the Charter. Therefore general practitioners must state their terms and lay down the principles which should govern negotiation. Sessional contracts should form the general basis of the service, and be similar to that for consultants. Full-time service should consist of eleven sessions, and maximum part-time service should consist of nine sessions. A part-time arrangement would enable a general practitioner to combine his work with sessions in hospital, industrial medicine, public health, insurance work, or private practice.

Work load must be clearly defined, said Dr. Manson. Under a salaried contract with rising demand and a decrease in the number of doctors, the profession could no longer accept corporate responsibility for covering any particular number of the population. Doctors would be responsible only for the amount of work for which they had contracted. It would be for the Government to provide additional doctors to meet additional demand. There must be radical changes in disciplinary arrangements. Doctors should be answerable only for their actions during the sessions for which they had contracted. It was vital that no final decision should be reached until a full report had been considered by the Conference.

Dr. SPEAKMAN (Liverpool) moved as an amendment: "That at the end be added the words: 'and the majority of general practitioners in the N.H.S., if necessary by plebiscite.'"

The amendment was carried.

Dr. G. P. WILLIAMS (G.M.S. Committee) believed that there should be flexibility, and both patients and doctors should be able to exercise a wide choice in the arrangements for medical care. It was right that those doctors who did not want a salaried service themselves should support those who did. They must insist on sessional terms and on limiting the work load to a level consistent with good medicine. The actual work load was what should be considered, and not the list size. The terms of service must be tailored to match.

Doctors must state their own terms, and state them in public. If there was any rejection to be done, let the Government do it. The Government should be seen to refuse for general practitioners terms and conditions of service which the consultants already enjoyed. Doctors who advocated a salaried service had their heads in the clouds, because the Ministry could not agree to the sort of salaried service which the profession would accept, nor could the profession accept what the Ministry was likely to propose without creating a dangerous precedent for general practice as a whole. He hoped the motion as amended would be passed.

Dr. CAMERON agreed that the use of a plebiscite was the best way to ascertain the opinion of the profession.

The motion was carried.

A similar motion by Kent was ruled to be covered by the last motion.

Other Motions on Remuneration

The following motions were withdrawn:

Motion by LEICESTER: "That this Conference, while not being in favour of payments for special experience and service to general practice, considers that payments for general experience are inadequate and should be revised."

Motion by WARWICKSHIRE AND SOLIHULL: "That, though we recognize that the present system relieves some anomalies, our negotiators should still press for adequate payment for optimum list size."

Dr. J. RUFFELL (Kent) moved: "That, in the opinion of this Conference, the overall level of remuneration contained in the 1966 Review Body award is too low and is unlikely to increase recruitment or to stem emigration."

He said that the Review Body award bore unfairly on different sections of the profession, and it had been bedevilled by Government intervention as a result of the national economic policy. A proper comparison ought to be made with other countries which were successfully competing for doctors. In Canada, U.S.A., Australia, and New Zealand general practitioners received an average of about £10,000 gross per annum. In this country they received far less and for unlimited work. Since the award there had been no significant drop in emigration and no significant upward trend in recruitment. The conclusion was that the Review Body award had been too little and too late.

The motion was carried.

Dr. J. C. KNOX (Tynemouth) moved: "That the Review Body's urgent attention be drawn to the fact that up to April 1967 Government implementation of their recommended award in respect of general practitioners falls short by approximately £18m. and that the Review Body be asked to recognize this fact in their next review."

The motion was carried.

Refund System

Dr. WHOWELL (Leicestershire and Rutland) moved: "That the effect of the recent doctors' charter is likely to lead to a salaried service unless active steps are taken to prevent this, and that this Conference urges further consideration of a refund system of payment for general-practitioner services."

Notice of an amendment by North-east London was given: "To delete all the words up to and including the word 'and.'"

Dr. WHOWELL said he accepted the amendment. The idea of a refund to the patient had been mooted many times before, and the major argument against it had been the difficulty of administration. In view of the proliferation of forms required to obtain payment for the various items of service under the new pay structure this argument was no longer valid. Many countries had a refund system which apparently worked satisfactorily.

Dr. CAMERON said that the refund system should be given consideration. It was one of the methods of remuneration in European countries.

The motion as amended was carried.

Dr. LITTLE (Inner London) moved: "That additional payments should be made towards the employment of a locum for up to six weeks each year on the same scale and basis, and under the same conditions, as those provided in the scheme for additional payments during sickness."

He said that doctors should be encouraged to take holidays. Locum fees were an extra expense, and it was quite impossible to make provision for a holiday out of the basic practice allowance.

Dr. KENDRICK (Nottingham County and City) said that the Minister ought to pay the cost of a doctor's holiday locum and the Minister should be responsible for providing the locum, as in the hospital service. However, Dr. Kendrick said he was against the motion, because to start to negotiate now about itemizing the cost of holidays would weaken the doctors' overall case. The Conference had already asked the G.M.S. Committee to itemize each item in the basic practice allowance, and that included six weeks' holiday and a locum allowance.

The motion was lost.

Professional Negotiator

Dr. D. Clarke (Lanarkshire) moved: "That this Conference recommends the appointment of a suitably qualified and adequately paid professional negotiator to represent the profession in any future negotiations regarding remuneration."

He said that general practitioners were not suited to conduct the necessary detailed negotiations. By training they were too trusting. The present negotiators should continue to negotiate on broad principles, but the details should be left to people trained in the minutiae.

Doncaster and Sheffield moved as an amendment that the motion should read: "That this Conference recommends the appointment of a suitably qualified and adequately paid legal adviser who would accompany the profession's representatives during the course of all negotiations with the Ministry on remuneration and terms of service."

Dr. W. P. Lambie (Sheffield) said he was not in favour of a professional negotiator. The profession should be represented only by active general practitioners. However, he had been particularly impressed by the success of counsel who had presented the profession's case to the Review Body. A lawyer should accompany the negotiators. Dr. G. R. Outwin (Doncaster) supported the amendment. Dr. Cameron would say that legal advice was always available, and was frequently sought. But Dr. Outwin said he wanted the legal adviser to be present on the occasions when it was not expected that his advice would be needed.

Dr. Kendrick (Nottingham County and City) also supported the motion, but Dr. A. A. Brown (City of Edinburgh) told the Conference that it would cost in the region of £10,000 a year.

Dr. A. B. Davies (Staffordshire) said that to pass the motion would be a vote of no confidence in Dr. Cameron and his fellow negotiators. He had experience of negotiating, and he knew that when documents were being prepared expert legal advice was taken. But it would be nonsense to have a legal adviser at all negotiations with the Ministry. Their own negotiators were selected because they had a detailed day-to-day knowledge of every part of general practice.

Dr. R. A. Keable-Elliott (G.M.S. Committee) hoped the motion would be rejected. The negotiators had to negotiate. The only way to do that was to know the background to the whole matter and to know the feeling of the profession, and nobody was in a better position for that than Dr. Cameron and his team.

Facts Not Known

Dr. Kuenssberg (G.M.S. Committee) said it would be foolish to accept the motion. The proposers of the motion just did not know the facts. Whenever big issues were at stake legal advisers were always with the negotiators. Professional advisers were available all the time—that was what the Secretariat was. It had been said that a legal adviser would notice the flaws before the negotiators—what nonsense! The procedure of negotiation was that possible ways for making progress were discussed, and then something was committed to paper. Once it was on paper it was shown to all the experts.

Dr. A. M. Maiden (G.M.S. Committee) said that in the majority of negotiations the people required were those who knew general practice from the practical side. It was a waste of time and money to engage a highly paid legal adviser and it would not help. The G.M.S. Committee had always taken the view that *ad hoc* expert advice should be taken when it was needed.

Dr. Cameron said he had given much thought to the idea of a professional negotiator, but he had become firmly of the opinion that in negotiating on general practice matters it was better to have doctors facing the Ministry than professionals. Much money had been spent on legal advice during the course of negotiations, and looking back he did not think the profession had done too badly.

Dr. Clarke, replying to the debate, said that there was no question of a vote of confidence. General practitioners needed their present team, but they also needed legal advice, especially if they went into a field which was unexplored, such as salaried service. The cost could be dismissed.

The motion, as amended, was lost by an overwhelming majority.

Practice Premises

Dr. Cameron moved: "That paragraphs 82–91 of the report of the G.M.S. Committee be approved."

The motion was carried.

Dr. R. G. G. Gain (Hertfordshire) moved: "That, in view of the recent continuing reduction in bank rate, the interest rate charged by the Finance Corporation is unrealistic and unattractive and should be reduced forthwith."

He said he did not wish to decry the work of the General Practice Finance Corporation. Since it was set up the bank rate had twice fallen. It now stood at 5½%, whereas the Finance Corporation rate remained at 7¼%. His local medical committee thought it should be reduced to a lower and more realistic figure.

Dr. S. Wand, a member of the Finance Corporation, said that it had a statutory duty to secure that its revenue was sufficient, taking one year with another, to make provision for meeting all charges properly chargeable to revenue account, including allocations to reserve. The Corporation had been directed to set up a reserve. It did not necessarily follow that because the bank rate went down money could be borrowed at a lower rate at that particular time. The 7¼% charged by the Corporation did not leave much for the expenses of the Corporation and for providing a reserve. He had tried to get the rate as low as possible, and this rate was the lowest possible at the moment. The advantage of the Corporation was that it was possible to get 100% loan, including the expenses incurred in building or acquiring a property.

Dr. Cameron hoped that the Conference would not vote on the motion. Dr. Wand had said that everything possible would be done to keep the rate as low as possible. The Finance Corporation was independent, and it would be unfortunate if the motion was passed.

A motion to pass to the next business was put, seconded, and carried.

A motion that the speeches of movers of motions should be limited to three minutes and those of other speakers was moved and carried.

Terms of Service

Dr. N. S. Malimson (Salford) moved: "That this Conference recommends that there shall be no allocation of patients to a doctor's list without the doctor's consent."

He said that the profession had been inculcated with the idea that there was such a thing as compulsory allocation. There was no power of compulsory allocation. The profession had been deluded for too long. The Act placed on the Minister an obligation to distribute patients who could not find a doctor or who had been refused by a doctor. The Act did not place upon doctors an obligation to accept those patients.

Dr. Knox (Tynemouth) hoped that the Conference would pass the motion. For years lip service had been paid to the independence of the family doctor and his status; this would convert words into deeds. Dr. J. C. Arthur (Gateshead) said that the problem had grown in under-doctored areas, because the doctors could not take any more patients.

Dr. Kendrick (Nottingham County and City) opposed the motion. He was not worried about the existing allocation scheme, so long as doctors were sensible. Doctors had to preserve their right to be able to take a patient off their list without giving any reason.

Dr. Webb (Ipswich) asked whether the statement that doctors did not have to accept a patient allocated to them was correct.

Dr. Cameron said that further advice would have to be taken on that. The Minister took the view that the allocation scheme was necessary in order that he could fulfil his obligation to see that every citizen who wished was able to use the National Health Service. However, Dr. Cameron said he would resist doctors being compelled to take block allocations.

The motion was carried.

Dr. Ruffell (Kent) moved: "That this Conference considers that the G.M.S. Committee should negotiate list sizes beyond which no doctor should be required to accept the allocation of new patients."

He said his main concern was with block allocations. With the existing situation in which a declining medical force was still responsible for the continuous care of all people all the time he thought the allocation scheme was going to be used more and more. A figure of 2,000 was a list size beyond which no doctor could practise an adequate standard of medical service without undue physical and mental effort.

Dr. Keable-Elliott (G.M.S. Committee) said that the motion was meaningless, because it was asking the G.M.S. Committee to negotiate list sizes. What was important was the work that was done. Other things besides numbers determined the amount of work done, such as whether the doctor dispensed, whether he did his own midwifery, and so on.

Dr. Outwin (Doncaster) agreed that list size could not be negotiated, but it was the only tangible argument on which to approach the Minister. The Council had recently passed a motion to the effect that the profession could no longer accept overall responsibility for the preservation of standards of medical care which a modern community had a right to expect, and that tied in with the present motion.

Dr. CAMERON said that what was alarming him was the possibility of the allocation scheme being used for block allocation. The use of the scheme for that purpose would be resisted.

The motion was carried.

Dr. SPEAKMAN moved: "That any practitioner having a person assigned to him shall have the right of appeal to the local medical committee." The motion was carried.

Interim Treatment

Dr. T. K. COOKE (Yorkshire, North Riding) moved:

> "That this Conference requests the G.M.S. Committee to approach the Minister with a view to the immediate amendment of paragraph 2 of the allocation scheme so that it reads: 'It shall be the duty of a practitioner who refuses to accept a person who applies for acceptance to give the applicant such treatment, if any, as may be necessary.'"

He said that he realized that this point was currently under discussion, but in the meantime some colleagues might suffer from disciplinary procedure unless paragraph 2 of the allocation scheme was amended. The wording of paragraph 2 (*a*)—namely, to give the applicant such treatment, if any, as might be required by him pending his acceptance by or assignment to a practitioner—was, to say the least, ambiguous and wrong in substance. It was not for the patient to define the treatment. By inference, the motion implied that paragraph 2 (*b*) should be completely omitted. That read: "To inform the applicant of the name and address of any neighbouring practitioner, or practitioners, to whom application for acceptance might be made, and to inform him of the name and address of the council for the purpose of enabling him, if necessary, to secure assignment to a practitioner." However necessary that might have been in 1948, Dr. Cooke said, he could not see any reason why this entirely non-medical function should be placed upon doctors. A dentist on declining to accept a patient under the N.H.S. had no obligation to refer him to other dentists.

Dr. KNOX (Tynemouth) moved as an amendment: "Delete the words 'if any, as may be necessary' and substitute 'as the doctor may consider necessary at the time.'"

He said that the amendment set out the legal obligation. The original motion stated what they would do as their ordinary duty as human beings.

The motion as amended was carried.

Dr. SPEAKMAN (Liverpool) moved: "That a practitioner should be entitled to exercise his fundamental professional right to refuse treatment to a patient (other than in an emergency) in respect of whom he has no contractual obligation, and even then for limited duration."

He said that the motion only urged the Conference to restate a principle and give the G.M.S. Committee backing in order to preserve a right of the profession.

Dr. CAMERON accepted the motion, which was carried.

The following motions from Liverpool were also carried: (1) "That a practitioner's liability for the treatment of a patient must be defined in terms of time and place—i.e., the site where the patients elects to have any home treatment," and (2) "That, subject to adequate public safeguards, a practitioner must be capable of redefining his visiting area."

Dr. KNOX (Tynemouth) moved: "That a doctor who contracts out of evening and weekend work should be legally free of his contract with the National Health Service during the hours for which he has contracted out."

Dr. Knox said that under the new contract it seemed that a general practitioner could contract out of out-of-hours responsibilities provided he got someone else to do the work. Dr. Knox said he wanted to know whether the contract really meant that, and what was the exact position of a doctor who contracted out.

Dr. CAMERON said that contracting out freed the doctor from his obligations under his contract.

The motion was carried.

Minister's Unilateral Power

Dr. KNOX (Tynemouth) moved: "That the Minister's unilateral power to alter the terms of service is not acceptable to the profession."

Dr. Knox said he again wanted to know where the profession stood. In his view there should be a contract which was binding on both sides. It was true that the Minister could change the contract only "after consultation with the profession," but that did not mean after agreement with the profession.

Dr. KENDRICK (Nottingham County and City) opposed the motion. What the profession accepted was irrelevant, he said. What mattered was that doctors had stupidly signed a contract with the Minister in which the Minister could alter the terms of service without the agreement of the other party. It was quite legal and the doctors had been stupid enough to accept it.

Dr. CAMERON, in reply, said that under the new terms of service if the Minister put forward proposals which were unacceptable, the profession was at liberty to say they were unacceptable and that it was not prepared to carry on in the N.H.S.

Dr. SHERLOCK (East Suffolk) pointed out that the Minister's power could not be abrogated by the Minister or by anyone else.

The motion was carried.

Under-doctored Areas

Dr. CAMERON moved that paragraphs 79-81 of the G.M.S. Committee's report dealing with the special problems of acutely under-doctored areas be approved.

Dr. K. HACKETT (Wolverhampton) moved: "That, except where a request is made by an executive council to the Medical Practices Committee, all executive council areas should be 'classified' as a whole and not subdivided."

He asked leave of the Conference to insert after the first word "That" the words "in urban areas." The Conference agreed.

Dr. Hackett informed the Conference that Wolverhampton was divided into four areas for classification purposes, only one of which attracted designated area payments. The subdivision was unreasonable and irrational. Doctors in non-designated areas had patients in designated areas, and when a doctor left a designated area the repercussions were felt in practices all over the town.

Dr. MAIDEN (G.M.S. Committee) said that all executive councils were seeking to "display their wares" in the most suitable package in order to get the most money for the maximum number of doctors. That was fair enough, but it was important that the areas should be reasonable in size. Instability in designated areas must be avoided, and their size should not be too small. The Medical Practices Committee, of which he was chairman, thought in terms of 20 doctors as a minimum. There would be a better distribution of the money if areas were fairly large.

Dr. Maiden said that the whole question of payment for designated areas must be reviewed, but while the existing position remained it would be well not to have the Act altered.

Dr. G. M. TURNER (West Bromwich) said that West Bromwich had been asked to consider dividing its area into small groups of 15 to 20 general practitioners. That was thought to be the thin end of the wedge. It could be shown in West Bromwich that, though the figure was something like 4,500 patients per doctor, the area was over-doctored.

Dr. CAMERON said that if the motion were carried—and on balance he thought that it should be—it would go to the Medical Practices Committee.

The motion was carried.

Dr. G. MARTIN-JONES (Merthyr Tydfil) moved: "That the present method of assessing the under-doctoring of areas and work load of general practitioners is fallacious."

He said that the criterion based on calculation of lists was entirely fallacious. Doctors in Merthyr Tydfil were turned down on the figure of 2,505, which was only five over the figure required. He suggested the following criteria in evaluating an index or "points system": The Ministry of Social Security index; the average age of doctors in the area; the health of doctors in the area; the dependence of local hospitals and the public health service on general practitioners in the area; the demand of industrial concerns on general practitioners; the average number of contacts between patients and doctors; the number of patients aged over 60; the number of patients aged under 5; the total number of prescription forms; and the amenities of the area.

Dr. H. F. V. RIDDLE (Fife) said he came from an area which was partly industrial and partly rural. There had recently been a resignation in the industrial part leaving two doctors with something like 11,000 patients to look after. In the desirable, rural part of the area, where the doctors had their own cottage hospital and looked after a large number of patients, it had been possible to show that they were doing the work of an extra doctor between them, and on those grounds the area had been designated.

Dr. CAMERON accepted the motion, which was carried.

Health Centres

Dr. SMITH (North-east London) moved:

> "That, while not wishing to detract from any other form of practice, this Conference welcomes the Minister's response to the increasing demand of general practitioners for the opportunity to practise in health centres. Local medical committees, executive councils, and local authorities are requested to take all necessary steps to expedite provision of health centres for those doctors who wish to practise from them and to fully consult the practitioners concerned at the earliest possible stage of planning."

An amendment to insert the words "hospital authorities" after the words "executive councils" was carried.

Dr. SMITH said there was, and should be, variety in the methods of practice. Whatever form of practice a doctor had it was difficult for him to cope with the work load and to maintain satisfactory standards, but a rapidly increasing number of doctors were coming round to the view that when doctors worked as part of a team their difficulties were fewer. An increasing number of doctors considered that health centres provided a satisfactory vehicle for the work of such teams.

He recognized that many doctors would not accept that, and it was not the purpose of the motion to impose health centres on those who did not want them. The object was to ensure that doctors who wanted to work in health centres would be given the opportunity to do so.

Dr. RONALD GIBSON (Chairman of Council) said he opposed the motion not because he disagreed with it but because, in his view, it did not go far enough. He was concerned about the future of health centres. He had no doubt that they would play an increasing part in general practice, but not at the expense of urban and rural single-handed and group practitioners who were already properly housed, equipped, staffed, and sited. During his tour of the country he had encountered at least one group practice which had been disturbed by the possibility of a health centre being built literally across the road.

It was not sufficient merely to look at one aspect, said Dr. Gibson. In his view a complete appraisal of every facet and implication of working in a health centre should be asked for. There was the implication of a mass withdrawal from the Service, and the possibility or impossibility of a no-detriment clause to be considered. There was the question of security of tenure. But while doctors were thinking about these things health centres were being built.

It was not enough to talk about co-ordination and discussions between doctors. Dr. Gibson pleaded with the Conference, even though it might carry the motion under discussion, to carry unanimously a motion, appearing later in the Agenda, that called for a total investigation into all the implications of doctors working in health centres in the future.

Political Interpretation

Dr. SPEAKMAN (Liverpool) said he opposed the motion for one reason—namely, that he did not welcome the Minister's response. In his view the Minister's response had been so rapid that it was suspicious and spelt danger to the profession. "I think that the Minister is putting a political interpretation on health centres as opposed to a strictly medical interpretation," continued Dr. Speakman. "I have every sympathy with doctors who want to work in health centres, but would implore them to read E.C.N. 602 before they do anything."

Dr. ARTHUR (Gateshead) urged the Conference to reject the motion. It was dangerous, he said. He agreed with the Chairman of Council that the question of health centres should be looked into, but to press for the wholesale establishment of health centres was dangerous. Ever since 1948 practitioners had had to fight for their rights, and for many years their only weapon had been their independence. That independence was in turn dependent upon their owning the tools of their profession and their own premises. "Have health centres by all means," concluded Dr. Arthur, "but for goodness' sake own them yourself."

Dr. RIDDLE (Fife) supported the motion. There were many general practitioners who sincerely believed that they could practise better medicine in health centres, he said. Indeed, some 10% held that belief, and it was to be hoped that Conference would give them the backing they needed.

Dr. A. B. AISTROP (Brighton) suggested that the motion was most diabolically political. The words were ". . . this Conference welcomes the Minister's response to the increasing demand of general practitioners . . ." The Minister started it before he ever came into office. Before the Charter was negotiated the Minister was planning the setting up of health centres.

As to the "increasing demand of general practitioners," said Dr. Aistrop, one executive council magazine contained an analysis of inquiries made of general practitioners in different areas, and the number wishing to go into health centres greatly decreased when information on what it entailed was available.

A motion that the question now be put was carried.

Dr. SMITH (North-east London), in reply, rejected outright the suggestion that there was anything necessarily political about wanting health centres. There was nothing more political about wanting health centres than about not wanting them, he said. There was a rapidly increasing interest in health centres. Dr. Gibson had referred to security of tenure, but there was nothing in the motion urging doctors to go into health centres and accept bad contracts.

The motion was lost by 89 votes to 72 votes.

Dr. P. A. T. LOWDEN (Hampshire) formally moved: "That the British Medical Association be requested to issue a comprehensive memorandum on health centres."

He accepted an amendment, which was carried, that the words "British Medical Association" be deleted and the words "General Medical Services Committee" be substituted.

A further amendment, to add the words "when the N.H.S. is removed from direct political control," was not carried.

The motion, as amended, was carried.

Health Centre Tenancies

Dr. G. HIRST (South-west London and Surrey) moved: "That this Conference asks the G.M.S. Committee to safeguard the future independence of the profession by ensuring that health-centre tenancy agreements for practitioners shall be independent of the contract for services between executive councils and practitioners."

Dr. Hirst said that the Minister had promised some 500 health centres in the next 10 years. That would cover about 25% of general practice. The important point was not whether a health centre was a congenial place from which to practise medicine but whether practising from a health centre destroyed professional freedom. In the event of a disagreement between the profession and the Minister doctors practising from health centres would have no opportunity of withdrawing their services. If the Minister thought that health centres were desirable he should not offer them to the profession with strings attached.

Dr. B. D. MORGAN WILLIAMS (G.M.S. Committee) pointed out that the tenancy of a health centre would be a contract between the local health authority and the executive council, but if a doctor resigned from the service he would be in danger of eviction. That being so, health centres would be a menace to the health of the country. The health of the country depended on the efficiency of the profession and on the willingness of general practitioners to resign en bloc but still to be in the position to continue to provide medical services to the patients. If the contract was accepted in its suggested form, it would increase the doctors' reluctance to resign from the service. Dr. Morgan Williams suggested that if no changes were made in the contract the G.M.S. Committee should advise all practitioners to refuse to work in the premises provided. "We should continue to press for enough remuneration to own our own premises and ensure the health of the country by maintaining what is left of our independence."

Dr. OUTWIN (Doncaster) moved an amendment that the words "and Finance Corporation agreements" be inserted after "tenancy agreements." He submitted that the same principles applied to loans from the Finance Corporation as applied to health centres.

The amendment was carried.

Dr. F. C. RUTTER (Norwich) suggested that the profession could not afford to wait for a comprehensive memorandum. Norwich wanted to put up health centres in development areas, and here they would be in direct competition with established practices. A number of doctors were interested in going into health centres, but they thought it necessary to have a lease with the local health authority for at least 20 years, with the option of renewal.

"Licence to Practise"

Dr. A. M. FREEMAN (Middlesex) suggested that it would not be a tenancy agreement but a licence to practise. There had been a recent conference on health centres in London at which it was stated that a 30-year tenancy would be offered. The Ministry's document specified that there would be three months' notice in the event of resignation from the N.H.S., and among other conditions imposed by the Minister was one that would either involve a restriction of private patients or a close inquiry into practice income and expenses in order to determine the proportion which came from private practice. Dr. Freeman urged Conference to support the motion.

Dr. CAMERON said that representations had been made to the Minister to see what extension of security of tenure could be obtained, but the most that the profession's representatives had achieved was three months' notice and sufficient time, at the discretion of executive councils, to allow a doctor to make alternative arrangements. Dr. Cameron had pointed out to the Minister that that would be unacceptable to the profession, and general practitioners would be advised not to sign a contract unless greater security of tenure was offered. That remained the position.

Dr. Cameron said that it was doubtful whether a comprehensive memorandum could be produced for some months. He advised general practitioners to send any draft contract they contemplated signing to the G.M.S. Committee so that legal advice could be obtained on it. The Committee's own draft contract was being drawn up by its legal advisers, and it was hoped to issue this soon. The Finance Corporation circular insisted that a practitioner must be substantially employed in the Health Service, but if he had a large private practice it would be taken into consideration in fixing the rent.

Dr. KENDRICK (Nottingham County and City) opposed the motion. There were already many doctors negotiating and signing agreements with executive councils without taking legal advice, he said. There was no need to wait for a comprehensive memorandum. Doctors in the Cleckheaton health centre had negotiated an agreement which preserved certain rights should there be a change in the functions of the health centre. The doctors would have a say in the planning and siting of any new centre, which they insisted must be provided before they could be evicted from the first centre. The G.M.S. Committee should issue a warning notice to all practitioners immediately, stressing the importance of obtaining legal advice.

The motion, as amended, was carried.

Areas of New Development and Redevelopment

Dr. CAMERON moved that paragraph 92 of the G.M.S. Committee's report dealing with areas of new development and redevelopment be approved.

Dr. SPEAKMAN (Liverpool) moved the following amendment:

> "That the G.M.S. Committee will make representations to the Minister of Health that, where a local authority has failed to give a general practitioner or a group of general practitioners full and adequate opportunity to state his or their case in relation to dispersal of his or their practices or the siting of his or their practice premises in areas of redevelopment, all general practitioners in such areas shall receive compensation until a satisfactory agreement is reached and that this compensation shall include the maintenance of the level of their income at the level no less than it was on the date when the local authority's redevelopment or development plans begin to cause an outflow of population."

The purpose of the amendment, he said, was to give protection to the doctors in areas where local authorities went ahead with development plans without consulting the local doctors.

Dr. CAMERON said that the G.M.S. Committee was collecting evidence of cases where doctors had been severely hit in areas of redevelopment. If local medical committees would send in details of such cases, they could be taken up with the Ministry.

The amendment was carried. The motion, as amended, was carried.

N.H.S. Regulations

Dr. CAMERON moved that paragraphs 93–96 of the G.M.S. Committee's report dealing with N.H.S. (General Medical and Pharmaceutical Services) Regulations, 1966, be approved.

Dr. G. H. LLOYD (Devon and Exeter) moved the following amendment: "That, in the view of this Conference, the names of doctors seeing patients by appointment should not be specially marked in the lists of National Health Service doctors prepared by local executive councils and made available to the public."

Dr. Lloyd said that his local medical committee understood that if general practitioners who offered appointments systems had a special star against their name in public notices it was tantamount to advertising, and guidance was sought on this matter.

Dr. KUENSSBERG (G.M.S. Committee) suggested that such guidance should not be sought through a formal motion. The local medical committee could obtain the information from its representative, since the G.M.S. Committee had discussed the matter and it had seen no reason why general practitioners offering appointments systems should not be indicated in the executive council lists.

Dr. B. L. ALEXANDER (G.M.S. Committee) said that general practitioners had fought for the right to have an appointments system. Surely it was reasonable for a doctor to be able to indicate that he had such a system. To pass the motion would be a retrograde step.

Dr. CAMERON said that the question was under consideration by the Central Ethical Committee.

A motion to pass to the next business was carried.

Service Committees and Tribunal Regulations

Dr. MAIDEN took the chair in order to allow Dr. Ridge to present the report of the G.M.S. Committee's Working Group on Service Tribunal Procedure, of which he was chairman.

Dr. RIDGE moved that paragraphs 97–109 of the G.M.S. Committee's report dealing with N.H.S. (Service Committees and Tribunal) Regulations be approved.

He recalled that for years there had been motions on the Conference agenda criticizing service committees and tribunal procedure, calling for the abolition of the committees, and so forth. When the Fraser Working Party was set up its terms of reference had been to identify the cause of unrest in general practice, and to seek solutions and to make recommendations. Unfortunately, just when the working party's commentary was to be published the working party had come to an end, and its commentary on disciplinary machinery was never published. The Charter had demanded a drastic overhaul of the disciplinary machinery. A working group was set up, and it had produced a document for the negotiators which had the unanimous approval of the defence societies.

After the adoption by the Conference last year of the joint reports of the negotiations on the Charter as a basis for a new contract the working group was reconvened, and it enlisted the aid of legal experts and representatives of the defence societies. Dr. Ridge emphasized that, having studied the relevant paragraphs in the third joint report, the defence societies had declared that they were satisfied with the proposals. Nevertheless, the G.M.S. Committee had received expressions of disquiet from several local medical committees, executive councils, and B.M.A. Divisions, and it had re-examined the whole matter. After a long debate, and by a substantial majority, the Committee had decided to proceed with the proposals in the third report.

Unacceptable Proposals

Dr. A. C. DAWES (Warley) moved an amendment: "That this Conference considers that the proposals in the Third Report of Joint Discussions on the Family Doctor Service with regard to regionalization of medical service committees are unacceptable, and asks that the matter be referred back to the G.M.S. Committee for further consideration of all the implications involved."

Dr. Dawes said that some areas had managed to make the existing provisions work satisfactorily and others had not. In the view of his local medical committee the existing scheme should be amended to meet the needs of those who were dissatisfied. "The devil you know is always better than the devil you do not know," said Dr. Dawes, "and to introduce an absolutely new scheme is a dangerous experiment."

If the proposals for regionalization were implemented for years ahead the G.M.S. Committee would be busily amending the loopholes. It would be far better to amend the existing scheme to make it satisfactory. He failed to see what the opinion of the defence societies had to do with the Conference. The matter needed far more consideration, and he urged the Conference to refer it back to the G.M.S. Committee.

Dr. J. R. MILES (Gloucester County and City) supported the amendment. Time after time the local knowledge of members of a service committee had helped to avoid a miscarriage of justice. Dr. Miles did not think the appointment of a legally qualified chairman was a good thing. "If you have to be clobbered, it is much better to be clobbered by your own pals than by some civil servant in the next county."

Dr. M. R. SHERIDAN (Middlesex) opposed the amendment. Many general practitioners had had difficulty not only in dealing with uninformed lay members of service committees but uninformed chairmen, he said. Furthermore, in some executive councils almost every doctor was either a member or deputy member of the medical service committee. That led to invidious situations. A legally qualified chairman was a "must," in Dr. Sheridan's view.

Dr. H. N. ROSE (G.M.S. Committee) said that he spoke against the general view of the

G.M.S. Committee. He thought that in the proposals two essential safeguards were lost. One was the right to appoint the chairman of the medical service committee. Once the Minister was allowed to appoint the chairman general practitioners would not be able to appoint another one if they so wished. Secondly, if there were seven medical members of the executive council on the medical service committee they could get its recommendations modified by the executive council when they thought an injustice had been done. Furthermore, there were lay members of executive councils, and it was necessary to preserve their good will if medical service inquiries were to operate in a proper manner. The executive councils were against the proposition.

Independent Tribunal

Dr. I. M. JONES (G.M.S. Committee) opposed the amendment. It was, he said, a basic principle of justice that those sitting in judgement should be completely independent. The proposal for regionalization ensured that the majority of the tribunal would have no connexion with the case. Further, if the tribunal contained one layman and one doctor from the executive council area concerned the need for local knowledge was fully met.

It was important, said Dr. Jones, that there should be the maximum opportunity for relieving anxiety by the dismissal of a case at the earliest opportunity. That would be partly achieved by having legally qualified chairmen. It was equally important that a doctor who was arraigned should be able to count on getting justice.

Dr. A. M. READ (Portsmouth) asked the Conference to support the amendment. Before any changes were made in the existing procedure the views of all local medical committees should be canvassed so that the G.M.S. Committee could ascertain the amount of dissatisfaction with the present procedure.

Dr. G. JOLLY (Carlisle) said that his local medical committee was anxious to see "the end of this nonsense." It thought that, in a small area particularly, political considerations entered far too much into the matter, and too much pressure was apt to be put on a local chairman, who was placed in an impossible position. Carlisle wanted to see the matter taken as far away from local chairmen as possible.

Dr. R. W. RAE (G.M.S. Committee) said that, in his view, it was unnecessary to go to the lengths of setting up regional committees to rectify faults in the existing system. It was assumed that medical members attended the service committee hearings with an unbiased mind, and it had to be assumed that lay members did likewise. Therefore, it made little difference how the service committees were composed. He thought it would be better to leave matters as they were.

Dr. C. J. WELLS (G.M.S. Committee) suggested that a number of red herrings were being dragged across the debate. It had been said that executive councils resented a most important procedure being taken away from them. The Conference was not discussing the convenience of executive councils. It was discussing those unfortunate members of the profession who were arraigned before a service committee. "I think you would do a great disservice to your fellow practitioners were you to pass this amendment, because these are the ones for whom we have already a responsibility, and for whom we should do our best whenever we can."

Dr. WHOWELL (Leicestershire and Rutland) said he supported the amendment. His committee had written to every executive council in the country asking for their views and there had been over 20 replies strongly in favour of continuing the existing system. No replies had been received against. To state that it was necessary to consider only professional colleagues in the matter was scandalous. Justice must be done to all sides, and the existing system ensured this.

Securing Justice

Dr. RIDGE said that the endeavour was to secure that justice was done, and, more important, to secure that a very large number of doctors each year were not subjected to the anxiety of being involved in a formal service committee inquiry when there was no need for it.

The size of the problem was known exactly. In 1964 there had been 676 complaints. Of those 317 had been dismissed without a hearing. Yet those 317 doctors had had to suffer anxiety. Of the 359 hearings breaches had been found in only 118 cases, and of those breaches only 51 had been sufficiently serious to warrant a financial penalty. In the majority of cases —running into thousands—over the last eighteen years the defence societies had been involved and that was why their views were relevant.

The Ministry and the G.M.S. Committee thought that the Minister should nominate a chairman for appointment by the executive councils in the region, and the Minister would discuss the appointment with the Lord Chancellor. The appointment would normally be for one year, with the proviso that at the outset the initial appointment might be for longer. The Minister would consult the G.M.S. Committee about appointments and reappointments. There would be no deputy chairmen. Dr. Ridge assured the Conference that the G.M.S. Committee would not agree to anything in the way of new arrangements unless it was satisfied that they would be acceptable.

Judge, Jury, and Executioner

Dr. DAWES (Warley), in reply, said that it would be wise to refer the matter back to the G.M.S. Committee in order to provide a breathing space before regionalization came into effect, and time to see how the new Terms of Service were working. Under the regionalization proposals the Minister would nominate the chairman; would appoint the members of the service committee, apart from one medical and one lay member from the executive council; and would be the final court of appeal. He would, in effect, be judge, jury, and executioner, said Dr. Dawes.

The amendment was carried.

Dr. DAWES (Warley) moved a further amendment: "That this Conference considers that the chairman of a medical service committee should not be appointed by the Minister of Health, but should be elected by the executive council to which the committee is responsible, as at present."

He said the amendment was intended to ensure that a medical service committee was presided over by a chairman who had the confidence of the local people.

Dr. RIDGE said that the motion contained one glaring inaccuracy, that the service committee was responsible to the executive council. That was not so.

A motion to pass to next business was carried.

Dr. N. E. NATHANSON (Birkenhead) moved an amendment: "That, in the event of the new service committee procedure not coming into operation, the provision that complaints be considered informally by an *ad hoc* committee be added to the present procedure."

In the view of his local medical committee the most important part of the new proposals was that before any formal service committee procedure was brought into action there should be the most rigorous efforts to avoid it. That could well be done by an informal conciliation procedure.

Dr. A. WHITEWRIGHT (Bolton) suggested that an effort was being made to make a new law for a few bad cases.

Dr. RIDGE said that if Dr. Nathanson would withdraw the phrase "*ad hoc* committee" the amendment would be acceptable.

Dr. NATHANSON and the Conference agreed to the withdrawal of those words, and the amendment was carried.

Dr. DAWES (Warley) moved an amendment: "That this Conference considers that, while it is very desirable for the chairman of a medical service committee to be legally qualified, the proposals for reform of the machinery for hearing complaints against general practitioners should strongly recommend this qualification but not make it obligatory."

He pointed out that in some areas a legally qualified chairman might not be available, therefore the appointment of a legally qualified chairman should not be made obligatory.

Dr. RIDGE said that the amendment was in accordance with paragraph 40 of the third report.

The amendment was carried.

A further amendment standing in the name of Warley, to the effect that in the event of the chairman of a medical service committee not being legally qualified he should have wide experience of tribunal work, was carried without discussion.

Conciliators

Dr. E. PARKINSON (Dorset) formally moved an amendment: "That this Conference welcomes the formal recognition of the type of conciliatory work which has been successfully carried out for a number of years in many areas by clerks of executive councils, but instructs the G.M.S. Committee to make representation to the Minister of Health to ensure that each executive council shall have the option, in consultation with the local medical committee, to appoint as its conciliator either a lay member or the clerk of the executive council."

Dr. J. A. LEARNER (Derby) said that presumably the proposals in the third report for the appointment of a member of an executive council to act as conciliator arose because of unsatisfactory situations in some areas. In other areas, such as his own, the clerk and his staff had acted as conciliator for many years with complete impartiality and to everybody's satisfaction. When a local medical committee was satisfied the existing situation could remain undisturbed, but in areas where the committee was unhappy it could request the appointment of a member as conciliator.

Dr. Ridge referred the Conference to paragraph 36 of the third report which, he said, precisely covered the situation.

The amendment was lost.

Dr. Dawes (Warley) moved the following amendment:

> "That this Conference recommends that reform of the machinery for hearing complaints against general practitioners ought to provide that (1) the procedure to be adopted before, during, and after the hearing of a complaint is sensible, fair, and equitable to all parties concerned, and is adhered to in all areas as a standard practice; (2) the chairman of a medical service committee should have the right to view the initial documents of complaint and response, and be vested with power to reject those instances where a reasonable prima facie case is not implied by their content; (3) in the event of a formal hearing being decided upon, the practitioner against whom the complaint is made should have the right to be legally represented if he so wishes; (4) an appeal against the decision of the Minister of Health to a suitable higher authority should be possible, with proper safeguards against misuse; and (5) when the report of a service committee is sent by the Ministry to the G.M.C. the warning letter sent to the practitioner concerned should include not only the advice to consult his defence body before making a reply, but also to notify the secretary of his local medical committee that he has received a warning notice, so that the latter committee may advise the practitioner wherever possible."

A motion to pass to next business was put and carried.

Preserve Status Quo

Dr. Speakman (Liverpool) moved an amendment: "That in any alteration in medical service committee procedure the right of any local medical committee (with their executive council) to keep the status quo should be preserved."

He said the motion asked for justice for all local medical committees. Each local medical committee should be allowed to retain the status quo if it wished to do so.

Dr. Ridge said that the proposals in the third joint report did not concern procedure at all. They concerned solely the setting up and the election of chairmen. There was no suggestion that service committee procedure should be in any way amended.

The amendment was lost.

Dr. Dawes (Warley) moved an amendment: "That this Conference recommends that the mode of formation of medical service committees at present in use be continued, and that, suitably amended, it be made the basis for the formation of medical service committees in the family doctor service."

He said the amendment tied up the whole matter and made clear the decision of the Conference that it wanted a continuation of the existing procedure suitably amended to correct obvious shortcomings and to provide a medical service committee procedure acceptable to all.

A motion to pass to next business was put and carried.

Reimbursement of Expenses

The following motion by Inner London, incorporating an amendment by Denbigh and Flint, was formally moved and carried: "That a general practitioner who suffers the hardship of appearing before a medical service committee and is subsequently found not to be in breach of his terms of service should receive complete reimbursement for the expenses incurred in attending the committee, including the fee of a locum tenens. Reimbursement should also be made to general practitioners of expenses incurred in attending all N.H.S. (Service Committee and Tribunal Regulations, 1956) investigations."

At this point Dr. Ridge resumed the chair.

Forward Planning

Dr. Cameron moved that paragraphs 110 to 111 of the G.M.S. Committee's report dealing with forward planning be approved.

Dr. Ruffell (Kent) formally moved: "That this Conference requests the General Medical Services Committee to seek a re-appraisal and reorganization of the National Health Service in the light of current social conditions and of current available medical manpower. For this purpose it requests that the team of negotiators be broadened."

Dr. Noble (G.M.S. Committee) reminded the Conference of the unanimous decisions of the G.M.S. Committee and of the Council, supported by the Medical Practitioners Union: "(*a*) That the General Medical Services Committee believes that the present method of financing and organizing medical care in Great Britain requires re-examination and reassessment in the best interests of the community. (*b*) That the Committee is of the opinion that the Government should be requested to set up immediately an independent inquiry into the finance, administration, and staffing of the National Health Service." That request had gone to the Prime Minister, but no reply had been received so far.

The motion was carried.

A motion by Sunderland, that the N.H.S. should be removed from political control and vested in a public corporation which would administer the affairs and finances of the Service, and that the corporation should be empowered to take whatever steps it deemed necessary to make the Health Service a viable economic concern, was, by leave, withdrawn.

Dr. R. Hewitt (Salford) formally moved: "That this Conference deplores the lack of direct Government finance actively to promote the development of general practice and urges the Government to make immediate provision to provide general practitioners with the necessary facilities for improving the Health Service consistent with modern standards."

Dr. Cameron accepted the motion, which was carried.

Work Load

Dr. Cameron moved that paragraphs 112 to 114 of the G.M.S. Committee's report dealing with the work load of general practitioners be approved.

Dr. K. Hackett (Wolverhampton) moved: "That financial contribution by the patient at the time of service is essential to the maintenance of an efficient family doctor service."

The country could not afford the National Health Service, he said. There were still many doctors who were obliged to practise "soup kitchen" medicine, with two- to three-minute consultations, intuitive diagnosis, and blunderbuss therapy. It was the result of attempting to run family doctoring on a shoestring. The time had come when the provision of medical care must not be entirely a public responsibility. Part of it must be an individual responsibility. To ask a patient to contribute at the time of service would relieve the Chancellor of a responsibility which he could not fulfil and would restore a financial link between patient and doctor, thereby reducing frivolous demands upon the doctor's time.

Dr. F. C. W. Royle (Southampton) pointed out that the political climate was changing, and if the motion was passed it would show the Minister that it was what the profession wanted.

Dr. H. Glyn Jones (G.M.S. Committee) said it was fairly easy for a patient to pay the general practitioner at the time of his service but it was a very different matter when it came to hospital treatment. It would be an impossible state of affairs in which a patient paid his general practitioner but could go to the casualty department of the general hospital and receive free treatment.

A motion that the question be now put was carried.

The motion was carried by a large majority.

Dr. D. Gwyn Jones (Cardigan) moved: "That this Conference is of the opinion that nothing has been done to reduce the work load on general practitioners since the implementation of the Charter."

He said that during the last 12 months the work load had greatly increased.

Dr. Sheridan (Middlesex) moved an amendment to insert after the word "nothing" the words "material nor sufficient."

The amendment was carried, and the motion, as amended, was carried.

The following motion in the name of North-east London, moved formally, was carried: "That, because of the still serious situation in general practice, particularly with regard to the work load, patients should be expected wherever possible to attend surgery rather than to request home visits. The Conference strongly urges the Minister to take effective steps to achieve this objective."

Similarly, the following motion by Dundee was also carried: "That publicity be brought to bear on the working population to inform them that the deduction made from their pay packets for their 'National Health' stamps only pays for their general medical services in very small measure."

Dr. J. H. Marks (Hertfordshire) formally moved: "That the public ambulance service should be available to bring non-ambulant patients to general practitioners' surgeries."

Dr. G. D. Bolsover (Oxford County and City) moved as an amendment the addition of the words "and that the Minister should be urged to review immediately the whole problem of transporting non-ambulant patients to their doctor's surgery."

Dr. Webb (Ipswich) said that in Ipswich the ambulance service brought patients to doctors' surgeries as and when necessary. He advised representatives not to make an issue of the matter at the present juncture but to try to get their medical officers of health to provide the service.

The amendment was carried.

Dr. CAMERON said that this was a service that was certain to come about, and would probably be available in rural areas first. The sooner it was adopted as policy the sooner the G.M.S. Committee could begin discussions with the Ministry on the matter.

The motion, as amended, was carried.

Statistical Report

Dr. R. CONDIE (Midlothian, West Lothian, East Lothian and Peebles) moved: "That the G.M.S. Committee be instructed to produce a statistical report of the work load of general practitioners."

Dr. Condie said it might be argued that a comprehensive study of the work load in general practice had been done in the past. That was true to some extent, but the findings of various investigations had differed so widely that the Review Body in its Seventh Report had had to admit that it was difficult to base firm conclusions on them.

Dr. Condie said he had no illusions about the difficulties. Work load varied from practice to practice, from month to month, and from year to year. However, he was sure that had the profession been able to produce convincing evidence on work load for the Review Body on the last occasion it might have received a more sympathetic hearing. The proposed survey would give a base-line from which to judge figures obtained from similar studies in the future.

Dr. SHERLOCK (East Suffolk) was opposed to the motion. To carry it out, he said, would be too expensive and too time-consuming, and in any event doctors knew what their work load was.

Dr. W. O. WILLIAMS (Swansea) supported the motion, but pointed out that statistical evidence did not come down like manna from heaven. Wild guesses and opinions were a poor substitute for proper research. A detailed study of the work of the family doctor was being made in South Wales, and the G.M.S. Committee should actively support and encourage such projects.

The motion was carried.

Certification

Dr. CAMERON moved that paragraphs 115 to 116 of the G.M.S. Committee's report dealing with certification be approved.

Dr. WEBB (Ipswich) moved: "That this Conference considers the issuing of National Health Insurance certificates should not be a part of the general medical services provided by the National Health Service."

Dr. ARTHUR (Gateshead) said that certification had been simplified and more could be done. But he opposed the motion. As a general practitioner he was responsible for his patients, and if he was not to be the one to decide whether his patient was fit for work he would like to know who should.

Dr. CAMERON agreed that some progress had been made in the matter of certification but it was a difficult task, because so many people were involved. He asked the Conference to leave the matter to the G.M.S. Committee to carry out by stages.

Dr. WEBB (Ipswich), in reply, said that one of the objects of the motion was to try to raise the self-respect of the British employee by putting on him the responsibility of being honest.

The motion was carried.

Vocational Training and Continuing Education

Dr. CAMERON moved that paragraphs 117 to 120 of the G.M.S. Committee's report dealing with vocational training and continuing education be approved.

A motion by North-east London, that the Conference requested those responsible for medical education to see that more emphasis was placed on the importance of general practice as a potentially worthwhile career, was carried.

Dr. J. S. HAPPEL (G.M.S. Committee) informed the Conference that considerable progress had been made in the subject. In May the General Medical Council had approved recommendations on the curricula of medical schools for the next ten years, and general practice figured prominently in them.

Dr. H. S. HOWIE WOOD (G.M.S. Committee) moved: "That this Conference calls upon the General Medical Services Committee to collaborate with the Royal College of General Practitioners and the Ministry of Health in postgraduate educational activities for the general practitioner."

He pointed out that certain rewards had been offered to general practitioners who received some postgraduate instruction, but in practice it was not working out. Many general practitioners were attending a large number of lectures for which they would get no proper reward. As an example, Dr. Howie Wood instanced a full day's postgraduate course held in Winchester last December. At the end of the day those who attended were informed that the course had not been given prior approval so therefore no credits could be given. A request had been made six weeks before for one lecture to be recognized, but the Ministry had dragged its feet and after the lecture had been given the practitioners concerned were informed that no retrospective recognition could be given.

The motion was carried.

Dr. POLLACCHI (Dunbartonshire) moved: "That this Conference is of the opinion that regulations to permit a period of sabbatical leave of six months in each five-year period in general practice should be introduced, to enable general practitioners to broaden their experience in the medical and paramedical sciences."

He said the motion was to give the doctor something to look forward to. It gave him an opportunity to carry out some research in which he had an interest, and which would be to the benefit of himself and his patients.

The motion was carried.

Obstetric Courses

Dr. P. L. CONSTANTINE (Essex) moved: "That this Conference is of the opinion that continuing obstetric education courses for general practitioners should be conducted in designated postgraduate institutes which are academically incorporated into the university establishment, and calls for the initiation of discussions to that end."

He said that regrettably there had been little or no progress towards securing the necessary academic staff, facilities, and status for regional postgraduate obstetric centres. Those who had attended the residential course at Chelmsford would appreciate the need for adequate facilities. The Ministry recognized the desirability of those refresher courses. Attendance at them at intervals was one of the requirements for retention on the obstetric list. It was therefore difficult to understand why the Ministry's and universities' recognition had not been obtained.

The total number of doctors attending the course at Chelmsford in one year was greater than the number attending the courses at the "Mecca of obstetrics, Queen Charlotte's." Every month there was a perinatal conference at Chelmsford attended by the hospital staff and up to 50 local general practitioners. Once a year a weekend seminar was held at which distinguished consultants were present. That sort of work required time, money, and staff. Only by full recognition could those be obtained, and that question should be treated urgently. Dr. Constantine asked the Conference unanimously to support the motion.

Dr. CAMERON said that several times the profession's representatives, accompanied by Dr. David Brown, had been to the Ministry on the subject. If the Conference carried the motion it would give an opportunity of going back and reopening the whole problem.

The motion was carried.

Reimbursement of Expenses

Dr. A. M. FREEMAN (Middlesex) moved: "That direct payment for locum expenses for attendance at refresher courses should be restored."

Dr. CAMERON said he had sympathy for the motion, and it was something which the G.M.S. Committee could look at again. He reminded Conference, however, that on the previous day it had asked the Committee to get the basic practice allowance itemized.

A motion to pass to next business was carried.

A motion in the name of Berkshire, urging that reimbursement towards locum fees be continued when a doctor attended more than the minimum session requirements for qualification for basic practice allowance, etc., up to the previously accepted maximum of 22 sessions per annum, was, by leave, withdrawn.

Dr. MARKS (Hertfordshire) moved: "That a standard rate, applicable to general practitioners and consultants, be determined in respect of travelling allowances for attendance at refresher courses."

An amendment to delete the last five words, "for attendance at refresher courses," was carried.

Dr. Marks pointed out that general practitioners doing different types of work were paid at different rates though using the same car.

Dr. GLYN JONES (G.M.S. Committee) asked the Conference to reject the motion, which, he said, was dangerous. There was a standard rate for travelling in the hospital service which had been agreed under the Whitley procedure, and it covered all employees of the hospital service. It was in fact one farthing a mile more than it was 15 years ago. The rate had been regarded by the Central Consultants and Specialists Committee as unsatisfactory. If the motion was carried the Conference would be agreeing with the rate which the C.C. and S. Committee disapproved of.

The motion was lost.

Rural Practice

Dr. J. S. HAPPEL (Chairman of the Rural Practices Subcommittee) moved that paragraphs 127 to 132 of the G.M.S. Committee's report, dealing with rural practices, be approved.

Referring to his predecessor in the chair, Dr. C. F. R. Killick, Dr. Happel said that he had been a member of the Rural Practices Subcommittee for the past 20 years and its chairman for 17 years. He had served the Subcommittee well and faithfully. At the Ministry he had been "a tiger in the interests of rural practitioners." He had served for 13 years on the Government's mileage committee, and it was owing to his personal efforts that the Rural Practices Fund had remained almost intact. For those and all Dr. Killick's many other services to the profession the Conference would no doubt be glad to pay tribute. (Applause.)

On taking over the chair, Dr. Happel said he had found that his tasks fell into three parts. Firstly, to tackle the urgent problems of dispensing; secondly, the short-term question of the impending review of the Rural Practices Fund; and, thirdly, the need for a good look at the future of rural practice.

A Working Group had been set up to examine the problems of dispensing in detail, and its views were reported at several meetings with the main negotiators and with the Ministry. No more had been heard from the Ministry, in spite of a number of requests, until new proposals had been received on 24 May—some four and a half months later—and too late to put before the Conference. Dr. Happel said the Ministry's proposals were not very exciting. Preliminary consideration had been given to them, and counter proposals were being drafted in readiness for further talks. A report would be made to the profession when a decision was reached. Dr. Happel said he was grateful for the support in some of the motions on dispensing, but the Conference would understand if he asked that they be treated as references, since negotiations were going on.

When it became obvious that the talks would not be completed before the Conference met the Rural Practices Subcommittee obtained the consent of the G.M.S. Committee to have a special meeting of rural practitioners to discuss, among other things, whatever proposals might emerge. Constitutionally such a meeting could not have the power of the Conference, but he was sure Dr. Cameron would give an assurance that the G.M.S. Committee would carefully consider any resolutions passed.

Dr. Happell said that consideration of the future of rural practice had been entrusted to a working group of some of the younger members under the chairmanship of Dr. Michael Wilson. He had already commissioned some preliminary studies by individual members of the group into such things as patterns of rural practice overseas, including Europe; transport in rural areas; telecommunications; future financing of rural practice; and, last but not least, the place of single-handed rural doctors in the new contract.

A number of motions on dispensing and amendments thereto were, by decision of the Conference, referred to the Rural Practices Subcommittee *en bloc.*

Rural Practices Fund

Dr. HAPPEL moved that paragraphs 127 to 132 of the G.M.S. Committee's report dealing with the Rural Practices Fund be approved.

Dr. MANSON (Denbigh and Flint) moved that paragraph 131 of the annual report be referred back to the working group. It was, he said, disturbing to all rural practitioners to learn that it was not envisaged that any major alteration in the scheme would be necessary in 1968.

Dr. KILLICK (G.M.S. Committee) thanked Dr. Happel for his kind remarks. He had, he said, enjoyed every "battle." Referring to the amendment by Denbigh and Flint, Dr. Killick said the Conference would be amazed if it knew how many hours the Subcommittee had taken in dealing with the points raised by Denbigh and Flint. All the disputes and problems raised by that local medical committee had been investigated, and everything possible had been done to sort them out. Denbigh and Flint still had the right to appeal for the matter to be looked into again, and he suggested that was the proper course to take at the present stage.

Dr. A. J. ROWE (G.M.S. Committee) added that the question of the Rural Practices Fund had been looked at very carefully. Every local medical committee had been written to, and the replies had shown no major anomalies had arisen in the administration of the scheme. It might well be that at a later date the Fund could be administered in a different fashion, but at the moment there were no grounds for a major alteration in the mechanics of the scheme.

The amendment was lost.

The CHAIRMAN formally moved the following motion in the name of Cumberland: "That, in the event of the 10% increase in the Rural Practices Fund being found to be inadequate on revision to recompense divergencies between urban and rural practices under the revised provisions for payment of remuneration to general practitioners, any adjustment in the Fund should be retrospective to October 1966."

Dr. HAPPEL suggested there was some confusion. The amount was fixed by the Review Body.

The motion was carried as a reference to the Subcommittee.

Dr. E. PARKINSON (Dorset) moved: "That, having regard to the fact that profits from dispensing and rural practice payments constitute a financial subsidy for rural practice, the General Medical Services Committee be urged to ensure in its negotiations with the Minister of Health that any reduction in the former should be offset by a substantial increase in the latter, and in any case, remuneration under these headings should be considered in relation to each other."

Dr. HAPPEL said that the Minister had views on the subject. In the view of the Subcommittee subsidy in rural practice should be provided from inducement funds.

The motion was carried as a reference to the Subcommittee.

Planning Care in Rural Areas

Dr. HAPPEL moved that paragraph 133 of the report dealing with the planning of medical care in rural areas be approved.

Dr. A. M. SMEATON (Hampshire) moved: "That the General Medical Services Committee be invited to give special consideration to the problems of rural areas surrounding developing towns."

He said that he represented general practitioners in a market town in Hampshire which had become the victim of a "take-over bid" by the Greater London Council which would increase the population from 30,000 to 80,000 over the next seven years. One of the many problems concerned mileage payments. Until recently, 16 of the doctors in the town were eligible for mileage payments, serving a large rural area, and having at least 10% of their patients living outside the three-mile limit. Within the past year or so six doctors had fallen below the 10% and were no longer eligible for mileage payments. As the urban population increased, that trend would continue, and doctors would be more and more reluctant to accept patients living four to eight miles from the surgery. That must seriously affect the ability of patients in rural areas surrounding developing towns to get medical care, particularly from the doctor of their choice.

The motion was carried.

Maternity Services

Dr. CAMERON moved that paragraphs 134 to 135 of the G.M.S. Committee's report, dealing with general practitioner maternity services, be approved.

The following two motions, in the names of Southampton and of Devon and Exeter, were carried:

> "That when a maternity patient is transferred to hospital during labour where the general practitioner is in attendance, the full maternity service fee should still be payable."
>
> "That this Conference deplores the proposed closure of the existing general practitioner maternity units, which is against the interests of both patients and general practitioner obstetricians."

Compensation

Dr. A. N. MATHIAS (former Chairman of the Compensation and Superannuation Committee) moved that paragraphs 136 to 139 of the G.M.S. Committee's report, dealing with compensation, be approved.

He said he was presenting those paragraphs of the report with the permission of the chairman of the Compensation and Superannuation Committee, Dr. J. B. S. Morgan.

Approximately 500 repayments of compensation had been made to practitioners aged over 70, and the number of those expecting to receive compensation was set out in the report. The policy of the Committee remained unchanged, and at the appropriate moment, so soon as the "freeze" allowed, representations would again be made to the Ministry for the question of compensation to be looked at again. It was scandalous after all these years of continuous inflation that the matter still remained unresolved.

The following motions in the names of Gateshead and of Cardiff were carried:

"That this Conference reaffirms its firm adherence to the resolution of the Conference of 1966 on the subject of compensation."

"That this Conference strongly supports the action of the G.M.S. Committee on compensation. Nothing less than the proposals in paragraph 138 are acceptable."

Dr. A. B. DAVIES (Staffordshire) moved: "That this Conference deplores that even after 1972 some 3,000 doctors will still lack repayment of their compensation. The injustice to doctors at age 60 or with twenty years' service must be remedied forthwith."

He paid tribute to Dr. Mathias for the progress which had been made in the last year of his office. There were, however, still some things which had not yet been achieved, and the motion in the name of Staffordshire was an invitation to stimulate the negotiators to do even more.

The motion was carried.

Superannuation

Dr. MATHIAS moved that paragraphs 140 to 170 of the G.M.S. Committee's report dealing with superannuation be approved.

Dr. A. B. DAVIES (Staffordshire) moved: "That this Conference considers that the reply of the Minister of Health to the deputation on 12 October 1966 is regrettable. In the matter of older doctors with twenty years' service no special treatment is requested but an urgent reconsideration on both moral and actuarial grounds."

He said that again the motion was an invitation to Conference to stimulate those concerned to work even harder.

Dr. MATHIAS accepted the motion, and added that it was "a tough bit of negotiation." It was quite scandalous that the people who made the service tick for the first 10 to 12 years, underpaid and increasingly overworked, with little prospect, because of increasing years, of serving long enough to add to their pension, should be denied a backdating of the 1¾%. The Committee would press on, and when the freeze was over would go back and see what could be done in the matter.

The motion was carried.

Dr. WEBB (Ipswich) moved: "That this Conference considers it should be possible for a general practitioner to retire after 20 years' service with the pension accrued at that time."

He said that a practitioner should be able to retire in the circumstances described, and go to an underdeveloped country and do work there without prejudice.

Dr. MATHIAS said that the matter was under consideration in a much wider field by the National Joint Advisory Council of the Ministry of Labour, and the Committee had been asked to hold its horses until such time as Government policy on the whole of the report had been determined.

The motion was carried.

A motion by Cardiff, "That those doctors who opted out of the N.H.S. Superannuation Scheme in 1948 should now be given a fresh option as from 1 April 1967," was carried as a reference to the Committee.

Constitution

Dr. CAMERON moved that paragraphs 171 to 175 of the G.M.S. Committee's report dealing with the constitution of local medical committees, the Conference of Local Medical Committees, and the G.M.S. Committee be approved.

A representative asked whether a quorum was present.

The CHAIRMAN moved formally the following amendment by Cumberland: "That the election of direct representatives on the General Medical Services Committee shall be by voting power vested in individual general medical practitioners and not, as at present, by voting power vested in local medical committee members."

Dr. W. KEITH DAVIDSON (G.M.S. Committee) pointed out that at present the G.M.S. Committee was responsible to the Conference. If the retention of that situation was the desire of the Conference the motion must be rejected. The attitude of a member of the G.M.S. Committee depended on the advice and, in some cases, the instructions of his local medical committee. Under a system of direct election of the G.M.S. Committee by the periphery the policy adopted by the G.M.S. Committee would depend on the system of communications between the periphery and the G.M.S. Committee member and not necessarily through the local medical committee. Machinery existed at present, and if it were not perfect in all areas the present position might be improved. Communications, both ways, between the local medical committees and the G.M.S. Committee representative and, of course, between the periphery and the local medical committee might be improved.

The Conference had shown that it wanted to retain the right to advise and in some cases to instruct the negotiators. Passing the motion would mean that the negotiators would be directly responsible to the periphery, who elected them, and would have a diminished responsibility to the Conference.

Conference members, as far as representatives were concerned, were appointed by local medical committees, and it was quite illogical that the Conference executive, the G.M.S. Committee, should be elected differently.

The amendment was lost.

No Quorum

A demand was made, on a point of order, for the number present to be counted to determine whether there was a quorum.

A motion to suspend Standing Order 25, which stated that no business shall be transacted unless there be present at least one-third of the representatives appointed to attend, was not carried by the requisite majority.

On a count being taken, the CHAIRMAN ruled that a quorum was not present, and that the official business of the Conference terminated with the motion by Cardiff concerning doctors who opted out of the N.H.S. Superannuation Scheme in 1948.

Vote of Thanks

On the motion of Dr. SPEAKMAN (Liverpool) a vote of thanks to the Chairman was carried unanimously, a standing ovation being accorded Dr. Ridge, and the Conference terminated at 6.15 p.m.

Removal Expenses

The joint first report of negotiations between the Health Ministers and representatives of hospital medical and dental staff (*Supplement*, 27 May, p. 135) announced an extension of the existing removal expenses arrangements for medical and dental staff. A circular embodying these improvements has now been published (H.M.(67)39: Scotland, S.H.M. 39/1967), and the new arrangements began on 22 June.

The effect of the agreement is chiefly to extend the existing arrangements to include house-officers who transfer, on expiry of their appointments, to other posts in their existing grade, and medical assistants who move to another grade for approved training purposes. Consultants will also be included in certain approved cases.

The Minister will also consider reimbursement of removal expenses to doctors moving to a whole-time or maximum part-time consultant post when it is considered that there is a special need to attract candidates to a new post or where there has been or is expected to be difficulty in filling a vacancy in an existing post. Doctors taking up maximum part-time contracts will receive nine-elevenths of the sum payable to a doctor accepting a whole-time contract.

Doctors taking up appointments of up to six months' duration will be eligible for assistance with expenses, except the legal expenses of house purchase and sale, unless there is an established commitment to take a subsequent appointment in the same area.

Hospitality

A French doctor living in Paris would like his 18-year-old daughter to stay *au pair* with a British medical family from July for 6 months. In exchange the doctor would be pleased to receive a British girl aged about 18 to stay *au pair* with his family to help look after his other daughter aged 18 months, from September for 6 to 12 months.

A French doctor living in Rugles (Eure) would like his 22-year-old daughter to stay with a British medical family *au pair* for the month of August.

Would anyone who is interested please get in touch with Dr. R. A. Pallister, Medical Director, International Medical Advisory Bureau, B.M.A. House, Tavistock Square, London W.C.1.

British Medical Association

Supplementary Annual Report of Council, 1966-7

Since the publication of its Annual Report (*Supplement*, 6 May, p. 31) the Council has other matters which it wishes to report to the Representative Body.

Preliminary

Vice-President

289. It is with great pleasure that the Council recommends that Dr. John Oubridge Mercer, of Wellington, New Zealand, should be made a Vice-President of the Association.

Dr. Mercer has been Honorary Editor of the *New Zealand Medical Journal* for 28 years in addition to the many other outstanding services which he has rendered to the Association and to his colleagues in New Zealand.

> **Recommendation:** That John Oubridge Mercer, C.B.E., M.B., Ch.B., F.R.C.P. (London), F.R.A.C.P., M.A.C.P., be elected a Vice-President of the Association in recognition of his outstanding services to the Association and to the profession.

Private Practice

Fees for Part-time Services for Government Departments

(Continuation of Paragraph 145 of Annual Report)

290. The Council is now in a position to report that, following negotiations with the Treasury, agreement has been reached to increase the fees payable to general practitioners and consultants in respect of part-time services for Government departments by 10% on 1 July with retrospective effect to 1 October 1966.

Organization

Roll of Fellows

(Continuation of Paragraph 219)

291. The Council has approved the undermentioned for admission to the Roll of Fellows in 1967:

Division Making Nomination	*Nominee*
Nottingham Division	Vartan, Ronald Hepworth, M.B., Ch.B.

Other Association Activities

Ancillary Help

292. Council has noted the motion appearing in the Agenda for the forthcoming A.R.M. requesting an explanation why there is no reference in the Annual Report of Council to the following Resolution of the A.R.M. in 1966:

> 363. **Resolved:** That this Meeting wishes to draw attention of B.M.A. members to Medical Management Services Ltd.

During the debate on this item at the A.R.M. in 1966 reference was of course made to the services offered to members of the profession by Medical Management Services Ltd., and a full report of the debate appeared in the *Supplement* of the *B.M.J.* of 23 July 1966. To this extent the wishes of the A.R.M. have been fulfilled.

No further opportunity has been taken to draw the attention of the membership to M.M.S., because discussions with M.M.S. regarding the scope of the services offered by that body have not been completed.

The Council will therefore make a further statement as soon as it is in a position to do so.

Discount Trading

293. Independent Medical Services Ltd. has informed the Council that it has made an arrangement with a reputable discount trading organization which is prepared to offer its facilities to doctors. The Board of I.M.S. agreed, if Council so wished, that the scheme should be restricted to members of the Association, on the understanding that any established subscribers to I.M.S. who are not members should not be excluded. The Council has accepted this offer, and the scheme will be promoted by the Association as a benefit of membership. In order that this enterprise may be self-supporting it will be offered to members in return for a modest annual subscription to cover administrative costs.

The scheme will be administered by I.M.S., which will publish a catalogue containing a wide variety of branded goods on which the discount will, in the main, be of the order of 17–20%. A copy of the catalogue, with order forms, will be sent to each subscriber. Orders accompanied by remittances will be forwarded through the I.M.S. office, and the goods will be dispatched directly to the customer. The present range of goods is largely of personal, domestic, and household articles. Cars are available in certain areas of the country already, and arrangements are being developed elsewhere. Arrangements for trade-in value are being made. Furthermore, I.M.S. has on its own account arranged reduced rates for contract car hire for its members. In addition, the discount firm is prepared to deal in any type of goods for which there is a reasonable demand. The supply of professional equipment is under investigation.

The Council commends these arrangements to members.

RONALD GIBSON,
Chairman of Council.

Annual Representative Meeting 1967 Supplementary Agenda*

(Items received up to 26 June 1967)

Report of Agenda Committee

Order of Business

(To follow Item 10)

Amendment by TYNESIDE: That Item 557 be taken immediately after Item 270.

Amendment by EAST SUFFOLK: That Items 572 and 573 be taken immediately after Item 419.

Preliminary

Election of Vice-president

(To follow Item 15)

Motion by the Chairman of Council: That John Oubridge Mercer, C.B.E., M.B., Ch.B., F.R.C.P.(London), F.R.A.C.P., M.A.C.P., be elected a Vice-President of the Association in recognition of his outstanding services to the Association and to the profession.

Public Health

Fluoridation

(To follow Item 42)

Motion by KINGSTON-UPON-THAMES: That this Meeting notes with concern that many local authorities have not yet implemented the valuable preventive health measure of fluoridating the water supplies and urges all such authorities to review the situation immediately.

Free Milk in Schools

(To follow Item 46)

Amendment by WINCHESTER: That Item 46 be reworded as follows:

That this Meeting recommends that the issue of free milk to schoolchildren should be discontinued, except in the cases of medical necessity.

Amendment by TOWER HAMLETS: That the following be inserted immediately after the word "Meeting" in Item 46:

"being of the opinion that supplementary milk supplies are no longer necessary for the nutrition of the population of this country."

Medical Screening of School-crossing Patrol Staff

(To follow Item 50)

Motion by KINGSTON-UPON-THAMES: That this Meeting urges the appropriate authorities to institute medical screening (at least a check on visual capabilities) of school-crossing patrol staff.

Medical Ethics

Family Planning

(To follow Item 64)

Amendment by DARTFORD: That the following words be added immediately after the word

---

* The Agenda of the Annual Representative Meeting was printed in the *Supplement*, 10 June, p. 149.

"patient": "unless the treatment is carried out with the prior consent of the patient's own general practitioner."

General Medical Services

Remuneration and Terms and Conditions of Service

(To follow Item 70)

Amendment by TOWER HAMLETS: That Item 70 be reworded as follows:

That, with reference to paragraph 17 of the Annual Report of Council, the standard capitation fee is inadequate and should be raised to a realistic level.

Seniority Payments

(To follow Item 96)

Amendment by WINCHESTER: That Item 96 be reworded as follows:

That until 1972 family doctors over the age of 70 years providing full-time general medical services should continue to enjoy seniority payments.

Inducement Payments

(To follow Item 97)

Amendment by SOUTH SHIELDS: That Item 97 be amended to read:

That the criteria at present laid down for inducement payments are wrong and should include unattractive industrial areas where the doctor–patient ratio remains constantly high.

Night Visits
(To follow Item 106)

Amendment by CARDIFF: That the following sentence be added to the Motion: "This should be made to apply equally to subsequent visits, after the first, when the condition of the patient indicated that such further visits be made."

Organization

Constitution

Representative Body and Autonomous Bodies
(To follow Item 300)

Motion by SUNDERLAND: That paragraph 28 of the Report on the Constitution of the B.M.A. (Doc. A.R.M. 8) be amended by the addition of the following words: "provided such reference back is passed by at least a two-thirds majority of the Representative Body."

(Paragraph 28 reads as follows: "We therefore propose that the Representative Body should normally receive and approve reports on the work of the autonomous bodies, but when it wishes to exercise its right to disagree in any respect it would normally refer the matter back to the autonomous body before reaching a final decision.")

Second Tier—Regional Councils
(To follow Item 307)

Amendment by CLEVELAND AND MIDDLESBROUGH: That the words "a few" be substituted for "three."

Representative Body
(c) Proportional Representation
(To follow Item 321)

Amendment by CAMDEN: That the words "the seat becomes free and any member of that Division may be elected to fill it," be substituted for the words "the seat remains void."

(d) By-law 40 (Doc. A.R.M. 2, Appendix XIII)
(To follow Item 325)

Amendment by RUGBY: That the words "apply for" be substituted for the word "claim."

(f) Constituencies for Election of Representatives
(To follow Item 335)

Amendment by TEES-SIDE: That the proposals published in Appendix II of the revised Report on the Constitution of the B.M.A. be amended as follows:

"That constituency No. 45 should consist of three Divisions—viz., Cleveland and Middlesbrough, Hartlepools, and Stockton—returning three representatives, and constituency No. 46 should consist of the Darlington Division alone, returning one representative."

Council
(j) Elected Members of Council
(To follow Item 349)

Amendment by MID-GLAMORGAN: That the Motion be reworded as follows: "That the Council of the B.M.A. should always include a woman member of the B.M.A."

(To follow Item 360)

Amendment by NORTH GLAMORGAN AND BRECKNOCK: That, of the five members of Council proposed under the new constitution to be elected at the Annual Representative Meeting, three should be elected by the Representative Body as a whole and one each by the Scottish and Welsh Representatives respectively.

(m) Term of Office

(To follow Item 371)

Amendment by HALIFAX: That Item 371 be reworded as follows:

That with the aim of combining the benefits both of reasonable continuity and infusion of new ideas, the Council be requested to investigate the question of terms of office and eligibility for re-election as they affect officers, representatives, and committee members throughout the Association, centrally and locally, and to report the recommendations.

Private Practice

Fees for Services Outside the National Health Service

(To follow Item 390)

Amendment by NORTH MIDDLESEX: That the Motion 390 be reworded as follows:

"That comprehensive medical examinations and medical reports without examination required prior to the employment of individuals by local authorities, and reports required by local authorities in connexion with sickness of their employees, should in future be included in the Whitley agreement on remuneration of practitioners employed part-time in England and Wales, and fees should be at the same level as those recommended or agreed by the Association in other fields."

Statutory Fee for Notification of Diseases
(To follow Item 417)

Amendment by DERBY: That this Meeting feels that the statutory fee for notification of diseases to local sanitary authorities should be modified to take into account the diminution in the value of money which has taken place since 1889 when the present fee was fixed.

Therapeutic Abortion

(To follow Item 445)

Additions to List of Divisions after Item 445: Belfast, North Devon, Tower Hamlets.

Hospital and Consultant Services

Memorandum on the Current Problems of Hospital Medical Staff

(To follow Item 478)

Motion by BROMLEY: That this Meeting welcomes the first joint report of the negotiations with N.H.S. doctors and dentists which contains many important points. Even, however, on those points where agreement has been reached with the Ministry of Health, they regard it as doubtful whether these can be implemented in some areas as certainly they cannot be unless additional finance is provided for the hospitals.

Allocation of Distinction Awards

(To follow Item 501)

Amendment by DERBY: That this Meeting disapproves of distinction awards for consultants and considers that these awards should be replaced by seniority awards.

Domiciliary Consultations

(To follow Item 520)

Amendment by DERBY: That, in the case of whole-time consultants and S.H.M.O.s, all domiciliary consultations should be paid for.

Association Notices

Proposed Amalgamation of Redbridge and Stratford Divisions

Notice is hereby given by the Council to all concerned of the proposal to amalgamate the Redbridge Division and the Stratford Division to form a Redbridge and Stratford Division. Any member affected by this proposal and objecting thereto is requested to write to the Secretary of the Association by 29 July 1967.

DEREK STEVENSON,
Secretary.

Formation of the Hannover Branch

The Council hereby gives notice of the formation of a new Branch of the Association to be known as the Hannover Branch. The area of the new Branch is eastern Lower Saxony, West Germany.

DEREK STEVENSON,
Secretary.

Diary of Central Meetings

JULY

6	Thurs.	**Annual Representative Meeting** (at Bristol), 9.30 a.m.
7	Fri.	**Annual Representative Meeting** (at Bristol), 9 a.m.
8	Sat.	**Annual Representative Meeting** (at Bristol), 9 a.m.
10	Mon.	**Annual Representative Meeting** (at Bristol), 9 a.m.
10	Mon.	**Annual General Meeting** (at Bristol), 12.30 p.m.
10	Mon.	**Council** (at Bristol) (at conclusion of A.R.M.).
10	Mon	**Adjourned Annual General Meeting and President's Address** (at Bristol), 8.30 p.m.
19	Wed.	Joint Formulary Committee, 10.30 a.m.
20	Thurs	Planning Unit, 5.30 p.m.
24	Mon.	North-west Metropolitan Regional Consultants and Specialists Committee, 5 p.m.
25	Tues.	Joint Consultants Committee, 10 a.m.
25	Tues.	Vocational Training Advisory Committee (G.M.S.C.), 2 p.m.

SEPTEMBER

22	Fri.	Planning Unit, 4.30 p.m.

British Medical Journal Supplement

LONDON SATURDAY 8 JULY 1967

CONTENTS

Proceedings of Council - - - - - - - - 15
More Consultant Posts - - - - - - - - 17
General Medical Services Committee - - - - - 18
Central Consultants and Specialists Committee - - - 21
Highlands and Islands Medical Services - - - - - 23
Flashing Light for Doctors' Cars - - - - - - 23
Hospitality - - - - - - - - - - - 23
Association Notices - - - - - - - - - 24

Proceedings of Council

The Council of the Association had a short agenda for its last regular meeting of the session 1966–7. It approved a reorganization of the representative machinery in the B.M.A. for hospital junior medical staff. *It also* approved a Supplementary Annual Report (Supplement, 1 July, p. 13), in which, among other things, proposals for a discount trading service for B.M.A. members organized by Independent Medical Services Ltd. were commended to the Representative Body.

The Council of the Association held its last regular meeting of the session on 21 June. Dr. RONALD GIBSON was in the chair.

The CHAIRMAN expressed the Council's pleasure that Dr. J. C. Cameron, Chairman of the General Medical Services Committee, had been presented with the Claire Wand Award at the Annual Conference of Representatives of Local Medical Committees (*Supplement*, 24 June, p. 191).

Resolutions from Divisions

The Council considered resolutions from Divisions on various matters, including merit awards in general practice (Sutton Coldfield), security of tenure for general-practitioner clinical assistants (Sutton Coldfield), and fees for medical certificates for employees (South Staffordshire). The South Staffordshire resolution, which suggested that when an employer asked for a medical certificate about an employee the employer should pay not less than 10s. 6d. for it, was referred to the Private Practice and General Medical Services Committees for consideration.

The Coventry Division had requested that the Council "should press for the setting aside of the present proposed legislation on the medical termination of pregnancy until all relevant facts and beliefs had been advanced to, sifted, and considered by an independent body such as a Royal Commission."

The CHAIRMAN said that the Bill was now in the report stage and he believed the Government would give time in order to get it through Parliament. At this late stage nothing the Representative Body said would have much effect. The Council, in conjunction with the Royal College of Obstetricians and Gynaecologists, had been successful in getting a number of important amendments to the Bill, and there was only one outstanding amendment needed to bring it into line with the recommendations of the B.M.A.'s special committee (*B.M.J.*, 2 July 1966, p. 40). The Council would continue to press for this amendment, which concerned the qualifications of the doctors who performed the abortions.

A resolution from the Harrow and Hillingdon Division, that the Minister be asked for a radical simplification and reduction in the size of certificate forms used by general practitioners, in particular forms E.C. 73A, 73B, 73C, 74, and 81, was considered. Dr. CAMERON said that he hoped that these points and others would be settled shortly.

Another resolution from the Harrow and Hillingdon Division congratulated the Council on its efforts to back public health medical officers in improving their conditions of service.

Cervical Cytology Service

The Council considered a letter from the Chief Medical Officer, Ministry of Health, commenting on the Council's views on the progress towards establishing a nation-wide cervical cytology service. The Chief Medical Officer stated that the Ministry had established a committee on gynaecological cytology, under the chairmanship of Professor J. McClure Browne, which was considering certain of the points which had been raised by the B.M.A. The aim was to provide facilities for the examination of all women aged over 35 once in five years, and the service was now more than half way to that target, which would involve screening 2,600,000 women each year. The Chief Medical Officer said that the question of how best to extend the service to include those at greatest risk in the younger age groups was being considered.

The Ministry intended to ensure satisfactory liaison and co-ordination in all areas, and it welcomed the Council's support in this aim. The Ministry also gave full support to the Council's views on the provision of training facilities for taking smears, but pointed out that this training must be provided by gynaecologists who were, in many areas, hard pressed.

The CHAIRMAN said he thought that this reply from the Ministry was very satisfactory. Dr. CAMERON said that the G.M.S. Committee would continue to press for the age limit to be abolished. Clinics had never observed this rule.

Discount Trading

Dr. IVOR JONES (Chairman, Committee of Management, Independent Medical Services Ltd.) reported on Independent Medical Services's offer to provide a discount trading service to B.M.A. members. The legal and administrative aspects of providing discount trading facilities had been discussed, and the advantages in providing this service had been measured against its practicability and the advisability of such activities on the part of a professional association.

An *ad hoc* B.M.A. committee had examined the proposals and its recommendations to the Council were that the offer of the I.M.S. discount trading service should be accepted; that it should be restricted to B.M.A. members; and that existing subscribers to I.M.S. who were not members of the B.M.A. should not be excluded. There would be no entrance fee. The B.M.A. would promote the service and I.M.S. would run it. The B.M.A. would have no legal or financial obligations. The question of the advisability of a membership card and number would be remitted to the Organization Committee for consideration. The promotion of the scheme would also be the responsibility of the Organization Committee.

Dr. Jones said that the service could be offered to all doctors on payment of an annual subscription which would probably be about two guineas and would cover administrative and printing costs. Alternatively there could be a concessional level of subscription to B.M.A. members or the scheme could be limited to B.M.A. members only. The Committee of Management of I.M.S. would accept the B.M.A.'s decision on this point. The Association would be involved only in promoting the scheme, at its discretion, as a service to members.

Unsatisfactory Scheme

Dr. A. M. **Rankin** thought it was an unsatisfactory scheme. He objected to it, chiefly as a shareholder in I.M.S., on three counts. Firstly, when I.M.S. was formed Dr. Jones had asked general practitioners for financial support, and 6,000 doctors had subscribed. Dr. Jones was now inviting doctors to put their hands in their pockets again to give benefits to those who had not supported I.M.S. in the first place. Secondly, Dr. Rankin thought there was a patronizing tone in the statement that the service should be restricted to members of the B.M.A. but existing subscribers to I.M.S. who were not members of B.M.A. should not be excluded. It looked as though these doctors were being given something they were not entitled to. Thirdly, doctors who joined I.M.S. in future were not going to get discount unless they were members of the Association. The scheme ought to go back to I.M.S. to be looked at again, said Dr. Rankin.

Dr. **Jones** said that Dr. Rankin's points were contradictory, since he had started by suggesting that the scheme should be limited to people who contributed to I.M.S. in the first place. A different rate of subscription for those who had contributed to I.M.S. to those who had not had been considered, but the original appeal for funds to I.M.S. had been restricted to general practitioners, and I.M.S. wished to make this scheme available to all doctors. The enthusiasm for a scheme of this kind was greatest among hospital junior doctors, and it would have been contrary to Council's wishes to make the cost to these doctors any higher.

After discussion with the officers of the Association, it had been agreed that the solution lay not in using existing I.M.S. funds to administer the scheme but to found it as a service for all doctors financed by a uniform subscription for all doctors. There might be a handful who were not members of the B.M.A. but who had subscribed as general practitioners to the original I.M.S. fund, and they would feel harshly dealt with if they were excluded from the scheme. It had therefore been decided that an exception should be made in their cases.

Dr. G. R. **Outwin** said that once again the Council was being asked to associate the B.M.A. with an I.M.S activity. Those doctors who subscribed originally might say that their money was being used for a purpose for which it was not intended, and once again the B.M.A. would be linked with criticism of I.M.S. The I.M.S. was a "dead duck," and the B.M.A. should consider what the original purpose of I.M.S. was, though the B.M.A. was committed to supporting I.M.S.

Dr. J. S. **Happel** said that, since the B.M.A. itself was not allowed under its articles to organize a discount scheme, Dr. Jones was to be congratulated on providing one.

Dr. **Joan Chappell** asked when the matter would be reported to Divisions and B.M.A. members, so that they could make their views known.

Encouraging Membership

Dr. J. S. **Noble** said that the Organization Committee had been given powers to seek ways of increasing B.M.A. membership. One of the things considered had been a discount service. Every junior doctor to whom he had spoken had been impressed with the idea. The I.M.S. had solved the constitutional difficulties, and this should satisfy those who objected to a professional association supporting such a scheme. Members could be made aware of the scheme through a supplementary annual report of Council before the Representative Body.

Dr. J. S. **Ross** said it was clear that under the Companies Act the B.M.A. could not take part in discount trading, since it brought gain to individual members of the Association. For this reason, said Dr. Ross, he felt uncomfortable that I.M.S., with its close association with the B.M.A., should provide a discount trading service.

Dr. **Jones** replied that the Association's solicitor had made it quite clear that there was no impropriety in the Association making an arrangement with I.M.S. which was analogous to the arrangements which the Association made in such matters as insurance. The original appeal for I.M.S. had been drawn up by the Association's solicitor, and the purposes for which I.M.S. could operate were specifically laid down in its Articles of Association. The present proposal was for financing a discount service by subscription, not for utilizing money which had been subscribed for another purpose. That was the main reason for financing the scheme by a special subscription. I.M.S. was certainly not a "dead duck." An increasing number of doctors were leaving the National Health Service and beginning to operate the scheme. Further, arrangements were far advanced for extending the scheme to hospital and specialist treatment.

Dr. A. V. **Russell** was in favour of the scheme, but Dr. C. P. **Wallace** thought that if it was improper for the B.M.A. to arrange it it was also improper for I.M.S. to do so.

Dr. A. **Skene** said that members of Council would be reassured that "the fiddle is legal," but he thought there was a matter of principle involved. There were many organizations which offered cut prices to their members, and any doctor could join one of those organizations if he wished. He was not sure that the Association would benefit by joining the "cut price racket."

Dr. G. R. **Smith** said it was important that I.M.S. should not become known as a discount trading company, and he was sure Dr. Jones did not intend that. I.M.S. was not a dead duck, and it was up to the Council to see that it did not become so. If the I.M.S. failed through lack of support then the profession failed. I.M.S. stood for independence and the ability and willingness of the profession to state its case. Discount trading could give a boost to I.M.S. to further its original aims.

The report on the discount scheme and the recommendations were accepted by the Council, and it was agreed that it should be reported to the Representative Body in a supplementary annual report (*Supplement,* 1 July, p. 13).

Medical Charities Year

Dr. R. **Cove-Smith**, Chairman of the Charities Committee, asked the Council to consider his committee's recommendation that "the proposal to launch a medical charities year in 1967 be accepted on the understanding that a professional organization be invited to conduct a preliminary survey at a cost of about £750, this cost to be met in the first place from the charities' own funds." The Finance Committee had taken exception to a medical charities year on the grounds that the costs of the appeal, estimated to be between 7 and 10% of the sum raised, appeared to be out of proportion to the target and scope of the appeal. The Charities Committee had envisaged a target of at least £50,000 gross, including covenanted subscriptions for seven years.

Dr. Cove-Smith said that two professional fund-raising organizations had now been consulted, and the conclusions drawn from the discussions were that a target of £100,000 gross over seven years was, if anything, too modest. The overall costs of the campaign should not exceed 10% and were likely to be less. A preliminary survey should be carried out by a professional firm to assess the viability of the proposal and the best methods of approach.

After discussion the Council decided that it would not reject the recommendation, but it asked the Charities Committee first, in the light of further information available, to reconsider whether it could not use its own resources to organize an appeal.

Mental Health

Dr. M. Sorsby attended the meeting by invitation to present a memorandum prepared by the Committee on the Mental Health Act (1959), of which he was chairman. The memorandum set out the committee's proposals for improving the mental health services, and it referred mainly to the services in the Greater London area.

Dr. **Sorsby** said that ten years ago representations had been made to the Ministry of Health about the mental health services, and the Ministry had indicated that in ten years everything would be all right. But, said Dr. Sorsby, after ten years everything was far from being all right. He asked that the recommendations in the memorandum should be put to the Ministry.

Dr. J. J. A. **Reid** moved the reference back of the memorandum. He agreed that there was cause for complaint, but the recommendations in their existing form must not be sent to the Ministry. The whole subject should be reconsidered on a broader basis and recommendations covering the whole country drawn up. If there was a special problem in London, as appeared from the memorandum, a special subcommittee should consider them and separate proposals should be sent to the Ministry.

Dr. **Wallace** agreed with Dr. Reid. The Council could not support a hotch-potch of comments, inadequate statistics, and opinions, though some of the conclusions and much of the information contained in the memorandum were most valuable.

Dr. H. L. LEAMING thought the Council could not approve the recommendations, but he suggested the memorandum should be referred to the G.M.S., the C.C. and S., and Public Health Committees for comments. The subject matter of the report was causing much concern in the Health Service, and action to improve the mental health services was urgently needed.

Dr. CATHERINE GRAY said that the report should be referred back, and it should be related to the country as a whole. If it was going to the Ministry it was no use dealing with one area only.

Dr. F. STEEL said that many societies were concerned with the problem, and he wondered if there had been any liaison.

Valuable Memorandum

Dr. CAMERON said that the impression might be gained from Dr. Reid's remarks that the memorandum was without value and that Dr. Sorsby and his committee had failed, but that was not so. Dr. Sorsby had pressed continously since 1960 to improve the arrangements under the Mental Health Act in the Greater London area, where all the mental hospitals were in Surrey and most of them were in one regional hospital board area. Dr. Cameron said doctors would have preferred other regional boards to take some of the hospitals over, but that had not been possible. He thought there should be a broader-based committee, and this was not the time for referring the matter to the other committees.

Dr. SORSBY, replying to the debate, said he would agree to consider the subject again on a wider basis. There were two problems, that of the London area and the general one of how to achieve improvements in the administration of the Act.

The Council decided to refer the memorandum back to the committee.

General Medical Services

Dr. CAMERON, reporting on the work of the General Medical Services Committee, said that it had been invited to consider the questionary issued by the Central Health Services Council's Committee on the Functions of the District General Hospital. General practitioners were not broadly represented on this committee, said Dr. Cameron, but Dr. Michael Wilson, a young doctor, had agreed to serve.

Because of its importance to general practitioners, a copy of the questionary had been sent to all local medical committees in England and Wales inviting them to submit their views to the G.M.S. Committee, and the Committee recommended that the questionary should now be sent to B.M.A. Divisions and Branches for their comment.

The Council accepted the recommendation.

Reporting on discussions with the Ministry on the question of payment by salary, Dr. Cameron said that it was important to differentiate between a salaried service and a salaried method of payment. No progress had been made on proposals put forward by the Minister of Health, which the G.M.S. Committee had found unacceptable. The Committee had decided to ask to see the Minister again, and its representatives would be accompanied by those of general practitioners in favour of a salaried method of payment. However, they had been overtaken by events, said Dr. Cameron, because the Annual Conference of Representatives of Local Medical Committees (*Supplement*, 1 July, p. 2) had carried a motion from Inner London that there should be no further discussions on the salaried method of payment until the Minister had agreed that payment by item of service was also made available for those who wished it.

Fees

The Council considered proposed increases in fees for part-time medical services for Government departments. Dr. IVOR JONES, Chairman of the Private Practice Committee, reported on the negotiations which had taken place with the Treasury. The Treasury had attached certain conditions to its agreement to increase the fees, and the Council decided that further clarification should be sought. Subject to that being satisfactory, it was agreed that the increase should be accepted.

Hospital Junior Staff

Mr. H. H. LANGSTON presented the report of the Central Consultants and Specialists Committee. The report was concerned solely with proposals for the reorganization of the Hospital Junior Staffs Group Council and the regional groups.

Mr. Langston said that the recommendations meant that the Association would provide a complete and comprehensive service for hospital junior doctors, and those who said that they were not adequately represented would no longer have substance in their allegations. If regional groups met regularly and worked efficiently and there was good communication with the centre many of the difficulties and misunderstandings which had occurred in the past would be overcome.

Mr. G. E. MOLONEY said he hoped there would be adequate representation of senior consultants' views.

In reply to Dr. J. S. NOBLE, Mr. LANGSTON said that the problem of communications with hospital junior staff was under consideration.

The recommendations were approved.

Other Reports

The Council also received reports from the Film Committee, the Finance Committee, the Journal Committee, the Scottish Council, and the Joint Committee of the B.M.A. and British Veterinary Association.

When presenting the report of the Journal Committee Dr. HAMILTON said that he was not seeking re-election to the Committee, and this would be the last time he would be presenting its report to the Council.

The CHAIRMAN paid a warm tribute to the long and valuable services of Dr. J. G. M. Hamilton to the Council and to the Journal Committee, of which he had been chairman since 1954.

Retiring Members

The CHAIRMAN thanked retiring members of the Council for their services. Those who made valedictory speeches were Dr. S. NOY SCOTT, who had been a member of the Council for 17 years, Dr. J. G. M. HAMILTON, Dr. H. C. W. BAKER, and Dr. G. R. SMITH.

More Consultant Posts

The Minister of Health has asked hospital boards in England and Wales to advertise over the next few months additional consultant posts and to readvertise unfilled posts. The consultant posts to be advertised are within those requested in the reviews of hospital medical staffing that resulted in the Platt report. The additional posts will be advertised in selected regions and mainly in general medicine, general surgery, traumatic and orthopaedic surgery, anaesthetics, and mental illness. The Minister has stated (*Supplement*, 27 May, p. 135) that doctors with satisfactory training will not be excluded from consideration for appointment to these posts on the ground that they have spent little or no time as senior registrars. Doctors in the medical assistant grade will also be eligible to apply for these posts.

The Ministry has stated that there is no intention of lowering the standard of entry to the consultant grade, but merely to allow every candidate to be judged by the Advisory Appointments Committee on the length and quality of his training and experience and on his other attributes without being debarred by any rigid requirement about length of service in one particular grade.

The negotiating team representing all National Health Service hospital doctors had represented (*Supplement*, 13 May, p. 93) to the Health Ministers that immediate steps should be taken to attain the establishment of consultants recommended by the Platt reviews, and that there were many senior registrars, including some who had not yet completed the normal tenure of their posts, and also long service registrars who had the necessary experience to fill consultant vacancies immediately. The profession's representatives stated that there were a number of well-trained registrars held up in the grade by the bottleneck in promotion higher up.

Discussions are taking place with the Ministry on the problem of time-expired registrars and senior registrars who have been only a short time in their existing grade but were a long time in the registrar grade.

General Medical Services Committee

Dr. J. C. Cameron was unanimously re-elected chairman of the G.M.S. Committee at its first meeting of the new session. The negotiating team for general practitioners was appointed with powers for the chairman to co-opt others when he wished. Members were appointed to various working groups on special subjects.

The Ministry of Health is to be asked whether, as one of its auditors seemed to think, the help that must be employed in a group practice before its members qualify for additional payment must be a full-time helper. The Minister of Health is to be asked to consider whether the terms of the N.H.S. Acts could prevent nurses, midwives, and health visitors from working in doctors' practice premises.

According to the Ministry of Health the betterment levy on land development value under the Land Commission Act, 1967, would not normally be payable by a doctor building a surgery or adapting or improving premises for use as a surgery.

The General Medical Services Committee held its first meeting of the session 1967–8 on 22 June. Dr. J. C. CAMERON was unanimously re-elected Chairman of the Committee, and was given a standing ovation.

The CHAIRMAN welcomed the new members of the Committee.

Negotiating Team and Working Groups

The Committee proceeded to appoint the negotiating team and working groups.

Dr. CAMERON said that the amount of work falling on the Chairman was so great that it was essential some of it should be delegated. He expressed his appreciation to all members of the Committee who had served on the working groups.

The negotiating team had been appointed by the Committee in the crisis after the fifth report of the Review Body in February 1965. It had been added to since, and the help of rural practitioners and of other members of the G.M.S. Committee had been called on from time to time. Dr. E. V. Kuenssberg had now given up his membership of the team.

Dr. Cameron said that the negotiations had reached a stage where it was not necessary for the full team of negotiators to go to the Ministry each time. It was essential, he said, to have a nucleus of two or three members who would attend most of the meetings. That would ensure continuity. But he would like to have the authority of the Committee to call on members with a knowledge of and interest in particular matters under discussion to assist the negotiators.

Dr. Cameron asked for the Committee's views on the policy to be adopted for the next session.

Dr. I. M. JONES thought there was some advantage in having as a nucleus those who had acquired valuable experience in negotiating in recent months. Apart from that, he thought the Chairman should be free to add to his team as he wished for specific occasions.

Dr. H. N. ROSE took the view that negotiations would virtually never be completed, and that a negotiating team would always be needed. There was much sound sense in what had been suggested, but he thought that it would be valuable to have a younger doctor included in the team.

Informing the Periphery

Dr. R. A. KEABLE-ELLIOTT said that it was important for the periphery to know that doctors from outside the negotiating team were called in on numerous occasions to assist. There was a feeling in some parts of the periphery that the team was a small group which did all the work and which might not always be the best suited to do it. He did not agree with this view, but if the members on the periphery knew that the team called on members of the G.M.S. Committee as well as other doctors outside to assist it would strengthen the team's position. Dr. C. J. SWANSON agreed with a suggestion that specialists in particular subjects should occasionally attend, and urged that the services of the Chairman of the G.M.S. Committee (Scotland) be used.

Dr. R. J. T. GARDINER said that under the new Charter it seemed there would be little latitude for varying the regulations in Northern Ireland, such as there had been in the past. The decisions taken in London would have greater repercussions than formerly. Though Northern Ireland would not ask to be included in the negotiating team, nevertheless it was hoped that the Chairman of the Northern Ireland G.M.S. Committee would be invited to attend as an observer or to contribute to the discussions on the matters affecting Northern Ireland. Dr. H. S. HOWIE WOOD thought that leaving it to the Chairman's discretion had worked well, and the Committee should leave it to the Chairman to carry on.

Dr. CAMERON said he was anxious to dispel any feeling there might be that there was anything like a caucus or a cabal.

Dr. A. SPEAKMAN said he had often marvelled at the stamina of the negotiators. He strongly urged Dr. Cameron to take other negotiators with him, so that in the event of illness or inability to attend the thread was not broken. Dr. W. W. FULTON said he agreed with Dr. Swanson that the Chairman of the G.M.S. Committee (Scotland) should be a member of the team.

Carte Blanche

Dr. G. CORMACK favoured the reappointment of the basic team, and suggested that the Chairman be given carte blanche to co-opt or appoint to the team whoever he thought best qualified to take part in the matters under discussion. Dr. Cormack accordingly moved that.

Dr. HOWIE WOOD seconded the motion.

Dr. T. K. COOKE urged the need for representation of rural practitioners' interests.

Dr. A. ELLIOTT said that appointing a negotiating team had been a new departure. The G.M.S. Committee had always been jealous of the fact that it was an executive committee. The Chairman had indicated earlier the strain that negotiating involved, and the heavy burden that fell on a few. Various plans had been put forward in the past for this or that committee to vet things, and when the negotiating team was set up some members of the G.M.S. Committee had been rather worried, thinking that the profession was putting its future into the hands of only a few people. As Dr. Keable-Elliott had pointed out, there were still certain suspicions in the periphery.

The Chairman had mentioned that the position had now changed, said Dr. Elliott. However, he was worried that doctors in the periphery might still feel uncertainty. The Chairman might also be put in an invidious position if he was given carte blanche to choose whom he liked to join the team. Dr. Elliott said that it would be useful if the names of those taking part in the discussions could be made known to the profession. He supported Dr. Cormack's motion, but wondered whether there might be a case for having a panel of doctors elected by the G.M.S. Committee from which the Chairman could nominate. That would strengthen his hand and prevent him from being put in an invidious position if any criticisms were made.

Dr. R. W. RAE said that the negotiating team was appointed for a special purpose when decisions had to be made quickly. There was a tendency to forget that it was the G.M.S. Committee that negotiated and was responsible for the results of negotiation, and that it was the Committee's responsibility to select whom it wanted to undertake the negotiations. It would be wise, he thought, to get back to the basic principle that the G.M.S. Committee was the responsible body. The important thing was to ensure that the right people undertook the negotiations.

Dr. J. S. HAPPEL supported Dr. Cooke, and recalled that at the Conference of Local Medical Committees the motions concerning rural practice had been dealt with in such a way that the movers of the motions were very angry. There was undoubtedly a feeling that the rural practitioners had not done well out of the negotiations, and that their problems had received scant consideration.

Scottish Representation

Dr. J. E. MILLER said that Dr. Kuenssberg had been appointed to the negotiating team when he was Chairman of the G.M.S. Committee (Scotland), and he considered that the continuity of this representation should be maintained. This was not because of any particular vested interests, said Dr. Miller, but because of the differences in the N.H.S. Acts as they applied in England and Wales and in Scotland. It was also of value to the Scottish negotiators to have the background knowledge when negotiating with the Scottish Home and Health Department. On occasions when there had been, for example, a difference of opinion between the Scottish G.M.S. Committee and the Scottish Home and Health Department, and Dr. Kuenssberg had been unable to be present at the meeting, there had been difficulties.

Dr. Miller therefore suggested that Dr. Cormack's motion and Dr. Swanson's suggestion should be married—namely, that there should be a basic team as before, merely replacing Dr. Kuenssberg by the present Chairman of the G.M.S. Committee (Scotland), and giving the Chairman of the negotiating team carte blanche to call for additional help from any member of the G.M.S. Committee when he considered it necessary.

Dr. Cormack said he would be happy to amend his motion in that way.

Dr. Cameron said the discussion had been useful. He was anxious not only to preserve continuity but also to make it clear that in the new negotiations the help of rural practitioners would be needed. The interests of Northern Ireland would also need to be covered. The strength lay in the working groups which studied various subjects in detail.

The motion, as amended, was carried.

The Committee appointed the following members to the Negotiating Committee: Drs. J. C. Cameron, I. M. Jones, A. M. Maiden, R. B. L. Ridge, and A. A. Clark (Chairman of the G.M.S. Committee, Scotland), with Dr. J. E. Miller as Dr. Clark's deputy.

Working Groups

The Committee then appointed the following members to the working groups for 1967–8.

Disciplinary Machinery Working Group: J. C. Cameron, E. Colin-Russ, B. Holden, I. M. Jones, N. S. Malimson, J. E. Miller, R. B. L. Ridge, C. J. Wells, the Secretary of the Medical Defence Union, the Secretary of the Medical Protection Society, the Secretary of the Medical and Dental Defence Union of Scotland, and the Association's solicitor.

Dispensing Working Group: G. Cormack, J. S. Happel, H. B. Muir, A. J. Rowe, G. Scott, and M. A. Weller.

European Economic Community Working Group: J. C. Cameron, G. Cormack, R. J. T. Gardiner, B. Holden, I. M. Jones, J. E. Miller, A. J. Rowe, and C. J. Wells.

Hospital Working Group: J. C. Cameron, W. W. Fulton, B. Holden, R. A. Keable-Elliott, R. B. L. Ridge, C. J. Wells, M. A. Wilson, and H. S. Howie Wood.

Maternity Services Working Group: J. C. Cameron, H. J. Eastes, A. Elliott, J. McGlone, R. B. L. Ridge, Joan K. Sutherland, and T. K. Cooke.

Planning Working Group: D. C. Bowie, J. C. Cameron, A. A. Clark, G. Cormack, A. Elliott, R. J. T. Gardiner, J. S. Happel, B. Holden, I. M. Jones, A. M. Maiden, J. E. Miller, R. B. L. Ridge, C. J. Wells, and M. A. Wilson.

Working Group on General Practice, Finance Corporation, and Practice Premises: W. E. Bowden, J. C. Cameron, E. Colin-Russ, G. Cormack, A. Elliott, W. W. Fulton, R. J. T. Gardiner, J. S. Happel, D. F. Heath, G. T. E. Jenkins, J. R. Preston, R. B. L. Ridge, and the Association's solicitor.

Health Centre Subgroup: J. C. Cameron, A. Elliott, W. W. Fulton, G. T. E. Jenkins, J. R. Preston, R. B. L. Ridge, and the Association's solicitor.

Terms of Service Working Group: E. Colin-Russ, W. Keith Davidson, R. A. Keable-Elliott, N. S. Malimson, A. N. Mathias, R. B. L. Ridge, A. Speakman, C. J. Wells, and the Association's solicitor.

Mental Health

Dr. Max Sorsby (Chairman of the Committee on the Mental Health Act, 1959) told the Committee that at the Council meeting on 21 June (see page 15) it had been resolved to refer the Committee's memorandum and its recommendations back. The Council thought the report was slanted towards the Metropolitan area and did not give a true picture of the whole country. Dr. Sorsby said that the memorandum had contained a great deal of information. The slant towards London was because he knew the Metropolitan area best. The Council had asked that a broader-based committee should present a further report setting out the national problems and the metropolitan difficulties separately. Certainly the troubles in London were great and something must be done to ease the position, said Dr. Sorsby, particularly on the north side of the river. The problem might be taken direct to the Minister of Health before the final report was produced.

Dr. Happel said that clearly there was a special problem in the Metropolitan area, but the report as presented to the Council bore no relation to the conditions in, for example, Hampshire. A much broader-based committee was needed.

Dr. Cameron said that Dr. Sorsby had rendered great service in the mental health field. The Mental Health Act had been in existence for about 10 years and most general practitioners would agree that the time had now come to look at some of its aspects, so the Council's decision to have a wider-based committee was a welcome one.

Ophthalmic Medical Practitioners

Dr. Sorsby referred to a communication from the Ophthalmic Group Committee after the G.M.S. Committee had considered the criteria for admission to the central professional list of ophthalmic medical practitioners. The G.M.S. Committee had suggested discussions within the profession before a formal reply was sent to the Chief Medical Officer, Ministry of Health, who had put forward suggestions on this matter.

Dr. Sorsby said he was not happy with the suggestion in the communication that general practitioners should appoint two representatives to take part in the discussions. That meant that the G.M.S. Committee representatives would be in a minority of two to six. (The other representatives would be two from the Ophthalmic Group Commitee, two from the Ophthalmic Qualifications Committee, and two from the Faculty of Ophthalmologists.) Dr. Sorsby thought this representation was grossly unfair, particularly in view of the comment at the end of the communication: "We are of the opinion that there is no real need to change the criteria as presently defined by regulations." He accordingly urged that the Committee should press for equal representation.

Dr. Malimson and Dr. Cormack supported Dr. Sorsby's request for equal representation.

The Committee agreed to take action to this effect.

Fees for Road Accidents

Dr. Fulton said that the G.M.S. Committee (Scotland) had suggested that representations should be made to the Private Practice Committee for a supplementary fee of 29s. 6d. for attendance at road accidents. The existing fee of 12s. 6d. was unrealistic. The item-of-service payment would be in addition to the fee, making a total of two guineas, and it would be in lieu of an emergency service fee. The fee would be payable by the executive council.

Dr. I. M. Jones said that the Ministry had agreed to discuss the amount of the fee.

The matter was referred to the Private Practice Committee.

Immunizations and Vaccinations

Dr. B. L. Alexander commented on the Ministry of Health's circular to local health authorities which stated that if records of vaccinations or immunizations not undertaken in pursuance of public policy were wanted ad hoc arrangements should be made with general practitioners through the local medical committee; and a fee of 5s. offered for each record. The Inner London Local Medical Committee, which had brought the matter to the G.M.S. Committee's attention, considered that a fee of at least 7s. 6d. should be negotiated.

The Committee agreed that a fee of 7s. 6d. was appropriate.

The Committee considered a letter from the Essex Local Medical Committee about the changed procedure for notifying vaccinations and immunizations since the introduction of the claim forms for item-of-service payments. The letter drew attention to the fact that, since the notifications were no longer sent direct to the local health authority, doctors might no longer receive reminders of the need for repeat or booster doses.

Dr. W. Hedgcock, Secretary of the Committee, reported that it was proposed that a fee of only 5s. should be paid in the case of patients who were vaccinated against smallpox and who went abroad immediately without giving the doctor an opportunity to check whether the vaccination was successful. A fee of 7s. 6d. implied that the doctor saw the patient twice, once to vaccinate and the second time to check.

The Committee rejected the proposal, and decided to refer the matter to the Public Health Committee.

Information to Hospitals

It was reported that a letter from the Ministry of Health had been received, in answer to an inquiry from the Committee, stating that a modification of the hospital letter H.M.R. 300 (informing a general practitioner when his patient was to be admitted) had been agreed in principle which would enable general practitioners to provide hospitals with information about treatment and drugs given to patients before their admission. The advisory committee on hospital medical records had also considered the problem.

Dr. C. J. WELLS said it would be a pity to let pass an opportunity for extending the use of modified Form H.M.R. 300. He said he used a treatment card, which he gave to patients under long-term treatment to carry with them. It was useful when they were on holiday, or were involved in an accident. Dr. Wells thought that Form H.M.R. 300 might be modified to be used for that purpose.

The Committee agreed to give the matter further consideration when the draft revised forms were available.

Employment of Ancillary Staff

A letter from Rotherham Local Medical Committee was before the Committee stating that, at the annual audit of the accounts of the Rotherham Executive Council, the Ministry of Health's auditors had questioned the clerk of the council on the additions for group practice which had been made to the doctors' basic practice allowance in several cases, in according with paragraph 11 of the "Statement of Fees and Allowances" (the "Red Book"). The auditor had particularly referred to proviso (iv) of paragraph 11, which stated that "a group must employ help to the extent of at least one person who can provide services of the secretarial, nursing-receptionist, or medico-social worker type." The sentence after that stated that "executive councils will exercise discretion in interpreting the terms of this definition."

The Rotherham Local Medical Committee wrote that it understood that the Ministry's auditor was trying to rule that under proviso (iv) the ancillary help must be full-time—i.e., for at least 38 hours a week. The auditor also disclosed that while payment for the ancillary services of a doctor's wife was not recognized for reimbursement such services could be recognized for the purpose of paragraph 11 (iv) for the group practice addition. The Rotherham Local Medical Committee submitted that the auditors were unreasonable, particularly in contending that a group practice must employ at least one full-time ancillary assistant for at least 38 hours. That conflicted with what executive councils and local medical committees believed to be the case, and it seemed to Rotherham that the auditor was seeking to impose his discretion in place of that given to executive councils.

Dr. WELLS said that the letter contained some disturbing information. He suggested that the matter should be taken up at the next meeting with the Minister, and the Committee agreed.

Attachments in General Practice

It was reported that the solicitor's advice had been taken on a letter from the Essex Local Medical Committee which the G.M.S. Committee had considered at its last meeting (*Supplement*, 3 June, p. 139).

The letter had stated that the attachment of nurses, midwives, and health visitors to general practitioners had been working well in Essex, but suggestions had now been made that local health authority staff might not carry out injections or other treatment in doctors' surgeries. Sections 23, 24, and 25 of the N.H.S. Act, 1946, dealing respectively with midwives, health visitors, and home nurses, specifically provided for the attendance, visiting, and nursing of people in their own homes. The Essex Local Medical Committee had thought that it would be unfortunate if strict regard to the statutory provision should prevent local health authority staff helping general practitioners in their surgeries. The Local Medical Committee suggested that the Minister should be asked to amend the statutory provisions if necessary.

The solicitor had advised that there was "no cause for concern." Section 22 of the National Health Service (Amendment) Act, 1949, enabled midwives "to render all services reasonably necessary for the proper care of the women upon whom they so attend." Section 24 of the National Health Service Act, 1946, imposed a duty on a local health authority to provide health visitors to visit persons in their homes for the purpose of giving advice. This was an obligation on local health authorities, but there was nothing in the obligation to prevent the authority from taking additional measures. The position of home nurses was dealt with in section 25 of the 1946 Act, and was similar to that of health visitors.

Dr. ROSE said that in some parts of Essex the area medical officer had suggested that it was illegal under the Act for the district nurse to perform services at the doctor's surgery. The Ministry must be convinced that that was not so.

Dr. J. R. PRESTON said that a number of local authority health committees were having difficulties in the matter, though they wished to co-operate with the general practitioner and the hospital services. The difficulty was in the words in the Act "in their homes." He hoped the matter would be cleared up with the Minister of Health.

Some Questions

Dr. G. T. E. JENKINS said that Middlesex Local Medical Committee was concerned over a broader issue. There was doubt about what duties district nurses would be allowed to carry out for general practitioners. Would they merely carry out their existing duties or would they be allowed to do more? Would co-operation between health visitors and general practitioners lead to clashes of views between the local authority and the individual doctor? Would ancillary workers be allowed to disclose clinical information they might have gained, through co-operation with general practitioners, in social case conferences held by the local authority? To whom would clerical staff be finally responsible? They would be employed by the local authority, but would the general practitioner be in a position to hire and to fire them? Who would take the responsibility for a breach of confidence or a breach of the agreed duties?

Dr. A. ELLIOTT said that these matters had been discussed before, and it had been agreed that it was undesirable to lay down regulations. He hoped that the Ministry would overcome any difficulties where they existed.

Dr. K. DAVIDSON said that there was concern over this problem in Scotland. If the Ministry was asked to tighten the regulations it might prevent advance rather than help to clear up the position. It would be better to leave it for the moment. Dr. MALIMSON said that in most cases district nurses visited patients and worked in the doctors' surgeries, and there were no difficulties. The Act did not say that they should work only in patients' homes. Dr. A. J. ROWE said that inoculations were not normally part of a district nurse's work. Who was legally responsible for any act or omission of a nurse who did something which was not part of her normal activities? Dr. E. TOWNSEND suggested that the Ministry should be asked to clarify the matter and to instruct local health authorities on how they should interpret the regulations.

The Committee agreed to approach the Minister to ask for clarification.

Restrictive Professional Practices

The Committee received a report from the CHAIRMAN that the B.M.A. had agreed to give evidence to the Monopolies Commission in its inquiry into restrictive practices affecting professional services, and that the G.M.S. Committee and other committees of the Association had been asked to consider this. However, the CHAIRMAN said the Monopolies Commission could not report on practices expressly authorized under any enactment or Royal Charter, and he thought a large field of general practitioners' activities were outside the scope of the inquiry. But he suggested that legal advice should be sought in case there were any aspects of the matter with which the G.M.S. Committee should concern itself.

The Committee agreed that legal advice should be sought.

Land Commission Act

The Committee had informed the Ministry of Health that, in the Committee's view, the betterment levy incorporated in the Land Commission Act, 1967, would halt improvements in surgery accommodation.

In a letter in reply, which was before the meeting, the Ministry had stated that there seemed to be some misconception about the levy. A leaflet had been published by the Ministry of Housing and Local Government entitled "Betterment Levy" [an explanatory memorandum on Part III of the Land Commission Act, 1967. H.M. Stationery Office, price 4s. 6d.] which explained the meaning of the levy. Broadly speaking the Act imposed the levy only when the owner of land realized its development value as distinct from its current-use value. Once a development value levy had been paid the levy was not charged again. When a doctor bought land to build a surgery the vendor, who ordinarily realized the development value, would pay the levy. There would normally be no question of a subsequent charge on the doctor, provided building of the surgery started within two years of buying the land. Even if building started more than two years later any liability to levy was likely to be small, since the price the doctor paid for the land would be the starting price in calculating the development value.

A doctor who bought a house or similar property for use as a surgery would not ordinarily have to pay the betterment levy, said the Ministry, even though some adaptation of the premises was needed. There would be no question of a levy when surgery premises already owned were improved, unless the floor area was increased by more than 10% or 1,000 square feet, whichever was the greater. If these limits were exceeded a levy might be payable. In such a case the amount of a loan obtainable from the General Practice Finance Corporation would include the amount of the betterment levy.

Vocational Training

Dr. D. C. Bowie presented an interim report of the Advisory Committee on Vocational Training and Continuing Education for General Practice, of which he was chairman.

The Committee advocated that registrars in general practice should be seconded from the teacher's practice in search of additional experience. Doctors who received registrars on secondment need not be approved teachers, and if their practices demonstrated special methods and procedures they need not secure formal approval.

The G.M.S. Committee approved a recommendation that travel and subsistence allowances should be paid by executive councils to registrars on approved visits away from the teacher's practice, and that doctors who had not been approved as teachers and who received registrars on approved visits should be paid an appropriate fee. It also recommended that doctors in training should be paid on an incremental scale in accordance with increasing experience, and that experience in general practice should be taken into account in assessing remuneration for any subsequent hospital appointments.

Dr. Howie Wood commented on the general-practice training posts in the Wessex region. If Wessex was to be a prototype for other schemes there should be a closer tie between the hospitals and the local medical committee's training subcommittee.

Mr. Bowie pointed out that he was presenting only an interim report, and the point would be followed up.

Fees for Dental Anaesthetics

Dr. Cameron said that the Ministry of of Health had been pressed to increase the fees for administering general anaesthesia for dental surgery. One of the difficulties was that dentists were paid from a global sum, so that fees for dental anaesthetics affected dentists' pay. It had been made clear to the Ministry that doctors did not want to embarrass the dentists. The G.M.S. Committee's representatives had put forward a case for paying anaesthetic fees through executive councils. The Ministry would now receive representations from the dentists, and ultimately there would be a reply to the Committee's representations.

Constitutional Reform

Dr. Cameron referred to the fact that the Annual Conference of Representatives of Local Medical Committees had been counted out before completing its agenda (*Supplement*, 1 July, p. 12). The recommendations on the new constitution of the G.M.S. Committee and of the Conference had therefore not been debated. The only thing that could be done, said Dr. Cameron, was to postpone further consideration until a future Conference. The remaining motions, other than those on the constitution, could be taken as references to the Committee.

The Committee agreed to this course of action.

Central Consultants and Specialists Committee

The C.C. and S. Committee discussed changes in its composition and in that of the Joint Consultants Committee. The representation of the special groups on the C.C. and S. Committee is to remain. It was recommended that the College of Pathologists and the Royal Medico-Psychological Association should be directly represented on the Joint Consultants Committee.

A meeting of the Central Consultants and Specialists Committee was held on 29 June. Mr. H. H. Langston was in the chair.

Composition of Committee

The Committee discussed its previous recommendations to the Council for a number of changes in the Committee's composition. The proposal to abolish the 11 seats allocated to the special groups of the Association had been referred back to the Committee by the Council for further consideration.

Dr. E. Grey-Turner (Deputy Secretary) reported that he had written to the chairmen of the special groups stating that it had been suggested that the seats reserved for the 11 specialist groups should be converted into seats available for co-option, and that in the event of any of the specialties not being otherwise represented on the C.C. and S. Committee a representative of that specialty should be co-opted from the relevant group committee.

The C.C. and S. Committee's executive committee thought that the membership of C.C. and S. Committee could not be reduced to 50 or 60, and the fact had to be faced that it would continue to be a large committee. The Council had taken the view that no committee with a membership of 90 could possibly be efficient, and that something must be done to reduce the membership of the C.C. and S. Committee to between 50 and 60.

The Chairman said that the Council had made great play of its belief that a committee of 90 must be ineffective, but there were never 90 members of the C.C. and S. Committee actually present, and the number attending was less than the membership of the Council itself. The C.C. and S. Committee did not meet frequently, and it tried to keep its expenses down by appointing subcommittees to do much of the work. The Chairman said he believed their work was efficient. The C.C. and S. Committee had decided that it would not help to reduce the number of members elected by the regions or the junior staff membership. It was important to have the two representatives from each region. The suggestion to abolish the representation from the special groups had been made with reluctance as one of the few ways in which a substantial reduction in the membership of the C.C. and S. Committee could be secured.

Special Treatment

Dr. J. G. L. Cole, of the Radiologists Group, said that he realized the central committee was large, but it was a debating chamber in which all shades of opinion could be, and were, expressed. Items not covered in debate were usually discussed by the executive and reported on to the full committee. The Radiologists Group believed that its representation on the C.C. and S. Committee was most valuable, and in this it was supported by the Faculty of Radiologists and by the members of the British Institute of Radiology. While the Radiologists Group would welcome the co-option of any radiologist if radiologists were not otherwise represented, there were difficulties such as replacement at short notice.

Why should radiologists ask for special treatment ? Most consultants had a channel through one or other of the Royal Colleges as well as through their regional representation, whereas minority groups had only one member on the Council of the Royal College of Surgeons of England. Radiological departments had administrative problems, shared only by pathologists, which were not fully understood by their clinical colleagues. Today the radiology department was involved in nearly everything that concerned the hospital service, such as hours of working, the provision of capital and buildings, the future development of the National Health Service, and the recruitment and training of ancillary staff. They were also concerned with hospital junior medical staff. It had been suggested that the C.C. and S. Committee might call on the advice of radiologists when matters in their particular field were to be discussed. But those occasions, said Dr. Cole, would be difficult to predict in a specialty which was involved in so many different fields. He asked that the radiologists' seat on the committee should be retained.

Mr. H. G. Hanley said that the difficulties referred to by Dr. Cole were common to all groups, and that was the strongest argument against having any special group representation on the Committee.

Professor I. Rannie pointed out that there might be members of the C.C. and S. Committee who were pathologists but they would not be there as representatives of pathologists, as the Consulting Pathologists Group representative would be. There should be members of the C.C. and S. Committee who represented their specialty, and he opposed a compromise.

Mr. **WALPOLE S. LEWIN** asked whether money was the main consideration. He noted that the G.M.S. Committee met very much more often than the C.C. and S. Committee. If the C.C. and S. Committee thought its structure was right it should say so, and it should not try to reach a compromise solution without good reason.

The **CHAIRMAN** pointed out that the G.M.S. Committee paid for its meetings out of its Defence Trust funds.

Dr. A. J. W. **BEARD** pointed out that there were anaesthetists on the C.C. and S. Committee other than the one appointed by the Anaesthetists Group, and one of these also served on the Council of the Association. But it could well happen that the representative elected locally was not on the Council. It was difficult enough for anaesthetists to keep their link with the B.M.A., something which they valued, without reducing their representation.

Mr. N. G. C. **HENDRY** reminded the Committee that Scotland had agreed to reduce its representation, and he said he had thought that other groups would have disciplined themselves in the same way. If the C.C. and S. Committee (Scotland) found that there was no substantial reduction elsewhere it would wish to reserve its position.

The **CHAIRMAN** said that the recommendation about the representation from Scotland had been passed by the Council, and it would be before the Annual Representative Meeting in Bristol.

The Committee voted in favour of continuing the representation of the special groups on the C.C. and S. Committee.

Joint Consultants Committee

The Committee approved the proposed new terms of reference of the Joint Consultants Committee. The Joint Consultants Committee wished to adopt the terms of reference and had sent them to the C.C. and S. Committee for its formal consent. The terms of reference were as follows:

(A) To formulate policy and to consider all matters of policy that may from time to time arise relating to consultant and hospital practice including (i) the maintenance of standards of professional knowledge and skill; (ii) the encouragement of education and research; and (iii) the utilization to the best advantage of skills and resources; but excluding the remuneration and terms of service of hospital medical and dental staff and so that the Committee shall not engage in the pursuit of political purposes.

(B) To discuss (either alone or jointly with other bodies) with the Ministry of Health, the Scottish Home and Health Department, and other appropriate bodies all matters falling within the terms of the foregoing paragraph.

(C) To nominate members of such bodies as the Committee may from time to time decide.

Composition of Joint Committee

The C.C. and S. Committee then proceeded to discuss the composition of the Joint Consultants Committee.

The Royal College of Physicians of London had proposed that the representation on the Joint Consultants Committee from the Royal Colleges should be increased by three. There were also formal applications to be admitted as constituent bodies of the Joint Committee from the College of Pathologists and from the Royal Medico-Psychological Association.

The **CHAIRMAN** reminded the C.C. and S. Committee that the existing membership of the Joint Consultants Committee was one chairman *ex officio,* 11 representatives from the Royal Colleges, 10 from the C.C. and S. Committee, two from the Central Dental Consultants and Specialists Committee of the British Dental Association, and one observer from Northern Ireland.

Sir **JOHN RICHARDSON** said that the dilemma was that a small committee was desirable but it did not wish to alter its current representation, because it had been found to be very satisfactory. The representation of sectional interests had been pressed for in the past, and it had been pointed out that, for example, pathologists could be appointed through their constituent bodies. But there had been mounting pressure from large bodies of doctors to have representation on the Joint Consultants Committee as of right. If that were accepted others would follow suit. The wish of the Royal College of Physicians to have three more representatives from the Royal Colleges was so that it could be ensured that three more sections of the profession should be represented on the Joint Committee. Whether that was satisfactory to the bodies concerned was a different matter.

Sir John thought the Joint Committee was not a committee where the balance of interests was so important. To talk about "increased representation on the College side" was an unfortunate way of putting it. It was meant to emphasize that members should be chosen because of their academic position. Something should be done for the new colleges and those which were likely to be formed in the near future. The issue was whether this way of maintaining the principle of no direct representation but of ensuring that those who should have a voice had it was satisfactory, or whether, with all the grave disadvantages of enlarging the committee, the new colleges should be granted direct representation. On balance, he was in favour of the first course.

Dr. **JOAN TAYLOR** supported the direct representation of the College of Pathologists. It was the third largest specialty group, and should be directly represented. It was probably the largest group of whole-time employees, and some of the troubles affecting the hospital service were not always covered by those who were employed part-time.

Knocking at Door

Dr. E. A. **HARVEY-SMITH** emphasized the need for good will. Both pathology and psychiatry were knocking at the door of the Joint Consultants Committee. It was better that they should be invited in with magnanimity rather than have to put up a fight. When the Joint Consultants Committee was set up there were only a certain number of Royal Colleges and they were represented directly. Had the other colleges been in existence then they would also have been represented directly.

Dr. H. **GLYN JONES** said that the balance between the representation of the C.C. and S. Committee and that of the other constituent bodies of the Joint Consultants Committee had to be borne in mind. It had been said that hospital doctors in the provinces were less interested in the affairs of the Joint Consultants Committee because it was no longer involved in negotiations. But the new terms of reference seemed to him to be as concerned with the interests of peripheral consultants as were the old. Surely, said Dr. Glyn Jones, the representation of the Royal College of Surgeons of England and of the Royal College of Physicians of London should be reduced from three to two, and there would then be two spare places which could go to the new colleges. If further colleges appeared in due course then, logically, the College's representation could come down to one each.

The C.C. and S. Committee agreed that there should be separate representation, directly, of the College of Pathologists and of the Royal Medico-Psychological Association on the Joint Consultants Committee.

The **CHAIRMAN** said that the question now remained whether that representation should be by three additional representatives, as suggested by the Royal College of Physicians of London, or by any particular number of additional representatives, or whether there should be a rearrangement of the representation of the existing constituent bodies.

Dr. A. **SKENE** said that the matter of proportionate representation was less important now. A possible answer was to suggest that the C.C. and S. Committee's own representation should be reduced from 10 to 9, making a place for one of the new bodies, and perhaps the Royal College of Physicians of London could reduce its representation by one.

In reply to a question, the **CHAIRMAN** said that proposals that the Full-time Medical Teachers and Research Workers Committee of the B.M.A. should have representation and that the Scottish Royal Colleges should be given increased representation would have to be considered in due course.

The C.C. and S. Committee voted against any increase in size of the Joint Consultants Committee, and it was decided that it should now be left to the Joint Consultants Committee to look at the matter further.

(A report of the remainder of the proceedings of the C.C. and S. Committee will be printed next week.)

B.M.A. Car-badge Scheme

The Chief Superintendent of the Hampshire Constabulary has agreed to the introduction of the B.M.A. Car-badge Scheme in the area of the city of Southampton. Application forms for badges for doctors practising in this area may now be obtained from the Secretary of the Association, B.M.A. House, Tavistock Square, London W.C.1.

Dangerous Drugs Act: Withdrawal of Authorities

The Home Office announces that Dr. Paul Coling (Chichester, Sussex) is no longer authorized to be in possession of or to prescribe those drugs to which the Dangerous Drugs Regulations, 1965, apply.

Highlands and Islands Medical Services

The Report of the "Birsay Committee"* was published last month. The Committee was appointed in 1964 by the Secretary of State for Scotland "To consider the arrangements for the provision of general medical services in the Highlands and Islands within the framework of the health services generally; and to make recommendations." The chairman was Lord Birsay and the four medical members were Drs. R. S. C. Fergusson, Thomas Scott, C. J. Swanson, and E. R. C. Walker.

The "Highlands and Islands" includes the counties of Argyll, Caithness, Inverness, Orkney, Ross and Cromarty, Sutherland, and Zetland, and covers 14,000 square miles out of the 30,000 square miles of Scotland. Only seven of the 118 inhabited islands had more than 2,000 inhabitants in 1961, and of the whole Highlands and Islands there were fewer than 278,000 people (about 1/20 of the Scottish population). In the ten years ending 1961 the population declined by 2.8%, despite an increase in some of the burghs, when the total population of Scotland increased by 1.6%. In the Committee's view these facts justified special measures. "Only a radical reshaping of the health service which succeeds in transcending the past administrative divisions," the report states, "will . . . be successful in creating the conditions for a steady development and improvement in the services to the public."

Problems of Practice

The Committee does not consider that there are too many doctors in the Highlands and Islands, and states that there will be a continuing need for general practitioners in the foreseeable future. The general medical services were not likely to become a function of hospital outpatient departments or clinics. Grouping of practices in certain areas would be valuable to ease the burden of continuous responsibility and to facilitate the provision of diagnostic and other equipment. Notwithstanding the importance of refresher training for doctors working in isolation the Committee did not think it should be compulsory. Close links between general practice and universities should be encouraged, and general practitioners should have responsibility for a "substantial element" of public health work and school medical examinations.

Attention is drawn to the special position of a rural doctor's wife as an ancillary helper, and it is recommended that this should be recognized in future reviews of the scheme for direct payments in respect of ancillary staff. It is also recommended that the standards to which new houses are built by executive councils for doctors should be kept under review, and the power of executive councils to provide residential accommodation should be widened to include separate main or branch surgeries. Hospitals might have to loan diagnostic equipment if good doctors are to be attracted to remote areas. The report suggests that part of the responsibility for providing locums could be borne by health service bodies without disturbing the "independent contractor" status of general practitioners.

The Committee does not favour a policy of extreme centralization of specialist services, and, in addition to frequent visits by consultants to peripheral areas, it considers there should be resident consultant physicians in the Orkney and Shetland Islands. It also considers that general practitioners must work more in hospitals.

Remuneration

The Committee sees no difficulty in principle about paying a salary to doctors who want to be paid in that way and who work in health centres in isolated areas where they are not directly in competition with professional colleagues. It would not favour any measures to change the independent contractor status of any doctor against his will. Experimental patterns of salaried medical provision in self-contained areas such as Orkney should be encouraged, but an organized salaried service for the whole of the Highlands and Islands area is not recommended.

The Committee believes that inducement payments to provide general practitioners in sparsely populated areas with a predetermined income no longer provide an adequate basis for settling remuneration, and it recommends that there should be a special Highlands and Islands practice allowance to take the place of both mileage payments and inducement payments. The allowance should be determined by the nature of the practice.

Administration

The existing administrative structure of the National Health Service is criticized. The Committee states that it is clear that shared membership of the three administrative arms of the service did not overcome the tendency to uncoordinated development. The Committee recommends that there should be a Highlands and Islands Health Board responsible for all aspects of the National Health Service, with nine area boards to undertake the day-to-day running of a unified service in various parts of the region.

Reservation

In some reservations on the report Dr. Fergusson thought that there was a danger in the proposal for a Highlands and Islands Health Board of creating something remote and impersonal. Dr. Fergusson also did not consider that the existing remuneration structure would attract and keep good doctors, nor did he think the introduction of a Highlands and Islands practice allowance in the form proposed in the Committee's report would do so. He thought that a much smaller practice allowance in addition to all other payments, including mileage, and tapered along similar lines to those suggested in the report had much to commend it.

---

* *General Medical Services in the Highlands and Islands. Report of a Committee Appointed by the Secretary of State for Scotland*, 1967, Cmnd. 3257. Scottish Home and Health Department, H.M.S.O.

Flashing Light for Doctors' Cars

The new Mediflash emergency light for doctors' cars (see advertisement page xxi) may be purchased subject to the following conditions. (1) It is to be used only by registered medical practitioners when travelling to medical emergencies. (2) The use of the light confers no exemption from the observance of traffic regulations and of speed limits. (3) In the event of the light being lost or stolen the B.M.A. must be informed immediately. (4) The light must not be sold or transferred to another practitioner.

The question of an emergency sign for use on doctors' cars was referred to in the Annual Report of the Council (*Supplement*, 6 May, p. 58). Doctors wishing to buy a Mediflash light should write to the Secretary of the British Medical Association for an application form.

Hospitality

A French doctor living in Yerres, Essone, would like his 14-year-old son to stay with a British medical family from 5 to 31 August. In exchange the doctor would be pleased to receive a British boy of similar age at a mutually convenient time.

A French doctor living in Louveciennes (Seine-et-Oise) would like his 16-year-old daughter to stay with a British medical family for a month from 15 August. In exchange the doctor would be pleased to receive a British girl of similar age at Christmas or at Easter or in the summer of 1968.

A French doctor living in Dieppe would like his 18-year-old daughter to stay with a British medical family in the south of England or in London for 2 weeks from 3 August. In exchange the doctor would be pleased to receive a British girl of similar age at a mutually convenient time.

A French doctor living in Anzin would like his 20-year-old daughter to stay *au pair* with a British medical family from October to Easter. She would be pleased to help look after children.

Would anyone who is interested please get in touch with Dr. R. A. Pallister, Medical Director, International Medical Advisory Bureau, B.M.A. House, Tavistock Square, London W.C.1.

Association Notices

Diary of Central Meetings

JULY

10	Mon.	**Annual Representative Meeting** (at Bristol), 9 a.m.
10	Mon.	**Annual General Meeting** (at Bristol), 12.30 p.m.
10	Mon.	**Council** (at Bristol) (at conclusion of A.R.M.).
10	Mon.	**Adjourned Annual General Meeting** and **President's Address** (at Bristol), 8.30 p.m.
14	Fri.	Interim Negotiating Subcommittee (C.C. and S. Committee), 2.30 p.m.
19	Wed.	Joint Formulary Committee, 10.30 a.m.
20	Thurs.	Planning Unit, 5.30 p.m.
24	Mon.	North-west Metropolitan Regional Consultants and Specialists Committee, 5 p.m.
25	Tues.	Joint Consultants Committee, 10 a.m.
25	Tues.	Vocational Training Advisory Committee (G.M.S.C.), 2 p.m.
27	Thurs.	General Medical Services Committee, 10.30 a.m.

SEPTEMBER

22	Fri.	Planning Unit, 4.30 p.m.

Branch and Division Meetings to be Held

Honorary Secretaries of Branches and Divisions are asked to send notices of meetings to the Editor at least 14 days before they are to be held.

Members proposing to attend meetings marked ● are asked to notify in advance the honorary secretary concerned.

BIRMINGHAM DIVISION.—A summer party was held on 8 June at Charlecote Park, Warwickshire, by invitation of Major Sir Brian Fulke Cameron Ramsay-Fairfax-Lucy, Bt. In addition to the grounds, members were able to visit the deer park, the malt house, and the museum.

BRIGHTON AND MID-SUSSEX DIVISION.—At Postgraduate Medical Centre, Brighton General Hospital, Tuesday, 4 July, 8.30 p.m., meeting to instruct Representatives and to consider motions to Annual Representative Meeting.

LANCASTER DIVISION.—At Postgraduate Medical Centre, Ashton Road, Monday, 3 July, 8.30 p.m., general meeting to instruct representatives to Annual Representative Meeting.

NORTH BEDFORDSHIRE DIVISION.—At Medical Institute, Bedford General Hospital, Thursday, 13 July, 8.30 p.m., general meeting to receive report of representative to Annual Representative Meeting.

NORWICH DIVISION.—Thursday, 13 July, 2.15 p.m., visit to Sewage Purification Works, Whitlingham. Guests are invited.●

WEST NORFOLK DIVISION.—At King's Lynn Golf Club, Wednesday, 5 July, 12.15 for 12.30 p.m., annual general meeting followed by lunch.●

PUBLIC HEALTH MEDICAL OFFICERS: BIRMINGHAM REGION.—At 36 Harborne Road, Edgbaston, Tuesday, 11 July, 5.15 p.m., meeting.

Meetings of Branches and Divisions

BURY DIVISION.—The annual general meeting of the Division was held on 16 May at the Royal Hotel, Bury. Dr. J. B. Law was in the chair, and 20 members were present.

Branch and Division Officers Elected

BIRMINGHAM DIVISION.—Chairman, Dr. D. F. Heath. Vice-chairman, Dr. M. Sim. Honorary Secretary and Treasurer, Dr. A. L. Lloyd.

BLACKPOOL AND FYLDE DIVISION.—Chairman, Dr. I. McD. G. Stewart. Chairman-elect, Dr. A. C. Ferguson. Honorary Secretary and Treasurer, Dr. L. W. Atkinson.

BORDER COUNTIES BRANCH.—President, Dr. J. S. Moffat. President-elect, Dr. R. B. Wilson. Vice-presidents, Dr. A. M. Rankin, Dr. H. Maclean. Honorary Secretary and Treasurer, Dr. J. Hogg Smith.

BROMLEY DIVISION.—Chairman, Dr. J. C. Brocklehurst. Chairman-elect, Dr. G. A. Griffin. Honorary Secretary and Treasurer, Dr. E. M. Shipsey.

BURY DIVISION.—Chairman, Dr. J. B. Law. Vice-chairman, Dr. G. A. Levell. Honorary Secretary, Dr. J. S. Guinan. Assistant Honorary Secretary, Dr. A. E. Fishburn. Honorary Treasurer, D. R. S. Savidge.

CAMBERWELL DIVISION.—Chairman, Dr. S. Slovick. Vice-chairman, Dr. A. Clark Jones. Honorary Secretary and Treasurer, Dr. W. B. J. Pemberton.

CAMDEN DIVISION.—Chairman, Dr. Lena Williams. Vice-chairman, Dr. L. Stoll. Honorary Secretary and Treasurer, Dr. T. P. Linehan. Assistant Honorary Secretary and Treasurer, Dr. S. E. Josse.

CHESTERFIELD DIVISION.—Chairman, Dr. D. R. Lewis. Vice-chairman, Dr. W. G. Wells. Honorary Secretary, Dr. L. L. Ralph. Assistant Honorary Secretary and Treasurer, Dr. D. J. Hunt.

CITY OF EDINBURGH DIVISION.—Chairman, Dr. Betty C. Hamilton. Vice-chairman, Dr. W. S. Dalgetty. Honorary Secreary and Treasurer, Dr. Joan K. Sutherland. Assistant Honorary Secretary, Dr. A. G. Donald.

CLEVELAND AND MIDDLESBROUGH DIVISION.—Chairman, Dr. G. Blair. Chairman-elect, Dr. R. H. R. Renwick. Vice-chairman, Dr. W. M. Morgan. Honorary Secretary and Treasurer, Mr. R. Cowley. Assistant Honorary Secretary, Dr. D. S. Strachan.

CONSETT DIVISION.—Chairman, Dr. D. H. Bailey. Chairman-elect and Vice-chairman, Mr. G. I. B. Da Costa. Honorary Secretary and Treasurer, Dr. J. I. McL. Forsyth.

COUNTY OF ANGUS DIVISION.—Chairman, Dr. J. B. Miller. Vice-chairman, Dr. Ewen Taylor. Honorary Secretary, Dr. William Dodd. Honorary Treasurer, Dr. E. G. Jenner.

COVENTRY DIVISION.—Chairman, Dr. J. Catto. Chairman-elect, Mr. Richard Shaw. Vice-chairman, Dr. A. C. Kendall. Honorary Secretary, Dr. D. G. Scott. Honorary Treasurer, Dr. D. Patchett.

CREWE DIVISION.—Chairman, Mr. H. Hassall. Vice-chairman, Dr. Gretel Bergheimer. Honorary Secretary, Dr. R. D. Currie. Honorary Treasurer, Dr. F. W. Blacklay.

DEWSBURY DIVISION.—Chairman, Dr. E. B. Harrison. Chairman-elect and Vice-chairman, Mr. H. N. Burwell. Honorary Secretary and Treasurer, Dr. Valerie Platts.

DONCASTER DIVISION.—Chairman, Dr. W. E. McPhillimy. Vice-Chairman, Dr. C. F. Coutts-Wood. Honorary Secretary, Dr. W. J. B. Templeton. Assistant Honorary Secretary, Dr. G. C. McGlone. Honorary Treasurer, Dr. H. F. Clay.

EAST KENT DIVISION.—Chairman, Dr. D. O. Davies. Vice-chairman, Dr. Q. F. Evans. Honorary Secretary, Dr. G. W. Stuart. Honorary Treasurer, Dr. W. Sutcliffe.

EAST AND MIDLOTHIAN DIVISION.—Chairman and Chairman-elect, Dr. A. S. Watson. Vice-chairman, Dr. H. D. Wilson. Honorary Secretary and Treasurer, Dr. C. C. Lutton.

EAST YORKSHIRE BRANCH.—President, Dr. J. N. Redfern. President-elect, Dr. R. L. Luffingham. Vice-president, Dr. B. Reffold. Joint Honorary Secretaries, Dr. R. L. Luffingham, and Dr. S. T. Lunt. Honorary Treasurer, Dr. O. G. Prosser.

ENFIELD AND POTTERS BAR DIVISION.—Chairman, Dr. C. Crampton. Chairman-elect, Dr. L. E. L. Ridge. Honorary Secretary and Treasurer, Dr. H. R. Shepherd.

HASTINGS DIVISION.—Chairman, Dr. L. G. Scott. Vice-chairman, Mr. C. F. Mayne. Joint Honorary Secretaries, Dr. T. K. Bradford, Dr. A. J. Mitchell. Honorary Treasurer, Dr. T. K. Bradford.

HENDON DIVISION.—Chairman, Dr. A. D. Manning. Vice-chairman, Dr. H. Maxwell. Honorary Secretary and Treasurer, Dr. J. W. McCarthy.

HUNTINGDON AND PETERBOROUGH DIVISION.—Chairman, Dr. H. M. Weaver. Vice-chairman, Dr. K. D. Allanby. Honorary Secretary and Treasurer, Dr. J. K. Murphy. Assistant Honorary Secretary, Dr. J. Harkness.

ISLE OF ELY DIVISION.—Chairman, Dr. J. R. Morton. Vice-chairman, Dr. G. A. H. Cookson. Honorary Secretary and Treasurer, Dr. H. McColl.

LAMBETH DIVISION.—Chairman, Dr. T. A. V. Brooks. Vice-chairman, Dr. R. J. Smith. Honorary Secretary, Dr. J. A. Gavin. Honorary Treasurer, Dr. T. A. V. Brooks.

LANCASTER DIVISION.—Chairman, Mr. G. Freeman. Chairman-elect and Vice-chairman, Dr. S. Smith. Honorary Secretary, Dr. Jean L. Ward. Honorary Treasurer, Dr. R. J. Howat.

LEEDS DIVISION.—Chairman, Dr. J. R. B. Turner. Vice-chairman, Mr. T. F. Redman. Honorary Secretary, Dr. G. W. J. Hawbrook. Assistant Honorary Secretary, Dr. J. M. Thomas. Honorary Treasurer, Dr. G. E. Welch.

MORPETH DIVISION.—Chairman, Dr. D. Irwin. Vice-chairman, Dr. T. S. Blaiklock. Honorary Secretary, Dr. F. J. Wilkinson. Honorary Treasurer, Dr. G. F. G. Woodman.

NORTH BEDFORDSHIRE DIVISION.—Chairman, Dr. M. G. L. Lucas. Chairman-elect and Vice-chairman, Dr. J. D. Harte. Honorary Secretary, Dr. V. E. Collinson. Assistant Honorary Secretary, Dr. M. A. Cole. Honorary Treasurer, Dr. A. Obertelli.

NORTH DEVON DIVISION.—Chairman, Dr. J. S. T. Searle. Chairman-elect and Vice-chairman, Dr. A. J. Bray. Honorary Secretary, Dr. B. J. Muir. Assistant Honorary Secretary, Dr. A. J. Edwards. Honorary Treasurer, Dr. E. Lindsay.

NORTH LANCASHIRE AND WESTMORLAND BRANCH.—President, Dr. F. T. Madge. Vice-presidents, Dr. J. L. Skene, Dr. A. B. Lishman. Honorary Secretary and Treasurer, Dr. W. M. Thomas.

NORTH STAFFORDSHIRE DIVISION.—Chairman, Dr. A. J. McCall. Chairman-elect, Dr. B. Hyde. Honorary Secretary, Dr. S. R. Fee. Assistant Honorary Secretaries, Dr. A. E. Hugh, Dr. B. Hyde, Dr. W. N. Stirling. Honorary Treasurer, Mr. J. S. Ramage.

SOMERSET DIVISION.—Chairman, Dr. B. J. Douglas Smith. Chairman-elect, Dr. M. M. Johnston. Vice-chairman, Dr. A. Parry Jones. Honorary Secretary and Treasurer, Dr. M. J. Forth. Assistant Honorary Secretary, Dr. G. R. Stevenson.

SOUTH STAFFS DIVISION.—Chairman, Dr. H. A. S. Walker. Chairman-elect, Mr. R. G. Hughes. Vice-chairman, Mr. C. M. C. Potter. Honorary Secretary and Treasurer, Dr. H. R. Marker. Assistant Honorary Secretary, Dr. N. McLeod.

STAFFORDSHIRE BRANCH.—President, Dr. C. H. Catlin. Vice-presidents, Dr. H. J. Browne, and Mr. J. C. Newbold. Honorary Secretary and Treasurer, Dr. R. W. Rae.

STIRLING BRANCH—President, Dr. G. C. Chessor. President-elect, Mr. G. L. Reid. Vice-president, Dr. G. Smith. Honorary Secretary and Treasurer, Dr. R. T. Campbell.

SUNDERLAND DIVISION.—Chairman, Dr. B. Gordon. Vice-chairman, Dr. P. Inman. Honorary Secretary, Dr. C. Nelson. Honorary Treasurer, Dr. B. Tindle.

THAMES VALLEY DIVISION.—Chairman, Dr. M. Webber. Vice-chairman, Dr. P. H. A. Willcox. Honorary Secretary and Treasurer, Dr. D. Paton. Assistant Honorary Secretary, Dr. M. Charrett.

WEST LONDON DIVISION.—Chairman, Dr. J. L. Kearns. Vice-chairmen, Dr. W. Gunn and Dr. D. J. Thomas. Honorary Secretary, Dr. G. Moses. Honorary Treasurer, Dr. M. M. Marks.

British Medical Journal Supplement

LONDON SATURDAY 15 JULY 1967

CONTENTS

Annual Representative Meeting, Bristol - - - - 25
Hospital Junior Doctors - - - - - - - 65
Central Consultants and Specialists Committee - - - 65
Association Notices - - - - - - - - - - 68

British Medical Association

Annual Representative Meeting, Bristol, 1967

Nearly 500 representatives from home and overseas constituencies attended the Annual Representative Meeting of the Association held in the Anson Hall, University Union, Bristol, from 6 July to 10 July, to debate an agenda of over 600 items. It was the largest agenda that the Representative Body had ever had to consider.

First day: Thursday, 6 July

DR. A. N. MATHIAS, Chairman of the Representative Body, was in the chair, and he was supported on the platform by Professor Hamid Ali M. Khan; Dr. Ronald Gibson, Chairman of Council; Dr. S. Wand, Treasurer; Mr. R. V. Cooke (Bristol), President-elect; and Dr. A. M. Maiden, Deputy Chairman of the Representative Body.

Preliminary

President 1969–70

On the motion of the CHAIRMAN OF COUNCIL, Dr. James William Howie, M.D., F.R.C.P.(London), F.R.C.P.(Glasgow) was elected President of the Association for the Session 1969–70.

Election of Vice-Presidents

On the motion of the CHAIRMAN OF COUNCIL, Dr. Thomas Rowland Hill, M.D., F.R.C.P., was elected posthumously a Vice-President of the Association in recognition of his valuable services to the Association; and Dr. John Oubridge Mercer, C.B.E., M.B., Ch.B., F.R.C.P.(London), F.R.A.C.P., M.A.C.P., was also elected a Vice-President of the Association in recognition of his outstanding services to the Association and to the profession.

Service Representative on Council

On the motion of the CHAIRMAN OF COUNCIL, Surgeon Captain P. G. Burgess was elected as the representative of the Royal Naval Medical Services on the Council for the three years 1967–70.

Civic Welcome

At 10.30 a.m. the Meeting suspended its business to receive the Lord Mayor of Bristol, Alderman the Rev. F. C. Vyvyan-Jones. The LORD MAYOR welcomed the British Medical Association to Bristol. After reviewing some notable events he expressed the hope that representatives would enjoy their stay.

The CHAIRMAN thanked the Lord Mayor for his welcome.

Presentation of Banner

Mrs. ANGELL JAMES, wife of the Chairman of the Bristol Division, presented to the B.M.A. on behalf of the Bristol Division a banner to mark the occasion of the Annual Representative Meeting being held in Bristol. The banner had been designed by the West of England College of Art, and the work had been executed by Miss Cook, who was on the staff of the Connaught Girls' School in Bristol.

The CHAIRMAN thanked Mrs. James on behalf of the Association.

Preliminary (Resumed)

The CHAIRMAN OF COUNCIL, on behalf of the Council, moved: "That the Annual and Supplementary Report of Council under 'Preliminary' (Doc. A.R.M. 2, paragraphs 1–16, and A.R.M. 2A, paragraph 289) and the Index of A.R.M. Resolutions, 1966 (Appendix I), be received."

Dr. GIBSON said it was his duty to give members an account of Council's work during the past year. Soon after the year started the Government's Prices and Incomes standstill had been announced. The Council had come to the conclusion that it should advise the profession to accept the freeze, with two strong reservations. The first was that if circumstances changed the Association would reserve the right to take any action necessary to preserve the profession's position. The second was that the Council would proceed to take strenuous action on behalf of the four small and important groups of the profession who had been most badly hit by Government's action—the medical officers of health, doctors in the armed Forces, university clinical teachers, and junior doctors in the hospital service. The Association had black-listed both the armed Forces and the local authority health services. In both cases it was proposed to maintain that argument until the effect became insupportable to those who were denying those doctors their just due. There had been remarkable and far-reaching changes within the hospital service. The new B.M.A. constitution would provide the widest opportunity for hospital doctors to make their voices heard and their influence felt. It was up to them to use the B.M.A. machine to the full. To split the ranks of young doctors at a vital stage in their negotiations could only weaken their cause at a time when it needed all the strength it could muster. It was not a time for treachery, but a time for loyalty and unity.

Dr. Gibson said he wanted particularly to emphasize the position of the university clinical teachers. They had had no increase in their remuneration since 1963. They had been excluded from an award of 14% in 1964, and, similarly, of 5% in 1965. The Review Body had made no specific reference to them. They were then offered 10%, and the B.M.A. calculated that 2,000 doctors were being offered the equivalent of an increase of 2.8% per annum since 1963. "This," said Dr. Gibson, "was taken by the Government as being substantial, and thus, under the latest White Paper, as subject to phasing, or payment by instalments. This was taken by us, on the other hand, as being disgraceful—and we said so.

"These doctors comprise probably the most important section of our profession, for they are charged with the training of the doctors of the future. This, therefore—to us at any rate—constituted a casting away of responsibility at the highest level. I am glad to say that the award—if such it can be called—is now to be paid in full retrospectively from October last year."

Dr. Gibson said that it had been a hard and testing year and one which had brought few rewards. But at least the B.M.A. had not stood on the fence or on the defence, nor would it do so in the year to come. The Association was charged also with the promotion of the medical and allied sciences. Here again the Association's activities had been many. They had included active participation with the Royal College of Obstetricians and Gynaecologists on the subject of therapeutic abortion, and a continuation of the role in the various discussions and debates on habit-forming drugs. Written and oral evidence had been given to the General Medical Council and to the Royal Commission on Medical Education, as a result of which the B.M.A. had been asked to produce a new edition of its booklet *Becoming a Doctor*, and to produce a new booklet on careers in medicine. "We are deeply concerned," said Dr. Gibson, "that the Association has not been included in the membership of the new Central Committee on Medical Education. All our efforts to obtain membership have been repulsed. Yet we are determined to pursue an active role in this important field."

Science Education and Planning

He was pleased to say that the Royal Colleges and some of the specialist associations had agreed to take a part in all future B.M.A. Annual Clinical and Scientific Meetings. That was a great step forward. Dr. Gibson referred to the development of the B.M.A.'s scientific and educational activities in the establishment of a department of audio-visual communications. He acknowledged the Association's debt here to the Life Offices Association and the Association of Scottish Life Offices in forming with the B.M.A. a trust for health education. The director of the department would be Mr. Charles Engel.

A managerial board for "Family Doctor" publications had now been appointed, and the new medical editor was Dr. Trevor Weston, who had already started work. Mr. Brian Edsall would continue as manager and Miss Evelyn Brown as subeditor. The reaction of the press and of the public to the regrettable but necessary closing down of the main magazine had more than ever persuaded the Council of the need for the Association's health education booklets. So *You and Your Baby*, parts one and two, *Getting Married*, and *Health on Holiday* could now continue to be published, and the Council also hoped to be able to expand in the health education booklet field.

Dr. Gibson said he hoped that so far he had been painting a picture of an Association which was active and forward-looking. That brought him "to one of the most important sections of my remarks, one of which I know the Representative Body would approve, and this is the formation of our Planning Unit under the direction of Professor Henry Miller, of Newcastle." Projects the unit had initiated to date included a panel on mechanical aids for the disabled, a panel on intensive therapy units, and an investigation into computer science in relation to medicine. A booklet on research projects was to be prepared. Organizational problems of the Health Service were being tackled from the beginning with an analysis into the problems of furnishing primary medical care. The unit intended to keep in touch with Divisions and Branches through specially appointed liaison officers.

Under planning, Dr. Gibson said he must also mention Dr. Ivor Jones and his team of workers who were researching into the history of the National Health Service from its original conception, and the successful conferences held by the Committee on Science, Education, and Research on computers in medicine.

The Council had had discussions with the Ministry of Health on Britain's possible entry into the European Economic Community. The B.M.A. had a special Common Market Committee and it had observers on the permanent Committee and on the Committee of Specialists of Common Market countries. The main effect that mattered to doctors was the mutual recognition of legally accepted medical qualifications. Once that was done doctors would be free to move about the community and to practise, but they would have to obey the laws affecting medical practice in the country in which they were practising. The Ministry had suggested, and the Council had agreed to, a small liaison committee by the B.M.A. and the Ministry which could keep each other informed of moves affecting Britain's entry into the Common Market, and this had been set up.

Communications

Dr. GIBSON continued: "I have talked about the Association being active and forward-looking, and I feel strongly that this is the theme that should dominate this meeting. But a theme, if it is to be sustained, has to be developed, broadcast, heard, and understood. And it is in this respect that we seem still to be failing. Yet why should this be?" Dr. Gibson listed the contacts that some of the officers and officials of the B.M.A. had had during the year. In November and December he and Dr. D. P. Stevenson, the Secretary, in between attending the World Medical Association meetings in Manila, a conference on medical education in Delhi, and the combined Annual Meeting of the B.M.A. and the Pakistan Medical Association, together with a Commonwealth Conference in Karachi, had met doctors in Hong Kong, Singapore, Malaysia, New Zealand, and Australia. Dr. D. Gullick, Under Secretary, had visited Malta, Cyprus, and branches or affiliated associations in East Africa. The Lebanon, Gambia, Sierra Leone, and Nigeria had also been visited, and the Treasurer, Dr. S. Wand, visited Mauritius on his way back from Karachi, and the Chairman of the Representative Body, Dr. Mathias, had been in New Zealand. He (Dr. Gibson) and Dr. Stevenson had attended a conference of B.M.A. Caribbean branches in Antigua, and had called at Jamaica. There had been the excellent clinical meeting in April in Londonderry. Dr. Gibson said he had visited Dublin, and Dr. Stevenson had just returned from addressing the Canadian Medical Association during its Centenary Meeting. Dr. Gibson hoped the meeting would agree that the Council was doing its best to help doctors within the Commonwealth in their many problems.

At home there has been considerable activity, said Dr. Gibson. He referred to the conference on the future of British medicine, held in Newcastle, and another in Manchester on drug addiction. He thought the Junior Members Forum was the best he had ever attended, and he hoped young doctors would find in the Forum a powerful platform from which to express their views. Members of the Secretariat had been visiting Branches and Divisions during the year. Dr. J. C. Cameron, Mr. H. H. Langston, Dr. J. S. Noble, and Dr. I. M. Jones—"to mention only four of our very active Chairmen of Standing Committees"—had been out and about all the year, and Dr. Gibson said he had done a tour in the course of which he had met and talked to over 500 doctors of all sorts and kinds.

"So it can be said with the utmost assurance (Dr. Gibson continued) that, wherever he or she may be, practically every member of the B.M.A.—indeed, every doctor, whether a member or not—has had an opportunity to see and talk to the officers and/or officials of the Association during the past year. This opportunity for personal contact has been supplemented by *B.M.A. News*, by means of which factual information on day-to-day affairs has been put through the letter-boxes of some 50,000 doctors six times during the year. "I know that six times is not enough, but there are difficulties here of which I may have an opportunity to speak later in the Meeting if the occasion arises."

Insufficient Impact

"Yet, Sir, I remain profoundly disturbed at the undoubted fact that we are still not reaching or making a sufficient impact on the mass of doctors in the profession. For example, I calculated that I had spoken individually to 500 doctors during my tour, yet, if my arithmetic is correct, I believe there were 5,974 doctors in the 14 areas I visited. From the point of view of personal contact—if from no other point of view—my tour was therefore a colossal flop, yet I do not know what more could be done to prove the good intentions of the B.M.A. and keep contact with and be of service to its members."

If it was to be accepted—as Dr. Gibson hoped it would be—that a policy of activity, of planning, and of increasing services to members was the right one, there was no point at all in pursuing the policy if the machinery for sustaining it was missing. "We are at present working in the 60's with a constitution that creaks in practically every joint and is not geared to progress in modern fields of medico-politics or of medico-science. We need for one thing active regional machinery, in which all branches of the profession, large and small, can see their interests being furthered and can find it worth while to take a personal role in the work there is to do. We need regional secretaries who can translate policy locally, make personal contact with members, recruit members, service regional councils and committees, and in general bring to life in all parts of the country the picture I have sketched here—albeit inadequately—of an Association that is on the move.

"The Council, Sir, finds no need or reason for standing on the defensive. We are prepared to attack, and indeed have done so on more than one occasion last year. We find no reason for looking backwards over our shoulders—we are looking into and planning for the future. But all this is a sterile policy if voices cannot be raised loudly enough or words written clearly enough for members who do not wish to hear or to read to be persuaded to do both, and to do it abundantly. It is only by the greatest number of doctors being fully and continually aware of what is going on and of taking an active part in it. . . . I appeal to the Representative Body, therefore, to give us the machinery we need for our work in 1967–8, and I in return, on behalf of your Council, will give you a pledge that it will be no fault of ours if the results this Body is expecting from us are not achieved."

Planning

Dr. D. **Burrell** (Winchester) moved: "That this Meeting considers that the lack of planning of total medical needs in all areas (and in particular in developing areas) is a national disgrace and that Council be instructed to initiate an inquiry forthwith to achieve a formula whereby the maximum efficiency of medical care may be ensured in all areas by effective overall planning."

Dr. Burrell said he wondered if during his tour of the regions Dr. Gibson had found that lack of planning had led to duplication of services—and worse to total lack of appropriate services and personnel.

New hospitals were still being built without adequate facilities for hospital junior staff and nursing staff. In a proposed new hospital in north Hampshire no junior staff quarters or nursing accommodation had been provided. Even now doctors were asked to start practice from a council house in the midst of an estate.

The profession needed to know how far general practitioners could be integrated with the hospitals, and to be able to assess the needs of general practitioners, consultants, nursing and auxiliary help, and a host of other medical factors in each area. Doctors needed to know how much could legitimately be done by ancillary staff, and how they could be freed to do the essential medical work for which they were qualified.

Dr. **Gibson** suggested that the motion should be referred to the Council, so that the mechanics could be worked out as quickly as possible.

Dr. **Burrell** agreed, and the motion was carried as a reference to Council.

•

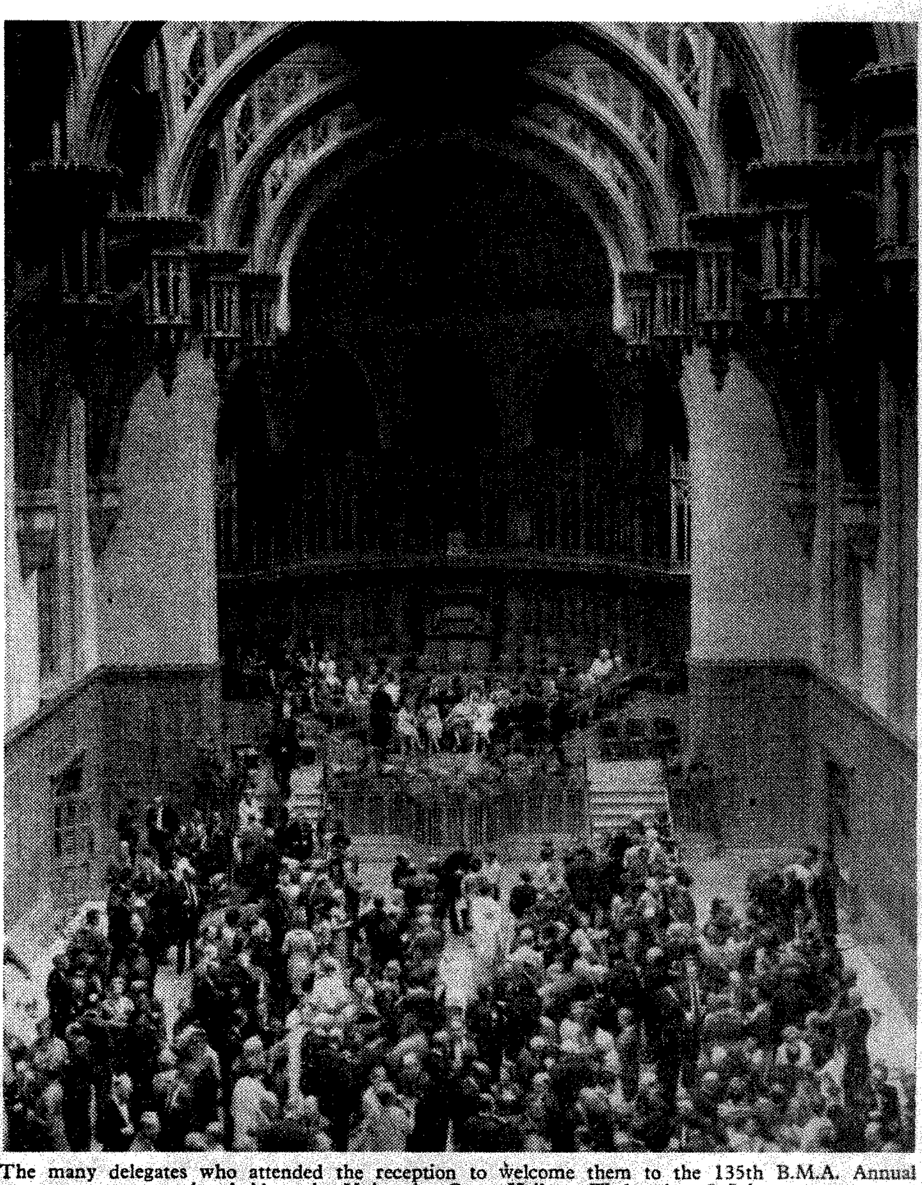
Alternative Service

Dr. W. S. S. **Maclay** (Guildford) moved: "That the results of the recent negotiations with the Ministry of Health have done little to alter the deficiencies of the National Health Service, the majority of which stem from the inadequate finance which is available at present, or will be available in the future, from direct taxation. The Annual Representative Meeting instructs Council to use whatever method it chooses to prepare an alternative Health Service. That this alternative shall be presented with adequate time for discussion by the profession before the Annual Representative Meeting in 1968."

Dr. Maclay said he was sure it would be agreed that some form of national health service was necessary in most countries. Britain's N.H.S. had remained basically unchanged for 20 years in spite of the fact that many of its faults and deficiencies had been recognized for many years. Recent negotiations and the Seventh Report of the Review Body had put money into doctors' pockets but had done little to ease their day-to-day work or to improve the standard of medical care. Among the faults of the N.H.S. was the fact that it remained irrevocably split into its three disciplines. Opportunities for an increase in preventive health services remained inadequate. There were insufficient beds and facilities for the care of old people. The conditions of many of the country's mental hospitals were so poor that doctors would not like to see one of their own relatives admitted to one. In-service training programmes for hospital junior doctors were not good enough. There were many other examples.

The present system of financing the N.H.S. from Treasury funds had produced insufficient money to carry out the improvements everyone wished to see. The percentage of the gross national product expended on medical care remained less than that in many other Western countries, notably the U.S.A. Patients should be given the opportunity to pay for extra service and medical attention. It was evident many were keen to pay for better medical care from the recent expansion of B.U.P.A. Since the introduction of the N.H.S. in Britain in 1948 other countries had started health services, but none had considered Britain's to be a good enough example to copy. Health services now existed in many countries. Britain could learn from the experience of others and prepare an alternative form of health service.

The general practitioner's "Charter" had been produced in one week-end, said Dr.



The many delegates who attended the reception to welcome them to the 135th B.M.A. Annual meeting held at the University Great Hall on Wednesday, 5 July.

Maclay. The B.M.A. could and should produce an alternative national health service within six months, so that it could be discussed in the Divisions before the A.R.M. of 1968.

Inaccurate and Irrelevant

Dr. E. TOWNSEND (Cornwall) opposed the motion as being inaccurate, tendentious, and irrelevant to the real business of the Association. It was inaccurate, said Dr. Townsend, because it was untrue to say that the negotiations had done little to alter the deficiencies of the N.H.S. There was solid evidence that quite a lot of good had come out of the recent negotiations. One example was that the Ministry of Health returns for the last quarter showed that for the first time for nearly 18 months there had been an increase in the number of general practitioners.

The effect of the negotiations on general practice had been considerable—new premises, ancillary help, health centres, preventive measures—and it could not be said that these had had no effect. The new contract had been introduced only three months before. It was untrue that the majority of deficiencies in the Health Service stemmed from insufficient finance, Dr. Townsend went on. The real faults of the Health Service now were its faulty administrative structure, the lack of creative and long-term planning and direction of the resources that existed, faulty use of resources (particularly faulty use of medical manpower), and failure to educate the public in how the Health Service should be used.

It was not, he said, the business of the B.M.A. to produce a health service. It was their job to see that any existing health service was run reasonably and properly.

Dr. G. R. OUTWIN (Council) said that a year ago the Association had had its chance to set the profession apart from party politics and to leave the economics of the Welfare State as a matter to be negotiated between the patient and the Governmnt. Surely, said Dr. Outwin, representatives must realize that the profession would never achieve what it really required by negotiation, because no politician would ever release his hold on the Health Service. The Association had been given the power to force the issue and had failed—but not because it did not know where it wanted to go or how to get there, nor because it had no alternative to follow. The Amending Acts Committee had produced an alternative scheme much better than that produced in a different context since then.

Was the profession to go on producing schemes for evermore, Dr. Outwin asked, without putting the ultimate weapon into effect? The B.M.A. could achieve these ends, but a new spirit of aggressiveness would have to be injected if the profession was to place its faith in the B.M.A. in the future.

Dr. J. H. NEWMARK (Sutton) supported the motion. On the last occasion that a similar type of motion had been brought before the A.R.M. the Review Body had been considering general practice. This position no longer existed, and if the motion was accepted the Council would be given ample opportunity to suggest a health service which could integrate all sections of medical practice in a way which would satisfy everybody.

Efficiency

Dr. G. E. CRAWFORD (Liverpool) said everyone agreed that the National Health Service as at present organized required increased efficiency, mostly in the hospital service. It would be well to let the public know what the results of using modern techniques could be. He quoted the following passages from Payne's *Introduction to Medical Automation*, which he thought were relevant. "At the margin of progress there are computer storage devices which can store ten million records and select any particular one in less than one-fiftieth of a second. . . . It is technically feasible, and indeed many such systems exist outside the medical field, to have data entered directly into the computer from teleprinters and such like stationed locally in wards, clinics, laboratories, the pharmacy, and so on so that the central computer file is immediately updated. Equally it could be directly interrogated at any time by anyone requiring the answers to specific questions."

These techniques would be available to the Government in the near future. The country had been aghast when the Home Secretary had suggested that everyone's fingerprints should be taken for record purposes. The Minister of Health and the Government would have data which would make fingerprints seem like "a mere drop in the ocean." When the public knew what was going on it would demand an alternative health service, said Dr. Crawford.

Dr. I. M. JONES (Council) hoped the Meeting would overwhelmingly support the motion. It was part of the task which had already been remitted to the new Planning Unit and to the panel of which he was chairman. The N.H.S. was inadequately financed, under-manpowered, and imperfectly organized to bring all the resources of modern medicine to the community. All over the world health services were coming into being, and time was showing each of them to be deficient in some respect or other.

His criticism of the motion was that it asked for something to be done within twelve months, and it could never be accomplished in that time. An alternative scheme would be not merely a matter of money or of laying down a pattern of organization. It involved planning into the use of many resources which were in short supply. He asked the meeting to support the motion, but not to make it incumbent on Council to give a final report by next year.

Dr. H. C. W. BAKER (Council) said that there was already an alternative medical service in the Independent Medical Services. (Cries of "Poppycock.") An alternative medical service must be available so that if the N.H.S. broke down it would be there to offer to the public.

Dr. GIBSON said he had no objection to the motion. He supported it to the extent that the previous year he had asked Dr. I. M. Jones to set up the working party on the N.H.S., before the Association's Planning Unit had been set up. The only objection he had was the time limit. He asked for the withdrawal of the words "in 1968" from the motion. He was happy to accept it with the omission of those words.

Dr. MACLAY, in reply, said he wanted a new national health service which might run parallel with Independent Medical Services, to include all branches of medical care in the country as a whole. So far attempts at reform had been limited to amendments to the National Health Service on its present course. Doctors felt they needed a new and better service to give better care to all patients in the country and to give themselves a better and more satisfying career. He had to ask for some report within 12 months, because otherwise the subject would go on year after year. He understood the difficulties in devising a complete alternative national health service within a year, but some comprehensive report should be asked for within 12 months.

The Meeting agreed to the deletion of the words "in 1968" and the substitution therefor of "as soon as possible."

The motion, as amended, was carried.

The 100% Issue

Dr. J. G. FREEMAN HEAL (Brent) moved: "That the motion (Minute 88) carried by S.R.M. of May 1945 be now rescinded.

Minute 88 of the S.R.M. of May 1945 read as follows: "88. Proposed by the Chairman of Council: 'That the following recommendation of Council should be adopted. (E) That the Association, regarding the 100% issue as one for Parliament to decide, is willing to negotiate terms and conditions for such a 100% service, if such be decided upon, provided that ample safeguards are introduced to ensure that any member of the community, whatever his income, should be enabled to obtain his medical service, in part or in whole, privately, as, for example, by grant-in-aid provision.'"

Dr. Freeman Heal said that the proviso mentioned had been ignored by successive Governments and every Government had discouraged private practice. At the same time every Government had leaned heavily on the 100% agreement with the profession, offering the public a comprehensive health service free on demand. The anxiety of the Government on that point had been evident in the first conversations on the Charter, when the Minister had asked the negotiators if they still stood by the 100% commitment.

Since 1945 such changes had taken place in the circumstances in which the 100% commitment operated that the speculative optimism of the profession's decision of 1945 had become an imprudence of the first order in 1967. He submitted that at the present time it was a physical impossibility for the profession to sustain an adequate medical service for the whole community within the present statutes and regulations governing the N.H.S.

The seriousness of the situation was enhanced by the risk that at any time general practitioners with excessive lists might have numbers of additional patients allocated to them. This was a liability which flowed directly from the 100% commitment. The hospital service had shortages of staff, which meant closing some casualty departments, long waiting-lists for appointments and admissions, and borrowing 46% of the junior staff from overseas. Aggravating the situation was the increase in population.

Dr. Freeman Heal submitted that the principle of 100% responsibility remained an article of faith given by the profession even though it proved unrealizable in practice. It formed the basis of any reorganization of the National Health Service. It circumscribed the Planning Unit and constituted a restrictive barrier to the consideration of a possible alternative service. Finally, it was the reliance of the Ministry on the 100% commitment which enabled it to expose the profession to the insatiable demands of the public.

Forced on Profession

Dr. C. M. SCOTT (Council) said that, judging by the reception the Meeting had given to the Guildford motion instructing the Council to prepare an alternative Service, and the majority by which it had been passed, he had little doubt that representatives were still seeing the light they saw at Swansea. He hoped that the motion by Brent would be given the necessary two-thirds majority. The motion was a compromise one. The 100% issue was one on which doctors were split. The proviso that ample safeguards should be introduced to enable people to obtain their medical attention privately had never been honoured, and he doubted if it ever could have been honoured.

Dr. Scott said that the mover of the motion wanted present policy rescinded so that the Planning Unit could look ahead and be given room for manœuvre. When the National Health Service Bill was under discussion Dr. Wand had been one of the out-and-out opponents of the 100% principle. If the profession in 1945 had stuck to 90%, and had simply accepted the existing National Health Insurance scheme for everybody at what was an appropriate income level, there would have been little argument and no acrimony since, Dr. Scott declared. Approval of the 100% issue had been forced upon the profession.

However, there was now a new climate of opinion in all political parties that the social services had to be completely recast at an early date. The Meeting should have no doubt whatsoever in rescinding Minute 88 of the S.R.M. in 1945. The motion was simply an attempt to make the National Health Service viable by going back to something like the 90% issue, which he hoped the Planning Unit would urge.

Dr. A. V. RUSSELL (Council) said that he thought the 100% decision taken in 1945 a disastrous one, and one from which had stemmed many of the difficulties that bedevilled the profession today. He remembered Dr. Wand saying at the time that if the profession accepted the 100% decision instead of 90% it was sunk. How right his prophecies had turned out to be, said Dr. Russell. Minute 88 was now dead wood. "Let us cut it out and clear the way to a viable and healthy Health Service." The State was no longer capable of financing an adequate service to cover 100% of the population. It was quite obvious that more than 10% of the population wanted to make their own arrangements. The grant-in-aid provisions suggested in the 1945 decision had never been honoured.

Dr. RONALD GIBSON wondered what exactly the movers wanted. If to pass the motion merely meant that the Planning Unit should have more room for manœuvre he could not say he had any objection to it. But if it meant that the B.M.A. must go to the Minister to demand that the N.H.S. should no longer cover 100% of the population that might become a resignation issue. What did the mover mean ?

Dr. FREEMAN HEAL (Brent) said the idea behind the motion was simply to give the Planning Unit an opportunity to manœuvre. It was not a challenge to the Government and was not intended to be a resignation issue. Dr. GIBSON asked for an amendment to that effect, as he thought the words should be included.

Dr. D. V. CASHMAN (Tyneside) said that the significant thing about the motion was the date quoted in it—namely, 1945. That was over 20 years ago. The resolution may have seemed wise at that time, but increasing demands had been made upon doctors, and with an increasing population doctors were now unable to fulfil their duties satisfactorily and get list sizes down. Doctors could not provide a 100% service.

Dr. J. C. CAMERON (Chairman of the General Medical Services Committee) said that the implementation of the 100% obligation had given great concern in the under-doctored areas. He was in sympathy with the difficulties doctors were facing in providing a 100% service, and he would support a motion which was up to date. Everything possible must be done to improve the conditions of general practice and reduce the work load. The present suggestions were constructive, and both Government and Opposition were having a re-look at the social security legislation.

Battles of Yesteryear

Dr. R. B. L. RIDGE (Council) observed that the motion was being used by old soldiers to fight again the battles of yesteryear. The results of those battles had no relevance to the existing situation. "The fact," said Dr. Ridge, "is that the only people who can give medical services to patients are doctors." The 100% issue was wholly immaterial, because only doctors could treat the people, whether there were enough doctors or whether there were too many doctors.

The policy of the Association was inherent in its acceptance of the three joint reports. The penultimate paragraph of the third joint report put the issue in the right perspective, stating that the profession would continue to recognize the collective responsibility of National Health Service doctors to provide family doctor services for all members of the population who desired them. The paragraph continued: "The Ministers have the duty of ensuring the provision of the services, but they can only do so through doctors. If the collective responsibility of the profession is to be discharged the conditions of general practice must be such as to attract and retain sufficient doctors for the purpose and enable them to deploy their services to the best advantage, but this is not a matter in which the Ministers can act alone: it must be carried through jointly with the profession."

It was on that basis that Dr. Ridge hoped the Meeting would plan its policy for the future.

Dr. OUTWIN (Council) moved an amendment: "That this Representative Body is prepared to support the resolution of Council that the profession can no longer accept collective responsibility for the preservation of a standard of medical care which a modern community should expect under the National Health Service.

He said that the Representative Body found itself in a difficult position on the Brent motion. He was sure everybody would support the fundamental principle. At the same time if it was possible it would merely be an attempt to remedy the past rather than to do anything constructive for the future. The matter was being left wide open for future negotiating committees to produce alternative schemes. If the matter was put forward in such a way the public might get

Mr. J. Angell James (left), chairman of the Bristol Division, and Mrs. Angell James welcome Mr. Robert V. Cooke, President Elect, at a reception to welcome delegates held at the University Great Hall on Wednesday, 5 July.

the wrong impression. To the credit of Council, it had passed a motion a month ago in the same terms as the proposed amendment. It was not suggested that 10% of the population should be refused treatment under the Health Service, although it was difficult to see how the 10% would be selected. The 100% issue could be very difficult to interpret and very easily misinterpreted.

Dr. I. M. **Jones** (Council) formally seconded Dr. Outwin's amendment.

Dr. A. **Elliott** (Redbridge) opposed the amendment. It would be very undiplomatic to pass it. The G.M.S. Committee was already on record as asking for an independent inquiry into the Health Service. In his view neither the resolution nor the amendment was necessary in those circumstances.

Dr. C. P. **Wallace** (Guildford) hoped the Meeting would accept the amendment as a reasonable and common-sense compromise. With respect, he disagreed with what the Chairman of Council had said. Although at one juncture the profession had had to accept the 100% issue, that did not mean that if the motion before the meeting was passed the profession would be forced to make the substance of it a resignation issue. The choice of what was a resignation issue lay with the Representative Body. There was anxiety about the standard of medical care in the country. Because of the brandishing of the 100% idea for political purposes, standards of care would suffer. When the time came doctors would be prepared to make the matter a resignation issue, but the time had not come and no one had suggested that it had.

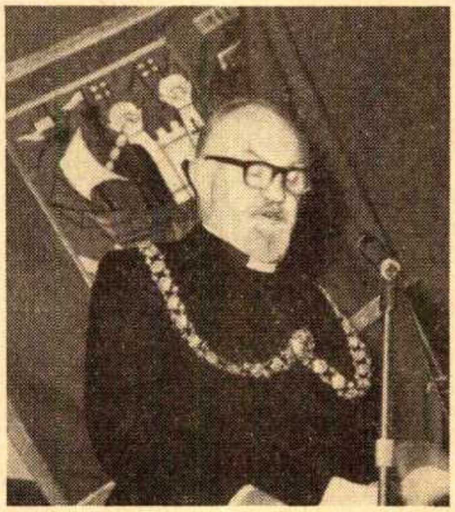
Dr. I. M. **Jones** (Council) said he had seconded the amendment for the very good reason that his opinion on the matter was supported by no less a person that a former Minister of Health, Mr. Enoch Powell, who had set out his views in a recent book on the problem of medicine and politics. Dr. Jones said Mr. Powell had stated that the existing Health Service did not enable a proper standard of medical care to be given to the public, imprisoned as the N.H.S. was by political considerations.

Accepted Duty

Dr. G. **Cormack** (Newcastle upon Tyne) said that it should be clear that what the amendment suggested was not that the medical profession was unable to provide medical care for 100% of the community. It had always been the honour, privilege, and cheerfully accepted duty of the medical profession to care for 100% of the population, and he was sure doctors would continue to shoulder that responsibility, no matter how the medical services were organized. The amendment stated that it was impracticable to provide 100% medical care under the present organization of the National Health Service, and under the present system of obtaining money mainly through taxation. Dr. Cormack thought that that was a statement of fact which should be obvious. Taxation could not provide the essential funds, and it was therefore only common sense that an alternative means of providing money should be available.

Dr. R. L. **Luffingham** (Council) said that in his and in other designated areas the number of doctors continued to fall. The Minister had said that anything the patient asked for he ought to have. What the profession was saying was that it was absolutely essential for medical care to be provided. When the average list had risen in five years from 2,400 to 2,800 it could no longer be said that doctors could provide a proper service. Therefore the profession was giving fair warning that, however hard it tried, whatever system it used, it could not provide adequate medical care on the 100% basis in the present circumstances.

Dr. S. **Freeman** (Manchester) thought the matter a simple one. As members of the medical profession they had to look after 100% of the community. If the motion was passed they were saying that they could not look after 100% of the population under the National Health Service but were prepared to do it if a section of the population were private patients. He concluded, "This, I think, is diabolical."



The Lord Mayor of Bristol, Alderman the Reverend F. C. Vyvyan-Jones, welcoming the delegates to Bristol.

Dr. **Freeman Heal** (Brent) said that his Division's original motion was straightforward. The amendment carried with it more implications of the subject becoming a resignation issue than the Brent motion, which was merely to rescind an agreement which had proved impossible to implement. If that were passed it did not present a resignation issue, whereas the amendment certainly did.

Dr. **Outwin** (Council) pointed out that the profession was not abrogating its responsibility to the community in any way. It was shouldering the responsibility of indicating sooner than later that it could not carry out its duties satisfactorily in the Health Service as it was organized at present.

The amendment, "That this Representative Body is prepared to support the resolution of Council that the profession can no longer accept collective responsibility for the preservation of a standard of medical care which a modern community should expect under the Health Service," was carried.

A motion to pass to next business was not carried by the necessary majority.

The amendment was carried as the substantive motion by the necessary majority.

Renal Dialysis

Dr. R. G. **Troup** (Havering) moved: "That this Meeting recommends that the matter of the supply and demand of renal dialysis machines should be considered under paragraph (vi) of the terms of reference of the Planning Committee."

He said he understood that 7,000 people died every year from renal failure. That was a matter of public concern, and the profession had to take steps to advise the public and the Ministry on the best use of dialysing equipment. His Division thought that a study of the need for the supply of renal dialysis machines was a matter for the Planning Unit.

The motion was carried as a reference to Council.

Health Centres

Dr. C. C. **Lutton** (East and Midlothian) moved: "That the Planning Unit should investigate the potential of medical services from health centres as a matter of urgency and make a report."

He said that health centres were being planned now. The Minister of Health had shown his enthusiasm for them. The number of 300 health centres being planned was itself rapidly being overtaken by more planning. There might well be more than 100 functioning within three years in England and Wales and four or five times that number within 10 years. The Minister had spoken of the increasing interest in health centres by the profession. Did the Minister want the profession to enter a room and he would then turn the key behind them?

The potential of health centres should be anticipated and planned by the profession. What was its policy on health centres? Were health centres needed? If so, why? If not, why not? Were there any alternatives for the future? Would general practice from health centres be the only way? If the profession failed to make the framework it would be in the power of the Ministry.

Dr. J. S. **Ross** (Council) said that there was no doubt that in certain areas health centres were desirable. There was scope for them in developing areas. In densely populated districts where surgery facilities were poor redevelopment offered an opportunity for health centres, particularly where the cost of land was prohibitive. However, the matter had to be considered carefully. The Planning Unit was the right unit to look at the problem, both from the professional and from the public points of view.

Dr. **Ross** said he was particularly concerned about general practice in health centres. The Government was offering every blandishment for doctors to work in them. There would soon be a headlong rush into them without considering the consequences. He feared, as a result of overwork and disillusion, doctors were becoming conditioned to the thought of an easier life and working from nine to five, but was this the sort of life they really wanted? They would be selling their freedom if they worked in these local authority premises and would never be able to resign from the National Health Service. If health-centre development became extensive they would soon be a salaried service.

With improvement grants doctors had means to provide a better service to patients, and to organize their practices properly in their own premises without sacrificing their freedom.

An amendment to add the words at the end of the motion, "and group practices and medical centres," was carried.

Dr. A. Elliott (Redbridge) opposed the motion, while agreeing that security of tenure and professional freedom of doctors in health centres had to be safeguarded. The working party of the G.M.S. Committee was looking into the whole question of health centres. He did not think that there should be several committees in the Association doing the same thing.

Dr. Ronald Gibson said that he had no objection to the motion, and he was well aware of the need to be prepared for practising in health centres. However, he was concerned that the matter was already being examined by the G.M.S. Committee, and he feared that if care was not taken the Planning Unit might end up by taking on more than it could cope with.

A motion, "That the question be now put," was moved and carried by the necessary majority.

Dr. Lutton, in reply, wondered whether the number of general practitioners who wished to go into health centres had ever been assessed. Doctors other than general practitioners were involved. Public health doctors were very interested in view of the changes in public health legislation.

The motion, as amended, was carried.

Developments in Science

Dr. E. E. Claxton (Dartford) moved a motion congratulating the Council on the concept of a planning unit and urging the unit to take cognizance of the effect on society of modern developments in science.

He said that Dartford wanted the Council to consider the rôle of medicine in a changing society and social causes of disease in modern life. The kernel of the matter was the future of the profession. Would it develop further as a responsible vocation or become a mere technology? In a rapidly changing world medicine, which represented both science and compassion, could be a stabilizing influence for mankind. His Division hoped that the Planning Unit would produce constructive ideas for the profession's share in the development of a healthy world.

As a profession, doctors should ask themselves where they were going? What were they doing? Was it enough to diagnose, to treat, or to prevent disease? Ought they not to discover a new and more radical aim? Ought they not to widen the scope of preventive and social medicine so that they were part of normal practice? Should not health education embrace the art of human relationships and communications? He believed the profession had a role to point and to pattern a way for mankind. It was for the Planning Unit to prepare the blueprint and for the profession to carry it into effect.

A motion that the question be now put was carried by the necessary majority, and, on being put to the meeting, the motion was approved.

Regional Organization

Dr. W. D. Gray (Liverpool) moved: "That this A.R.M. is opposed to the proposed regional office reorganization of the B.M.A."

He said that the Liverpool Division and other Divisions on Merseyside were now served by an excellent regional office in the new buildings of the Liverpool Medical Institution. Notices for meetings, letters, minutes, and all other business connected with the Divisions, the regional consultants and specialists committee, and other groups could easily be transacted through this office. The service had been available for these Divisions for many years. The Liverpool Division considered that it would be a retrograde step if the regional office in Liverpool became a mere post office, sending all work to be done to Manchester.

Dr. Gray said that the assurances received from Headquarters had been insufficient to satisfy his Division that the services to be provided under the new scheme would be as good as those provided under the old.

Dr. C. J. Wells (Sheffield) said the motion from his Division was slightly different from that of Liverpool. Sheffield wanted efficiently maintained regional offices.

Dr. H. Glyn Jones (Bromley) said he supported the motion not so much as a Divisional representative but because he was a member of a regional consultants and specialists committee. Regional consultants and specialists committees, unlike local medical committees, had no means of raising funds. They were therefore dependent on the Association for clerical services. In those areas where there were regional offices these committees were generally provided with a committee clerk and facilities. This was also the case in the Metropolitan regions. There was now a proposal to reduce the number of regional offices, and the services of the committee clerk which had been provided for the South-east Metropolitan Regional Committee were now being withdrawn.

Progress or No Progress

Dr. Gibson described the debate as "crucial." The choice was progress or no progress. Was it to be today's machine or yesterday's? There could be no question in his mind, from the visits he had made throughout the country, that the new regional offices were vital. What was needed was an active unit in the regions to do the work—in other words, decentralization.

Dr. S. Wand (Treasurer) said he wanted to say something about costs. To continue the existing organization would cost £50,000 a year. The proposals which had been outlined by the Chairman of Council would provide a medical secretary for certain areas. Some of the regional offices would remain in other areas. This would cost £75,000 a year. Last year Dr. Wand said that he told the Representative Body that the proposed new regional offices were a priority, and the money would have to be found even if something else had to go by the board. If all the present offices were retained as well as the new regional offices with their medical secretaries it would increase the cost by probably £15,000. That was a lot of money.

Replying to the debate, Dr. Gray said he was not entirely convinced by the arguments advanced against the motion. He agreed that regions needed the facilities described, but he did not think a regional medical secretary was going to fulfil all that was required.

The motion was defeated.

Dr. M. J. Forth (Somerset) asked permission to withdraw a motion standing in the name of Somerset: "That a main regional office should be maintained at Bristol."

He said that since the Division had put forward the motion it had learned that the Bristol office would stay much as it was, except that mailing would be done from London, and, in addition, it would have the services of a medical secretary. This fully met Bristol's requirements, and the motion became pointless. Dr. Forth paid tribute to Miss J. E. Ring, the regional officer for the West of England.

The motion was, by leave, withdrawn.

A motion by the Chairman of Council: "That the remainder of the Annual Report of Council under 'Preliminary' be approved," was carried.

Public Health

Dr. C. Metcalfe Brown (Chairman of the Public Health Committee) moved on behalf of the Council: "That the Annual Report of Council under 'Public Health,' paragraphs 106–122, Evidence to Royal Commission (Appendix V), Evidence to Seebohm Committee (Appendix VI), and Evidence to G.M.C. on Revision of Rules for Diploma in Public Health (Appendix VII), be received."

Dr. Brown said he wished to give the Representative Body some idea of the history of the present dispute on the pay of public health medical officers. In 1950 Whitley

Part of the Assembly in the Anson Room of the University Union listening to the Lord Mayor's welcome.

Committee C had been set up, a committee independent of any other Whitley Council, to deal with the salaries of public health medical officers. Since then the Management Side had persisted in trying to relate the remuneration of medical officers to that of other officers in local government service. The medical officers in the public health service had insisted that they wished to be paid on the same basis as other doctors. So far the Management Side view had prevailed, even so far as the Industrial Court was concerned, but time and time again the public health medical officers had persisted in their view.

Dr. Brown said that the pay for the commencing grade for a career in the public health service was £1,500 per annum. That alone illustrated the extraordinary hardships suffered by doctors in the public health service. It was against the interests of the public and of the profession that such a state of affairs should continue. Dr. Brown said he was glad that the Council had received the representations of the Public Health Committee with the greatest of sympathy, and had resolved unanimously that the public health service should have its full support. There had also been strong support from Divisions.

The Minister of Health at the time of the Royal Commission had assured the B.M.A. that the relationship of public health medical officers to other doctors would be taken into account in future negotiations. But the Management Side had still persisted in equating doctors with non-medical officers in the local authority service. So long ago as last June the Public Health Committee, with the approval of the Council, had put forward a reasonable claim. There had not been a word of formal reply to the claim from the Management Side, though over a year had passed. This action by the Management Side was, in his view, a gross avoidance of its obligations, and amounted to a great injustice. That had been the main reason why the Council had been asked to apply sanctions, which it had willingly done. He hoped that the Representative Body would support the Council. There would be no relaxation of pressure until the Management Side produced what the Council agreed was a firm acceptable offer.

Dr. Brown then discussed superannuation. The question of "added years" was a perennial one, he said. Local councils had the power to permit "added years" for a certain small section of public health medical officers. Some councils did so and some did not. The Council of the B.M.A. was applying pressure on the appropriate Ministries.

Local Government Services

The thread of the Association's memorandum submitted to the Royal Commission on Local Government in England was that in any rearrangement of local government areas in the future there should be much larger local authorities. This would be valuable not only from the point of view of providing the best services, medical and otherwise, but also because it provided a suitable background for the reorganization of the medical services.

An important problem had arisen as a result of the publication of a White Paper on the reorganization of the social services in Scotland. The White Paper suggested that there should be a combination of social services, and that was in accordance with the policy of the Association, but it then went further and said that the social services should not be under the control of the medical officer of health. If social workers were going to run the combined services, including the medical social services, it would mean that the social workers would be in charge of the local authority health services, and doctors would do no more than provide the necessary medical information. But medical provision in all the social services was so important that the B.M.A. could not agree with these proposals, and that view had been put to the Seebohm Committee.

Dr. Brown then discussed fluoridation. In his view any authority which failed to provide fluoridation in relation to the water supply was depriving children of good dental health, which they should have and would have where fluoridation schemes had been adopted. The policy of the Association was to get the Government to take central action. He hoped, however, that action would be taken locally so far as possible.

Mrs. Angell James presenting a banner to the Association during the welcome ceremony in the Anson Room at the University Union.

Dr. Brown reviewed the other work of the Public Health Committee described in the Annual Report of Council, including notifiable diseases, food hygiene, and the contamination of bathing beaches. He said that it was the policy of the Association that there should be provision of free milk in schools.

At this point it was moved, seconded, and carried that speeches should be limited to three minutes for movers of motions and two minutes for others.

Remuneration of Public Health Doctors

Dr. N. G. **Nicholson** (South Middlesex) moved: "That this Meeting considers that doctors in the local government service should have the same financial recognition as those in the armed Forces, where the precedent is already established that medical officers are paid at a higher rate than other officers of equivalent rank."

He said that the motion went to the root of the trouble between the local authorities as employers and the doctors working for them. The administration was afraid that if the pay of the local authority doctors was increased, to bring them in line with other doctors in the Health Service, it would create an imbalance in the local government service. His Division maintained that the principle had already been established. Doctors were paid more than any other officers of equivalent rank in the Army, Navy, and Royal Air Force. The Services recognized that doctors had to have long years of training before they received their commission, and that they were the most highly specialized branch. He asked the Meeting to pass the motion unanimously.

Dr. J. H. **Marks** (Barnet) said that, while agreeing with the desire to raise the financial status of local authority doctors, he opposed the motion, because to accept it would extend an undesirable system. Many service medical officers remembered the bitterness expressed by others, particularly technical officers, about the fact that the doctors' rates of pay were higher than theirs. He did not wish to see that extended to the local authority services. The Representative Body should insist that the pay of all doctors employed in all branches of the National Health Service should be related only to the pay of other doctors, and that these rates should be fixed by the Review Body.

Dr. **Harvey Gordon** (Council) said the Meeting should not get involved with the rates of pay of other staff. He asked the Meeting to vote against the motion.

Dr. **Metcalfe Brown** said the motion expressed sympathy and support for the dilemma the public authority medical officers were in, but the opposers had clearly indicated the best reason why it should not be accepted.

The motion was lost.

Deputies

Dr. R. C. **Greenberg** (Finchley) moved: "That in spite of the differential proposed in the salary claim for deputy medical officers of health, specialist medical officers should not be precluded from receiving remuneration commensurate with exceptional merit."

He said that the motion arose out of what had been B.M.A. policy and was in accordance with the claim, which said, "A deputy medical officer of health shall receive a salary in accordance with the scale of three-quarters of his chief, subject to the fact that his maximum should be £50 more than subordinate medical grades."

This policy acted in a reverse way. Instead of protecting the interests of deputies it degraded the status of distinguished physicians in the service. Some of the specialists who were dealt with under the heading of "subordinate medical grades" might be distinguished doctors who by specializing had been prevented from moving into higher-paid posts. Some of those in the mental health service were running within the public health service a clinical service equivalent to that of hospital psychiatrists. They were denied the appropriate fianancial recognition, and the present policy, if the motion was not passed, would continue to deny it them.

Dr. **Metcalfe Brown** said that the differential between a deputy medical officer of health and other members of the staff had existed for many years. He had found it invaluable in protecting medical officers rather than damaging them, and, he asked, who was to judge what was to be exceptional merit? On the other hand, it was a matter worth investigating, and he suggested the motion should be referred to the Council.

Dr. GREENBERG agreed that the situation had existed for years, but what the public health service had not recognized was that the clinical patterns of practice had changed. He was asking for a safety valve.

The motion was lost.

A number of agreed motions urging that support be given for obtaining a satisfactory level of remuneration for public health medical officers comparable with the other branches of the profession was accepted.

Off-duty Work

Mr. R. K. ALLDAY (Holland) moved: "That this Meeting considers that the conditions of service of public health medical officers which prohibit occasional work in the hospital and general-practice fields, and payment therefor, are unnecessarily restrictive and contrary to the national interests. While recognizing that no full-time public health medical officer should act as a principal in private or N.H.S. general practice, this Meeting urges negotiation to alter paragraphs 4 and 5 of section P of the Whitley Conditions of service to permit paid work out of office hours."

He said that medical officers of health and assistant medical officers of health, to whom the motion chiefly applied, should have the right to engage in other forms of medical practice which did not conflict with their duties as medical officers of health. One way of achieving this would be for medical officers of health to do occasional work in hospital and general practice. That was not at present excluded, provided permission was obtained from the authority, but that was not always easy to get. Furthermore any pay so obtained went to the employing Council. If a public health medical officer wished to engage in an occupation beneficial to him, to the National Health Service, and to his colleagues it seemed unjust that he should be penalized for so doing.

Dr. G. N. MARSH (Stockton) pointed out that, with general practitioners moving more and more into groups and shared premises, it would be a natural development for medical officers of health and assistant medical officers of health to find their work shifting towards group-practice centres. They should be able to play a recognized part in them. They could provide administrative and epidemiological knowledge. Any restrictive practice clauses which prevented closer integration of public health medical officers into the field of general practice were out of date.

Dr. A. W. MACARA (Junior Members' Forum) thought that to pass the motion at the present time would suggest that public health medical officers did not have enough to do. That might embarrass the negotiators.

Dr. METCALFE BROWN agreed with Dr. Macara. It would be unwise to introduce a new difficulty into the negotiations.

Mr. R. K. ALLDAY (Holland) thought that many assistant medical officers of health and medical officers of health were far too busy to engage in general or hospital practice, but that did not mean they all were. There were junior doctors in the public health service who wished to employ their leisure time in general and hospital practice.

The motion was carried.

A motion standing in the name of Portsmouth: That the Association continues to press for remedy of the haphazard situation which prevents public health medical officers obtaining a full pension," was accepted.

Royal Commission on Local Government

Dr. W. FERGUSON (E. Yorkshire) moved: "That in view of the brevity, lack of detailed argument, and positive proposals in the Association's memorandum to Royal Commission on Local Government, as detailed in Appendix V, Annual Report of Council, the Council be instructed to prepare and submit a supplementary memorandum, without delay."

He said that changes in the structure of local government would result in a major reorganization of local health authorities and social services. Despite the importance of the Royal Commission, the Association's evidence was brief, and practically the only positive suggestion in it was that local authorities should become larger still. There was no suggestion about the maximum or minimum size of the local government unit which would be suitable for health-service purposes. It did not necessarily follow that because a local government unit became larger it became more efficient. No suggestions were made on how the larger units would affect the two-tier system in county areas or the future functions of medical officers of health. No mention was made of the effect on local council areas or local medical committees. In rural areas general practitioners might find themselves having to travel much further to executive council meetings.

He questioned the statement in the document that larger units of administration would facilitate arrangements for final school-leaving medical examinations. In larger units of local government the school health service had been decentralized in order to make it work. He questioned whether the maintenance of uniform standards in housing was ensured if the administrative unit covered a wide area. Adequate standards were desirable but not uniform standards. He also questioned whether the administration of environmental health control by larger authorities would raise and maintain standards, or that the larger unit would provide a better ambulance service.

Dr. METCALFE BROWN said that most people with whom he had discussed the subject thought large areas were essential to provide a background not only for better services but against which to develop an improved, unified medical service. To say there was no virtue in uniformity in relation to housing was untrue. In his area he could see one standard in one place and one in another, and the Ministry was at present spending its time sending neutral inspectors round various areas to try to establish uniformity. Without uniformity there would not be correct standards in many areas.

Dr. FERGUSON, in reply, said he was not quibbling with the fact that larger units were required in many areas but because the document gave no guidance on what the size should be. Adequacy and uniformity did not necessarily go together.

The motion was lost.

Social Work and the Community

Dr. L. P. GRIME (Junior Members Forum) moved: "That this Meeting believes that it is in the best interests of the medical profession as a whole, and their patients, that the medical–social services provided by local authorities—as, for example, mental health, care and aftercare of the sick, and the care of the physically handicapped and of the aged—remain under medical direction and be not transferred to non-medical control."

He said that it was clear that it was the Government's intention to transfer to lay administrators the mental health services, the care and aftercare of the sick and physically handicapped, and various other services run by local health authorities. These services were better orientated under medical control.

Dr. K. A. WOOD (Portsmouth) supported the motions.

Dr. J. M. DUNLOP (Public Health Committee) said that feelings in Scotland were strong about this. The White Paper, "Social Work and the Community," applied to Scotland alone. A lay administrator would not be privy to the essential confidential details which a medical officer of health received from medical colleagues.

Dr. DORIS M. ODLUM (Bournemouth) said that as a psychiatrist she had no doubt that it would be fatal to divorce the medical and social services for the mentally handicapped, the aged, and the physically handicapped from medical control. It would be a completely retrograde step. There was no subject of more medical interest and more complex than mental health and mental health of the aged, which was becoming more and more a problem in the community.

Dr. D. R. COOK (Camden) said that the dangers envisaged had already come to pass. In one of the London local boroughs it had been decided to make a joint appointment of a social worker between the hospital and the local authority. It had then been discovered that this joint appointment would be between the hospital on the one side and the welfare department of the local authority on the other —with no medical supervision whatever of the medical social workers in their out-of-hospital activities.

Dr. METCALFE BROWN accepted everything that had been said. The position was very serious indeed, he said.

The motion was carried.

The following motions were accepted:

"That this Meeting notes with concern that many local authorities have not yet implemented the valuable preventive health measures of fluoridating the water supplies and urges all such authorities to review the situation immediately." (Kingston-upon-Thames.)

"That this Meeting considers that the list of notifiable diseases and the information required on the notification form should be reviewed." (Waltham Forest.)

"That great care should be taken that any advice in the form of health education given to the public is practical and supported by substantial evidence of its value. Resources must not be wasted and the public image of the medical profession harmed by advice which may later be shown to be insupportable" (East Herts.)

Contamination of Bathing Beaches

Dr. R. COVE-SMITH (St. Marylebone) moved: "That this Meeting recommends that sewage of seaside resorts and towns should be 'treated' in the same way as that of inland towns."

He pointed out that, while there were certain regulations about the quantity and quality of effluents put into rivers, there was none on the control of the effluent put into the sea. Most local authorities were concerned that sewage should be discharged at a safe position and that natural breakdown should occur. But there were difficulties about this and no method of treatment had so far been adequately established. One local authority was working out an electrolytic form of treatment which would be reasonably cheap. He hoped it would be acceptable to most authorities without undue expenditure.

Mr. A. LAWRENCE ABEL (St. Marylebone) asked what was the good of advising people to wash their hands after going to the lavatory when it was quite in order for them to bathe in sewage-polluted waters? It took a long time to sterilize effluents by exposure to the sun and by dilution. Seaside towns should have their disposal of sewage modernized, especially in view of the rapidly increasing population.

The motion was carried.

Free Milk in Schools

Dr. G. D. H. SHEPHARD (Gloucestershire) moved: "That this Meeting recommends that the issue of free milk to schoolchildren should be discontinued at the age of 11, except in cases of medical necessity."

He said that no one would deny the tremendous benefits the school milk system had had on the health of the growing children. Did the scheme now do what it was intended to do when it was first brought out? asked Dr. Shephard. The health of the community had improved, and he doubted whether many of the children who were getting school milk needed it. At the age of 5, when the child first went to school, it was easy to ensure a 100% distribution and consumption of milk. That was desirable as a health measure, and it was a good thing to teach the children the habit of drinking milk. But apparently when children got to the age of 11 they were asked at the beginning of the term by a teacher to hold up their hands if they wanted milk. Some did and were counted. For the rest of that term that number of bottles of milk were provided and only the children who had asked for the milk got it. That did not mean, however, that those children who really needed the milk got it. The B.M.A. should be able to examine this subject in an unbiased way. It should pronounce clearly without fear or favour on all matters with a medical aspect.

Dr. J. S. HAPPEL (Winchester) moved as an amendment, "That this Meeting recommends that the issue of free milk to schoolchildren should be discontinued, except in cases of medical necessity."

In Government grants to county councils and boroughs from 1 April 1967 the specific grants to cover free milk had ceased and were simply taken into account in fixing the general grant. So central Government was not so convinced of the need for the scheme. Free milk ought to take its place with other priorities. Winchester believed that there should be a drastic pruning of the whole scheme.

Dr. METCALFE BROWN described the subject as a matter of great importance. So far as he could see there seemed to be disapproval on the part of doctors who came from the more prosperous areas of the south. Those doctors, however, forgot the real problems in the Midlands and in the north in relation to nutrition. He drew attention to a recent article which said that there were some 630,000 in the low-income-group families who did not get enough food for optimum development. Milk was just one of the foods that were required. Children who wanted free milk could get it. No one forced them to take it. There were week-ends and holidays, and in practice the children who took milk got one-quarter of a pint a day. Was that going to make them fat?

The Winchester amendment was declared lost.

Dr. B. TAYLOR (Tower Hamlets) moved as a further amendment, "That after the word 'meeting' the following be inserted, 'being of the opinion that supplementary milk supplies are no longer necessary for the nutrition of the population of this country.'"

Deprived Children

Dr. Taylor said that he represented one of the poorer districts of London. His Division thought the Gloucestershire motion might cause the public to think, "Those wicked doctors are trying to deprive our children of their nourishment."

Dr. WALLACE (Guildford) hoped that the Representative Meeting would hesitate to pass any resolution which would urge that the supply of milk to the children should be discontinued. Dr. J. L. MCCALLUM (Westminster and Holborn) supported Dr. Wallace, and said that the amendment was disgraceful. He hoped the meeting would throw it out at once.

Dr. METCALFE BROWN reminded the Meeting that the Council did not favour any change in the existing arrangements for the provision of free milk.

The amendment was lost.

Dr. H. M. COHEN (Birmingham) hoped the meeting would reject the motion and referred to a report entitled "Malnutrition in the 1960s," which said, "In the area between chronic deficiency and optimum health more is known about animals than about men." The point he would emphasize was that there was optimum health. Only the day before the Ministry of Social Security had drawn attention to the fact that 1¼ million children belonged to families where the income was below the basic requirement.

The motion, "That the question be now put" was agreed to.

The motion was carried.

Constitution of Public Health Committee

Dr. C. METCALFE BROWN moved: "That the constitution of the Public Health Committee be amended so that the Public Health Committee (Scotland) appoints two representatives to the Public Health Committee, and the Society of Medical Officers of Health includes one representative from Scotland among its seven appointees to the Public Health Committee, and that there be no separate regional representation from Scotland."

Dr. J. M. DUNLOP (Public Health Committee) moved the following amendment: That the word "three" be substituted for "two."

Dr. Dunlop said that in an attempt to show more democracy it had been agreed that every regional public health committee in Britain was entitled to one seat on the Public Health Committee, apart from London, which, owing to its size should get two. Scotland with five regional public health committees was therefore entitled to five seats. Scotland agreed that would be over-representation, but thought the recommended number of two seats was too small and wished to have three seats.

Dr. METCALFE BROWN stated that the recommendation had been carefully considered by Council, and said he would leave the decision to the Representative Body.

Dr. S. WAND (Treasurer) opposed the amendment. There were too many committees of too big a size already. Indeed, a Scottish Public Health Committee existed to deal with Scotland. He urged the Meeting to reject the amendment.

The amendment was lost.

The motion was carried by the necessary majority.

On the motion of Dr. METCALFE BROWN, the remainder of the Annual Report of Council under "Public Health" was approved.

Immigrants

A motion by Thames Valley, "That this Meeting is disturbed by the absence of any arrangements for the medical screening of the dependants of immigrants, and requests that urgent representations be made to the Government to take appropriate steps," was carried.

Chiropody Treatment

A motion by Tower Hamlets, "That this Meeting considers that chiropody treatment should be an integral part of the National Health Service and that measures should be taken by the Ministry of Health to implement this," was carried.

School-crossing Patrol Staff

Dr. H. GORDON (Council) moved: "That this Meeting urges the appropriate authorities to institute medical screening (at least a check on visual capabilities) of school-crossing patrol staff."

Dr. Gordon drew attention to the possible dangers of employing crossing patrol staff with defective vision or other physical disabilities. No medical examination was mandatory before men and women were given the jobs. It was desirable that these people, who were directing others on the roads in this country and also looking after the children of the community, should be subjected to some form of screening.

The motion was carried.

Constitution of Central Consultants and Specialists Committee

Mr. J. R. BLACKBURNE (Central Consultants and Specialists Committee) moved:

(i) That the number of seats on the Committee allocated to the Hospital Junior Staffs Group Executive Committee be increased from 4 to 12, one to be filled by the Chairman of the Hospital Junior Staffs Group Council (Scotland) and another to be filled by a member of the Hospital Junior Staffs Group Council (Scotland) nominated by the Central Consultants and Specialists Committee (Scotland).

(ii) That the number of seats on the Committee allocated to the Central Consultants and Specialists Committee (Scotland) be reduced from 10 to five.

(iii) That the five seats allocated to "part-time specialists" be abolished.

(iv) That the four seats filled by the Representative Body be reduced to three, two to be elected by Representatives of Constituencies in England and Wales and one by Representatives of Constituencies in Scotland.

(v) That the number of seats allocated to the S.H.M.O.s Group Committee be reduced from two to one

(vi) That a seat be allocated to a medical assistant, to be elected by a method to be determined.

(vii) That the following clause in the Schedule to the By-laws be rescinded in relation to the Deputy Chairman only:

> "The person or body entitled to appoint a representative to the Committee shall be entitled to appoint an additional representative to be a member of the Committee during any period for which a representative appointed by such persons or body shall hold office as Chairman or Deputy Chairman of the Committee."

(viii) That the seat allocated to a representative of the Occupational Health Committee be abolished.

(ix) That the observer from the Central Dental Consultants and Specialists Committee be admitted as a full member."

Mr. Blackburne said the object of the motion was to try to comply with the request of the Council to the C.C. and S. Committee and other committees that they should look at their structures and see whether they could streamline themselves and make the committees smaller, and also—something the C.C. and S. Committee had already decided to do—to increase the representation of the junior staffs.

The first proposal was to increase the number of junior staff from 4 to 12. The Committee was in full agreement with that, and believed it was also the wish of the Representative Body.

The second proposal was to reduce the number of seats of the Scottish Committee from 10 to 5, about which the C.C. and S. Committee had been a little unhappy. All sections had been asked to look for places where reductions could be made. The Scottish representatives generously had agreed that they would cut down their representation in the hope that other sections would do the same. Since then it had emerged that the seats allocated to the special groups could not be cut in number, which meant that the sacrifice the Scottish Committee had made was not being followed by other sections. It was only fair to say that in his view, and he believed in the view of the Scots themselves, they were adequately represented. Under the new proposals there would be 12 representatives from Scotland out of an average of between 80 and 90, which was rather more than the one-in-eight representation. Mr. Blackburne therefore hoped the Scottish representatives would be prepared to carry on with the reduction to which they had originally agreed.

The third proposal was to abolish the five seats allocated to part-time specialists, since the seats had not been filled for some years. The fourth proposal was to cut down the number of representatives elected by the Representative Body from four to three. This would be the Northern Ireland seat, as there were already two Northern Ireland representatives on the Central Consultants and Specialists Committee. The fifth proposal was to reduce the number of seats allocated to the S.H.M.O. Group Committee from two to one. The S.H.M.O. Group was diminishing as a large number of S.H.M.O.s were made consultants and some were made medical assistants. No more appointments would be made. The extra seat might be allocated to the new group of medical assistants, which was the sixth proposal.

The seventh proposal, that the seats allocated to deputy chairmen should be out of the regional representation, would save another two seats. Next, it had been felt the seat allocated to the Occupational Health Committee could be abolished, to which the Occupational Health Committee had itself agreed. The final proposal was that the observer from the Central Dental Consultants and Specialists Committee should be admitted as a full member.

It had not been possible to make as complete a reduction as had been hoped, but those reductions proposed were reasonable and would, Mr. Blackburne hoped, receive the Meeting's approval.

The motion was carried.

Title of Committee

Mr. BLACKBURNE then moved: "That the title of the Central Consultants and Specialists Committee be changed to 'The Central Committee for Hospital Medical Services,' and that the regional consultants and specialists committees be styled 'The . . . Regional Committee for Hospital Medical Services.'"

Mr. Blackburne said that originally the Central Consultants and Specialists Committee had represented largely the senior members of the hospital staff, but in recent years it had done more and more representation of the junior staff, and, it was hoped, would now represent the whole of the hospital services. The suggested change of title was therefore proposed.

The motion was carried.

General Medical Services

Dr. A. M. MAIDEN took the Chair.

Dr. J. C. CAMERON (Chairman of the G.M.S. Committee) moved: "That the Annual Report of Council under 'General Medical Services' be received."

He said that the year had been one of the most trying that the Committee had experienced. He would not wish to go through the last 18 months again. A year ago the profession had been given just about enough in the Review Body's award and in the three joint reports to enable doctors to start remedying the ills of general practice. "As a result of the economic climate we had to accept phasing, freezing, and, worst of all, having to watch the continuing deterioration in our manpower and work load," he said. It had not been easy for any doctor in practice. It had been only the mild winter which had enabled them to pull through. Now, and only now, could doctors see what the Review Body had really intended. Representatives must not forget that in the first whole year of the two-year period for which the Review Body had made its recommendations doctors had received a quarter of what had been intended—they had lost £18m.

The Review Body had deliberately made an award favouring general practice, where it had seen the greatest need to encourage recruitment. Yet, though general practitioners were supposed to have the greatest award, the economic restrictions had caused them to receive only a quarter of their award. Hospital doctors had received twice as much. Thus the Government had completely reversed the differential proposals of the Review Body.

Dr. Cameron continued: "We shall bring all this to the notice of the Review Body and quote the very simple figures which show that the number of general practitioners has still failed to keep up with the increase in the population. In fact only in the last three months has there been any slowing up at all in the rate of deterioration of our manpower situation." So much, then, for those who said said that remuneration was not the real problem. But doctors must never forget that it was as important to improve the conditions of general practice. Without improvement of recruitment all the labours would be in vain. Family doctors had a responsibility to encourage young doctors to enter general practice.

During the year the General Medical Services Committee had had to undertake a difficult and detailed task. The translation of the recommendations of the Review Body and of the three reports into practical form had required long negotiation and consultation with experts in the various fields, leading to careful scrutiny and approved by the Committee. In a few instances iniquities and anomalies had appeared in the course of practical application, Dr. Cameron went on. The Committee had tackled them immediately, and he was glad to say it had been able to put many of them right. He was grateful to individuals who had drawn attention to those matters, and he could assure them that every case brought to the Committee's notice had been put to the Ministry of Health, either individually or as part of a general case. The urgent review the Committee was carrying out now with the Ministry had already produced some amendments.

The Minister recognized that the problems of the chronically designated areas could not be met just by the special payments for practising in those areas. An intensive inquiry was being carried out, and the Committee would join the Ministry in a special review of that serious problem. But as an interim measure it had been proposed that even if a doctor's main surgery was outside the specially designated area he would receive the whole payment if 80% or more of his patients lived in the area, and proportionately less down to 60%. Under that figure he would not receive the payment. The circulars would be produced shortly and payment would be with effect from 1 October 1966. In the case of groups which ceased to fulfil the conditions for group payments owing to departure of a member of the group the payments would continue as at present till the end of the quarter, and for a further four quarters where a replacement was genuinely being sought.

Dr. Cameron said it was proposed that doctors who had started postgraduate education but had not completed 10 sessions at recognized courses before 1 October 1966, so as to qualify for the £60 payment, should be paid for the sessions to their credit at October 1966 on a pro rata basis.

Vocational training payments would be made when a traineeship had been held for at least nine months and not necessarily the whole year. In the case of seniority payments breaks of up to 15 months spent in general medical services would not invalidate seniority as a principal. In breaks away from general practice seniority as a principal would be reaggregated after a further five years as a principal.

That was only a rough outline of some of the main points, said Dr. Cameron. Circulars would follow and other matters were being persisted in.

Conditions of Practice

There was much relating to the conditions of general practice other than pay. Some matters which had remained unchanged for at least 20 years were being dealt with. A great deal of revision was needed. In Dr. Cameron's view it was essential to do the job carefully, painstakingly, and without hurry. This was particularly the case in the review of the Regulations and Terms of Service. He would limit his remarks to main considerations.

First there was the problem of practice premises. The repayment of rent and rates had started. Owing to slowness of valuations it might be a little time before some doctors received all that was due to them. He was determined that they should get what was right, and he reminded the meeting that injustices which many doctors had suffered since 1948 were being remedied.

Health centres had a particular topical interest, and many were attracted to them. It was thought they would enable doctors to provide the up-to-date service for the patients in the most economical way. That perhaps was so, but there should be caution. It was expected, with the help of experts in many fields, that a summary of the present position, with general guidance, would be produced. If doctors went into these centres they should be careful to continue to provide the personal service that was the hallmark of good general practice. There was a risk of becoming institutionalized. In this age of automation and computers family doctoring had to remain a personal service, said Dr. Cameron. He was sure that the future of general practice did not lie in conveyor-belt methods nor in adopting the atmosphere of the worst hospital outpatient departments.

One aspect of health centres which was causing concern was the extent of security of tenure. Attractive as health centres could be, they must not be allowed to weaken the doctors' position as independent contractors. They should let the G.M.S. Committee look at agreements they were asked to sign. The Committee would have them examined by legal advisers.

If doctors worked in premises provided by a local authority they would not be able to continue indefinitely to practise in those premises if they left the N.H.S. They were premises provided for National Health Service practice. Those were the hard facts. The G.M.S. Committee would always insist that doctors were not precluded from practising in health centres privately as well as in the N.H.S., but if they left the Health Service all that could be hoped for would be a reasonable period of notice to find other premises. When doctors owned their premises the position was quite different. He thought it essential that general practitioners should maintain their position as independent contractors. (Applause.) The development of better premises for family doctors was something for which all must work, but Dr. Cameron hoped that many doctors would find it possible to own and improve their practice premises, and thus remain completely independent.

The independent General Practice Finance Corporation was now in existence. He welcomed it. It could lend money under terms that could not be obtained elsewhere. The Group Practice Loans Scheme was being wound up. It had been an outstanding success. Originally the money had come from the Pool at the rate of £100,000 per annum of the doctors' money from 1953 to 1960 inclusive. Since the Royal Commission reported the money had been provided by the Government, but the capital had been allowed to continue to circulate in interest-free loans. Information about repayment of the sum of £800,000 which doctors had provided from 1953 to 1960 would be given as soon as possible.

Dr. Cameron referred briefly to other matters in the section of the Council's report on general medical services. He referred to the proposals for revising the constitution of the G.M.S. Committee. It had been decided to defer that matter for a further year, and he asked Chairman's permission to withdraw paragraph 54 of the Annual Report of Council and motion 260 on the Agenda.

Dr. Cameron concluded by saying that doctors were in the middle of a complicated revolution in replanning the whole of general practice. He welcomed the chance of looking at some of the problems which had emerged from the original Charter negotiations and the new system of remuneration. The full effects would not be obvious for some time, but he was confident that it would be possible to overcome whatever difficulties arose. But it was unwise to make hasty judgements. There were still tough times ahead, but he was sure that in the end family doctoring could be made what it should be—the foundation of the practice of medicine in the country. (Applause.)

Remuneration and Terms of Service

A motion in the name of Cambridge congratulating the G.M.S. Committee on its firm stand " which insisted on the implementation of phase II of the Charter on 1 April 1967," was carried.

Dr. J. N. REDFERN (East Yorkshire) moved: " That, with reference to paragraph 17 of the Annual Report of Council, the standard capitation fee is inadequate, and should be raised to a level directly and realistically related to the consultation rate."

He said the motion was short and clear, and was very much in line with a similar motion carried unanimously at the Conference of Local Medical Committees in June. The average consultation rate varied throughout the country, but it had shown no sign of falling off since implementation of the Charter. In the past four years in his practice the annual consultation rate had risen from 3.5 to 4.2. The value of the pound fell as each year passed. The result of the Charter and the Review Body's Award had been to raise fringe benefits—ancillary help, rent and rate payments, group practice, and seniority and designated area payments. These were welcome and well fought for, but, taking an average doctor with none of those additions, the pay for general medical services had fallen far short.

Dr. B. TAYLOR (Tower Hamlets) moved an amendment: " That, with reference to paragraph 17 of the Annual Report of Council, the standard capitation fee is inadequate and should be raised to a realistic level."

He said his Division put this amendment because if from the beginning doctors had had a reasonable capitation fee there would not have been many of the problems which had arisen.

Dr. CAMERON accepted the amendment.

Dr. LUFFINGHAM (Council) spoke against the amendment, because it was a direct negative. The amount of the capitation fee needed to be calculated in a different way. The £1 bore no relation to the amount of work done. If the amendment was accepted it would not help.

The amendment was lost.

Dr. W. J. C. SCOTT (Dunbartonshire) moved an amendment to add the words: " and regrets that the statement of fees and allowances payable to general medical practitioners does not conform with the payments for items of service recommended in the seventh Report of the Review Body, and instructs Council to ensure that these payments be implemented."

He thought the immunization fees were too low. The Review Body had stated that the fee for these items of service should be 7s. 6d. per item. When it came to a course of, for example, cholera vaccine, which meant two vaccinations, the fee paid was for only one item of service. Attention had not been drawn to this anomaly, and the Council should take steps to see that the rates recommended were paid.

Dr. CAMERON said it was the Association's policy to get these payments made more realistic. The Review Body had recommended a standard fee for items or courses of service in pursuance of public policy, and it had been left to the health departments and the profession to agree on it. Seventeen shillings and sixpence had been agreed for a three-injection course. He did not oppose the amendment, but the facts were not as the Representative Body had been led to believe.

The meeting agreed that the amendment should be added as a rider to the motion.

The motion, as amended, was carried.

A motion in the name of Guildford " That this Meeting affirms its determination to maintain the freedom of general practitioners as independent contractors, notwithstanding the inclusion of a salary as a possible means of remuneration for a small minority of general practitioners," was carried without debate.

Unilateral Power

Dr. D. V. CASHMAN (Tyneside) moved: "That the Minister's unilateral power to alter the Terms of Service is not acceptable to the profession."

Difficult as it was to believe, he said, after 20 years of the N.H.S. the contract which the family doctor was compelled to accept bound him to terms of service which the Minister might later change, perhaps to the doctor's detriment, after he had accepted them. The relevant paragraph of the Terms of Service read: "The Executive Council may, with the approval of the Minister, alter the terms of service as from such date as he may approve, by giving to each practitioner, subject to subparagraph 3 of this paragraph, notice of the proposed alteration."

It was true there were recommendations that the Minister should consult "such organizations as he may recognize as representing practitioners," but he was not required to follow any advice he might be given, so that the terms of service could be altered without the profession's agreement. That would make nonsense of negotiation. It was no use saying it had not happened, or was not likely to happen. The Representative Body should declare that it would never happen "by insisting upon the immediate revocation of this iniquitous anachronism: the Minister's absurd and intolerable privilege in this matter."

Dr. CAMERON said that the offending passage had been extracted from the new draft Regulations. The National Health Service was based on an Act of Parliament, but it had been agreed that there would be no alteration of the terms of service without consultation with the profession.

Dr. CASHMAN, in reply, said that it might be suggested he was tilting at windmills. He had had a letter from the Windmill, or rather from the Elephant and Castle, as follows: "The terms of service are now being recast in consultation with the profession's representatives, and it would not be surprising if this particular provision disappeared. Yours sincerely, Kenneth Robinson." If the Minister himself accepted that the present position was inequitable "who are we to say him nay?"

The Tyneside motion was carried.

Another motion by Tyneside, "That the Review Body's urgent attention be drawn to the fact that, up to April 1967, Government implementation of their recommended award in respect of general practitioners falls short by approximately £18m., and that the Review Body be invited to recognize this fact in their next report," was accepted without debate.

Basic Practice Allowance

Dr. M. GOODMAN (Liverpool) moved: "That this A.R.M. considers that the present level of remuneration for the basic practice allowance is unrealistic."

He said they were dealing with the money which was needed for the basic requirements of general practice. He referred to some of the items it was supposed to cover, and he thought the amounts were unrealistic.

Dr. D. BURRELL (Winchester) said he would be glad to see the basic practice allowance itemized, but he would be sorry to see the motion carried completely. An increase in the basic practice allowance would approach nearer to a salaried service.

Dr. CAMERON said the question of the size of the basic practice allowance was something that had to be looked into.

The motion was carried.

Dr. JEAN E. LAWRIE (Dartford) moved: "That this meeting is disturbed to learn that executive councils are assessing the eligibility for basic practice allowance of part-time practitioners on the number of prescriptions they are writing."

She said the Dartford Division was disturbed to learn that in some areas executive councils were using the total number of prescriptions prescribed by a doctor in a given time as a yardstick to measure a general practitioner's activity. Dartford was utterly opposed to the practice; the number of prescriptions prescribed in any given time was not a valid measure of quantity or quality of work. It was degrading to doctors to be assessed in that way. She asked the Meeting to join Dartford in its concern at the implication of this activity of executive councils and to carry the motion.

Dr. D. R. COOK (Camden) said that there were executive councils using prescription counts as a way of measuring the activity of practitioners. It was a practice which the Representative Body should vigorously oppose for two reasons. Firstly, it was something being done as a check, unknown to the doctor, and, secondly, it was a most inefficient instrument to gain the required information. It was a wholly fallacious exercise which gave wholly fallacious information, and it had to be resisted.

Dr. J. S. NOBLE (Council) supported the motion. He had had instances brought to his attention where women doctors and others had almost been given the "third degree." If it was wanted to get women doctors back into part-time practice this treatment would not help. It was antiquated.

Dr. I. McD. G. STEWART (Blackpool and Fylde) said it was extraordinary that such a thing should be a criterion of worth in a practitioner. It was an active incitement to bad medicine to suggest that prescriptions should be written in greater number. He thought that if the number of prescriptions were halved or quartered the medicine practised would often be commensurably better. He supported the motion.

Dr. CAMERON said he was equally concerned. He asked any representative who knew of the practice to report it to the G.M.S. Committee and it would take it up with the Ministry.

The motion was carried.

Itemize Allowance

The Meeting agreed that the wording of a motion by Nottingham should be amended to read: "That this Meeting instructs Council to ask the Minister to agree to the publication of each item included in the basic practice allowance."

Dr. I. L. LOCH (Exeter), moving the motion, said that a year ago, at a special Conference of the Representatives of the Local Medical Committee, the Chairman of Council had proposed that a motion by Inner London, asking that information be sought about the way in which the £1,000 basic allowance had been built up, should be referred to the G.M.S. Committee. Dr. Cameron had stated at this year's Conference that the G.M.S. Committee had made an informal approach to the Review Body on the subject, but had been told that if a formal approach were made to the Review Body it would not give the information, since the figure was based on confidential inquiries. The confidential information must have come either from the Minister or from the profession. He was sure that representatives had no wish for that information to be confidential. The motion had asked specifically that the basic practice allowance be itemized. He assumed that the refusal by the Review Body was because the Minister himself wished to keep the information confidential. It was difficult to understand on what grounds the Minister wished this information to be withheld.

It had not been completely clear in the seventh report of the Review Body what the basic practice allowance was intended to pay for. The evidence from the profession to the Review Body stated that the basic practice allowance was intended to consist of, firstly, reimbursement of standing expenditure—a phrase which had not been defined—incurred by every general practitioner. Did that mean telephone costs, heating and lighting, car expenses? Nobody knew. There were so many anomalies that it should be insisted before the Review Body made recommendations in 1968 that the Minister and the profession should agree the content of the basic practice allowance.

Dr. J. R. EDWARDS (Exeter) said it was difficult to discover exactly what was covered by basic practice allowance. Until that was known he thought the matter could not be argued further. The facts must be known before further claims could be made. His only concern was that if the Minister refused and the Review Body refused where was the profession then?

Dr. S. J. CARNE (West London) wondered if the Meeting would accept the motion as a reference to the Council, with the clear understanding that it was not to be put off by vague phraseology such as "general expenses." The change in the wording of the motion had extracted much of the bite from it.

Dr. CAMERON said that, subject to the wishes of the Representative Body, it was in mind to seek an itemization of the basic practice allowance from the Ministry and the Review Body. What the Review Body had said was that it was dependent on confidential inquiries which it had made on its own account. That meant that the subject was not quite as simple as it had been put.

The motion was carried.

Seniority Payments

Dr. P. W. LUMLEY (Bromley) moved: "That this Meeting draws attention to the loss of seniority awards due to a break in continuity of service and urges the strongest possible representations to the Minister for immediate correction of this unjust anomaly."

He said that the agreement to permit the principle of seniority awards to be united with a penalty, which also acted as a disincentive, was irrational. It was a long haul to the final seniority payment—probably at the age of 60. As some wags would have it, it was "a senility award." That should be seen for what it was—an incentive bonus for those who could retire at 60 to stay on and to improve their final pension should they live to receive it. If seniority was so to be rewarded it should be rewarded without strings attached.

Dr. S. Copp (Cardiff) pointed out that there were conditions which could be altered by regulations. For instance, the Minister might suddenly decide that doctors would have to do a six-weeks refresher course each year to qualify for an award.

Dr. H. F. C. Johnson (East Norfolk) said that it was a classic example of one Ministry encouraging doctors to go overseas to serve in developing countries and another Ministry penalizing them for so doing.

Dr. Cameron said he was interested in what the last speaker had said about medical service overseas. The Ministry had been "hammered" on that question, and the Ministry would not relent. He took it that the motion would be passed and that it would be an instruction "to go back again." He thought it was quite wrong that a doctor should suffer in seniority because he elected to serve overseas.

The motion was carried.

Service as Assistant

Dr. R. T. F. Morrall (Grimsby) moved: "That all service in N.H.S. general practice should count towards seniority awards, including service as an assistant."

He said that every practitioner was eligible for a seniority allowance when his name had been continuously included in the *Medical Register* for 15 years from the date of registration and he had been a principal for the last five of those years. The motion sought to establish that the services provided by a doctor working in general practice, whether as a principal or as an assistant, should not differ in any material way from the point of view of seniority. He thought it particularly applied to a doctor moving to another practice, as an assistant with a view.

Dr. Cameron thought it might be impossible to get a blanket agreement. He agreed that it was something on which the profession should take to the Minister again. There were cases of doctors who were penalized.

The motion was carried without dissent.

A motion by Guildford, "That seniority payments should be payable at 15, 25, and 35 years from qualification and not from registration," was, by leave, withdrawn.

Dr. S. Copp (Cardiff) moved: "That the second point in the payment scale for seniority should be related to 20 years of service."

He said he had in mind doctors who had spent some of their medical life in the armed Forces, and as a result their service in the National Health Service had been limited. Cardiff thought that these doctors should be able to make up for the time they had lost in the armed Forces.

Dr. Cameron said that if the Meeting would approve the motion as a reference to Council he thought that should meet the case. He would hesitate to accept it as a binding instruction.

The motion was passed as a reference to the Council.

A motion by Dartford, "That seniority awards should increase annually after 15 years," was, by leave, withdrawn, and a motion by Cambridge, "That the pre-registration year should be allowed to count for seniority awards," was accepted.

Vocational Training Allowance

Dr. Joyce E. Brooks (Southampton) moved: "That the vocational training allowance should continue when the seniority award is granted."

She said that a young doctor who took the trouble to prepare himself for general practice by three years in hospital received £125 per annum when he went into general practice. When he had been on the register for 15 years he was presumed to have grown older and wiser, and yet he got only £200 per annum. Southampton thought that the vocational training allowance should continue for such a doctor.

Dr. H. S. Howie Wood (Isle of Wight), supporting the motion, claimed that the whole question of postgraduate grants needed looking into. Priority approval was essential, and that had been refused in many cases for lectures of a high standard. The Ministry should encourage general practitioners to take as much postgraduate training as they possibly could.

Dr. Cameron said that the vocational training allowance was set apart for a certain purpose. The seniority award had another function. Was it right that because a doctor did that extra time in practice he should have that allowance for the rest of his life? It seemed to Dr. Cameron it would be very difficult to justify it.

The motion was lost.

Dr. J. D. Sinson (Leeds) moved: "That this Meeting deplores the fact that when a practitioner receives a seniority award he loses the postgraduate training grant."

He said his Division thought that this was an important matter of principle. It was wrong that when a doctor qualified for one sort of allowance his entitlement to another and completely different allowance should then be ended. It seemed to Leeds that it was wrong that the postgraduate education allowance and the seniority awards should be grouped together. The doctor had earned his seniority pay for his work in the National Health Service and he should still be entitled to his postgraduate allowance.

The motion was carried.

Qualification for Payment

Dr. W. F. de C. Veale (Brighton and Mid-Sussex) moved: "That urgent action be taken to publish details of the requirements for attending a stipulated average number of sessions per annum of approved postgraduate training in connexion with qualification for payment or continued payment of an addition for seniority in accordance with paragraph 17 of the 'Statement of Fees and Allowances payable to general medical practitioners.'"

He explained that the only purpose in bringing the motion was to emphasize to the negotiators that there was considerable worry, if not alarm, that there had been no announcement about how much postgraduate training was required. No one wanted to have to crowd in three to four weeks' training in the last year, 1968 to 1969, to bring up their average to the required number of sessions. Under the new basic salary arrangement there had been a slight drop in the number of applications for postgraduate courses in the first half of 1967, but in 1968–9 it might be impossible to get a place on a postgraduate course if details of requirements were unduly delayed.

Dr. Cameron hoped the Meeting would pass the motion unanimously. The matter would be settled as quickly as possible and it would be seen to that the time was extended, so that doctors would find no difficulty in fulfilling the requirements. He gave that assurance.

The motion was carried.

Dr. G. L. Powell (South-west Wales) moved: "That, with reference to paragraph 17 of the Statement of Fees and Allowances as payable to general medical practitioners in England and Wales 1966, Council be asked to investigate the position of the doctor unable to attend the postgraduate training necessary to obtain a seniority award."

He reminded members that paragraph 17 stated that "On and after 1 October 1969, in order to qualify for a payment or continued payment of an addition for seniority in a period of 12 months from 1 October in any year, the practitioner must, during the years from 1 October 1966 (or since becoming a principal in general practice if this was later) to that date have attended a stipulated average number of sessions per annum of approved postgraduate training. Further details of the requirement will be issued in due course."

His Division thought it was iniquitous that a seniority award should depend on postgraduate training. However, the condition had been accepted with the Charter. But that was not to say that the Charter must not be under constant review and, when necessary, revised. All doctors knew the difficulty of obtaining a suitable locum. Single-handed practitioners had already lost their group-practice allowances through being prepared to work long hours in an isolated community. Must they now lose their seniority award for the same reason? In the later years of their professional life they would be losing £650 a year for these two reasons. Was the opinion of the profession so poor that it was thought a doctor was no good unless he did postgraduate training? Did the original years of training, the years of experience in practice, count for nothing? This required immediate action to rectify the position which at present interfered with the freedom of the doctor to practise where he wished as well as penalizing him financially.

Dr. Cameron said that if there were special cases of difficulty in isolated rural areas for single-handed practitioners particulars should be given and something done. He accepted the motion on the understanding that special cases would be investigated as they arose.

The motion was carried.

Elderly Doctors

Mr. R. J. Williams (North Glamorgan and Brecknock) moved: "That family doctors over the age of 70, providing full-time general medical services, should not lose seniority payments."

He pointed out that many doctors in this age group were still in active practice, and if it was allowed that a practitioner qualified for the basic practice allowance it must follow that he was undertaking full medical services. Why, therefore, cut down his income? It discouraged work by experienced, established, and known general practitioners at a time of extreme shortage. "In South Wales," he said, "the fact that a general-practitioner service can still be maintained is due in no small measure to the number of doctors over the age of 70 still in active practice."

Dr. J. S. HAPPEL (Winchester) moved as an amendment: "That until 1972 family doctors over the age of 70 years providing full-time general medical services should continue to enjoy seniority payments."

He said that the unique contribution of those approaching 70 was recognized, and the amendment limited the seniority benefits to a term of five years, when it could be reviewed.

Dr. F. E. GOULD (Birmingham) thought the original motion adequate and that doctors should continue in practice so long as they were capable of doing a full day's work. Dr. D. BURRELL (Winchester) supported the amendment, because it would be unfair to stop the seniority payments immediately of those doctors aged over 70. They should not in normal circumstances be practising full-time medicine, and this should not be encouraged by extra payments.

Dr. B. L. ALEXANDER (Manchester) said that there were 3,000 doctors over the age of 65 out of 23,000 general practitioners. Those in the 65-and-over age group were the doctors who had had to wait years and years for their compensation. They were the ones who would get poor pensions. They were the ones on whom the country was relying to keep the Health Service from falling apart. Yet at the age of 70 the seniority to which such doctors were entitled was being stopped. While there was a shortage of general practitioners the best possible should be done for all those who could do a full day's work.

Dr. CAMERON said that the overwhelming support of the Representative Body was needed. All the arguments had been used on the Ministry and no progress had been made. Two vacancies in the last few weeks had been filled by applicants aged over 70. He would be the first to say that a situation should not be perpetuated where doctors went on practising when they were past it. Nevertheless, as things were at present, it was a crying injustice that doctors asked to stay on because of the shortage of medical manpower should have to accept this cut in remuneration merely because they had passed their 70th birthday.

The amendment was carried by a large majority.

The amended motion was carried as the substantive motion.

Inducement Payments

Mr. R. J. WILLIAMS (North Glamorgan and Brecknock) moved: "That the criteria at present laid down for inducement payments to family doctors are wrong and should be urgently reviewed."

He pointed out that the basis of designation of an area simply on the doctor–patient ratio and the requirement for designation to be operative for a period of three years before the inducement payment could be offered were criteria which were not only too narrow but might be too late in operation. The system should be more flexible and rapid in operation. Work loads should be taken into consideration. Patient demand was also significant. In South Wales the load was twice the national average and three times that of the lightest areas. The morbidity among old doctors in those areas, because of sustained overwork, was high, making a still further increased burden on colleagues. Areas might be uncongenial. Terrain might be difficult. Building land might be scarce, or poor, or unattractive. Educational facilities might leave a lot to be desired. First-class district hospital facilities might not be readily available. Surgery accommodation might be inadequate. All those and similar factors should be appraised and perhaps an assessment made on the points system. That would provide a broader and more realistic basis and avoid the difficulties of the present system.

Dr. N. STRANG (South Shields) moved as an amendment: "That the criteria at present laid down for inducement payments are wrong and should include unattractive industrial areas where the doctor–patient ratio remains constantly high."

He explained that the purpose of the amendment was to draw particular attention to some of the industrial areas which were unattractive, where the work load was heavy, and the doctor–patient ratio high. It was to draw attention particularly to those which were not designated and to see that some inducement allowance was awarded to doctors in such areas.

The amendment was carried.

Dr. CAMERON said that when chronically designated areas had first been discussed it had been possible to define five such areas in England and Wales. The idea had been to encourage doctors to go into those areas, at the same time recognizing the heavy work load that they would have to cope with. The whole picture had changed since then, and there was no pattern of designation over the country. The question of designated areas, apart from the chronically designated areas, now had to be tackled. The new scheme would be without detriment to the doctors already in designated areas who at present came under the scheme of remuneration which had been agreed.

Dr. F. O. WELLS (East Suffolk) said that the suggested wording left the criteria wide open. It was said that the inducement payment would be paid in sparsely populated areas or for other reasons which made the area unattractive to doctors. If those criteria could not be fulfilled whatever Dr. Cameron had done might well be undone. Care must be taken about the manner in which the motion was accepted.

Dr. C. J. SWANSON (Council) said there were two entirely different problems. One was inducement payments, which had already been introduced in Scotland, and the other was special payments for unattractive areas. Special payments would not solve the problems in the unattractive areas, and an improved solution should be found, but it would not, on the other hand, be possible to carry on without inducement payments in Scotland.

Mr. WILLIAMS, in reply, said there were two types of criteria to be considered—those for designated areas and those for inducement payments. There was little doubt that many areas which were not designated in South Wales were grossly under-doctored, and inducement payments were needed to encourage doctors to go to these areas. Such things as work load and environment should be taken into consideration when criteria for inducement payments were being considered.

The motion, as amended, was lost.

Night Visits

The CHAIRMAN moved a motion drafted by the Agenda Committee under Standing Order 16 (iii): "That Council be instructed to negotiate more advantageous terms for night visits."

Dr. D. R. COOK (Camden) moved an amendment: "To add 'and to alter the statement of the practitioner on Form E.C. 81 to certify that the patient has been visited to avoid the need to introduce modified claim forms for the use of deputizing services.'"

Dr. Cook said deputizing services would become more important in the future and would spread to many new areas. Executive councils had issued modified claim forms for night visits in the areas where deputizing services were used providing for the signature of both the principal who would receive the payment and the deputizing doctor who had made the visit. That caused a lot of unnecessary trouble. The principal should be allowed to certify that the patient had been visited, and this should be all the executive council should require.

Dr. GOULD (Birmigham) disputed what Dr. Cook had told the Meeting. There was no need for a special form to be used for cases seen by a deputizing doctor. It was perfectly in order for the doctor to sign *per pro* the principal doctor, and the forms were sent to the executive council direct. The same principle applied in the rotas system.

Dr. R. G. TROUP (Havering) said in his area not only were there deputies for general practitioners but deputies for doctors in the deputizing services. The local executive council had produced a number of forms all amending the original form E.C. 81, which were becoming so complicated that it was difficult to understand them, and the interpretation put on them by the executive council might be entirely false.

The amendment was carried.

Dr. S. COPP (Cardiff) moved the amendment: "That the following sentence be added to the motion: 'This should be made to apply equally to subsequent visits, after the first, when the condition of the patient indicated that such further visits be made.'"

Dr. Copp said he understood the second visit could not attract a separate fee, although Dr. Cameron had indicated that this was not so. If Dr. Cameron was correct, and a second fee was available, he would be happy to withdraw the amendment.

Dr. CAMERON said if any doctor had difficulties with an executive council he should let him know and the matter could be investigated. It had not been envisaged the fee should be for only one visit. The doctor might well have to go back on a second occasion, and, if so, was surely entitled to a second fee.

The amendment was carried.

The Meeting accepted the following motion from Birkenhead and Wirral: "That this Meeting objects to the patient having to sign the night-visit form."

Dr. J. H. MARKS (Barnet) moved an amendment to add the words: "and all other forms for item-of-service payments."

Dr. Marks said that the signature of a doctor was important. It was accepted without question by private individuals and Governments on all forms of certificates, often involving large sums of money, yet to claim a paltry pound for a night visit or 7s. 6d. for a vaccination the doctor's signature was not enough. It had to be countersigned by the patient, who might not be able to read let alone understand the form. If patients bothered to read the form they realized that the doctor claimed a fee, and, not knowing this was a pittance, thought the doctor was making a fortune. Patients also realized they were acting as time-keepers to make sure the doctor clocked on and off between midnight and 7 a.m. If the Government did not trust the doctor why should the patient?

The amendment was carried, and the motion as amended was carried.

At this point Dr. MATHIAS resumed the chair.

Grants for Assistants

Dr. T. J. CARTER (Finchley) moved: "That a general medical practitioner should qualify for a grant for an assistant if he has a National Health Service list of 2,500 patients or upwards."

Dr. Carter said that the motion had been put forward because a general practitioner in his area felt aggrieved that payment for an assistant was made only when the list size was about 3,000. The figure of 2,500 or above went into the range of practices which were above average list size. In addition, in a group practice the doctors merely had to show that they had at least 2,500 patients each.

Dr. CAMERON said that there was of course a desire to make it easier to get the assistant allowance, but an even more urgent task was to obtain an amendment of the regulations to meet the case of rural general practitioners, and in particular single-handed ones, in areas where they could build up only a small list. It would be difficult to achieve both these things at the same time.

Dr. JOAN CHAPPELL (Council) supported the motion. She hoped the employment of both full-time and part-time assistants would be encouraged. Another type of doctor who might need help was the one with an average-size ordinary list but a large maternity list. She was particularly interested in opportunities for the employment of married women doctors and retired doctors as assistants.

Dr. CARTER, in reply, said that, in view of what Dr. Cameron had said, he would not like to think that the substance of his motion would get in the way of the rural practitioners, though in his view it might even help them.

The motion was carried.

Payment by Patients

Dr. W. S. S. MACLAY (Guildford) moved: "That this Meeting reffirms its support for the principle of a small charge to N.H.S. patients for each item of service rendered by general practitioners with exemptions in the cast of hardship."

The motion was carried.

Dr. J. C. OAKLEY (Medway and Gravesend) moved a composite motion: "That this A.R.M. remains of the opinion that an item-of-service payment by the patient at the time of usage, wholly or in part reimbursable by the State, is the only realistic method of limiting the increasing demand for service from the profession and of ensuring the intelligent and economic use by the public of the necessarily limited resources of the N.H.S., and firmly instructs Council to press this issue with the health departments."

Dr. Oakley said that the crisis in the National Health Service would continue unless the increase in demand by the patient for what he wanted could be limited to what treatment it was necessary for him to have. It had been said that ancillary help, group practice organization, appointment systems, and health-centre medicine would cut the doctor's work load, but many had found the work load had increased. Pharmacists had found their dispensing was now heavier than previously during peak winter months. The only way to achieve conscientious use of the doctor's time was to levy a fee for item of service.

Dr. A. I. McLEOD (York) supported the motion. It was essential to convey to the public that doctors were not, as was so often thought, crying out once again for a further increase in remuneration, but their policy was simply to ensure that people should realize that they could not, in the present economic climate of the country, receive more and more medical services at discount prices.

Dr. E. C. E. GOLDEN (York) supported the motion on economic grounds. The resources of the National Health Service were necessarily limited because it was competing with other Government financial commitments, such as pensions, roads, and education. On the other hand, the use of the Health Service was free, and the potential use of it by the public was limitless. The equation therefore did not balance and there was a state of disequilibrium between supply and demand. A charge on the patient would in some way help to restore the balance. Better still, it would remove the economic incentives that patients had at present to consult their doctors when they did not need medical advice.

Swing of Opinion

Dr. D. L. WILLIAMS (East Denbigh and Flint) said he was worried by the words "and firmly instructs Council to press this issue with the health departments." What had to be decided was whether a further approach to the Ministry now would bring nearer the day when the Government accepted this policy. Already there was a swing of opinion in all political parties towards selective social benefits and even towards the idea of payment by the patient. People were beginning to realize that the public purse was not bottomless, and that patients with money must help to provide a better service for all. If Dr. Cameron went to the Minister now the Minister would say "no," and that would make it more difficult to say "yes" later. Dr. Cameron would have to show that the proposed B.M.A. policy was designed primarily to benefit patients, and not doctors, that the additional money it produced would be used to increase the scope and efficiency of the service, and not to line doctors' pockets, just as doctors themselves must emphasize that the extra time given to them by the diminished work load could make possible a higher standard of medical practice. The Minister knew quite well what the profession wanted, and why. To approach him at the present time might do nothing but harm.

Dr. G. N. MARSH (Council) said that the increasing use by doctors of paramedical personnel was relevant here. An empire was being built geared to a free-at-the-time service, and it left the patient without any responsibility for its proper use. He was an enthusiastic supporter of the use of paramedical workers, but the profession might be creating a huge empire which when a fee was introduced would explode like an over-inflated balloon. If there were a fee-at-the-time instead of a free-at-the-time service doctors would know what were the genuine medical demands.

Dr. J. F. BURDON (Torquay) said he thought that a fee for item of service was a disincentive to get the patients well. It would mean forms galore. It created a problem which did not exist before—the patient with no cash. A charge was not the only realistic method of reducing the work load. There were other methods, some of them good and some of them bad. Dentists and pharmacists had recently received payments for certain services and already they were beginning to rue it.

Dr. H. GLYN JONES (Bromley) opposed the motion, because as it was written it would apply not only to general practice but also to the hospital service. He asked the Meeting to think of the problem that would be created. This motion was wide enough to cover even the casualty patient. It was not a reasonable proposition.

Mr. D. N. MENZIES (Liverpool) urged caution. If passed the motion would be political ammunition and the press would say that the doctors had given instructions to prepare an alternative health service. The motion was virtually proposing a non-free health service, and the B.M.A. should have regard to its public image.

Dr. OAKLEY, in reply, said the A.R.M. had reaffirmed the policy of a direct charge to patients, but this proposal would not refer to the hospital service. There had also been reference to the problem of diminishing responsibility to the patient. Doctors could look after patients better if they had fewer to see. Some item-of-service payment by the patient at the time of consultation would reduce the number of irrelevant consultations, and if there were some form of fee it would be much easier for the patient to go to the chemist and buy a bottle of medicine for the same fee.

A motion that the Meeting pass to the next business was carried.

A motion by Medway and Gravesend, "That this A.R.M. instructs Council to pursue further payment by item of service as an alternative method of remuneration as laid down in the Family Doctor Charter," was carried.

Evening Surgeries

Dr. D. J. ADDERLEY (Lewisham) moved: "That it is desirable that all evening surgeries should close by 6 p.m. in agreement with the Minister's letter and the executive council notice E.C.N. 570."

He said that the motion he proposed was not preoccupied with money but with easing the work burden of general practitioners. Doctors could in fact shorten their day's work if they wanted to. Why did they not do it? The first reason was that the traditional service which the general practitioners gave was a long day's service to fit in with the patient's free time. The second reason was fairness to patients. Many people thought that if doctors stopped at 6 p.m. they would be preventing patients from seeing them. That was untrue. In the past four years he had closed his door at 6 p.m. and there had been virtually no complaints, said Dr. Adderley.

Dr. R. P. HENDRY (Rugby) moved as an amendment to insert the words "be entitled to" after "should." He said he was appalled by Dr. Adderley seeking to dictate what time he (Dr. Hendry) should finish his surgery. If the motion was passed and he decided to go on to 6.15 or 7.30 p.m. then he was doing something that the Association said was undesirable. They were independent contractors.

Dr. R. COVE-SMITH (St. Marylebone) seconded the amendment.

A motion that the question be now put was carried, and the amendment was then approved.

Dr. J. H. MARKS (Barnet) said he believed that the whole concept of surgery work was an anachronism. Most doctors were in practice for two reasons: to make a living and to help their patients. To do both of those things they needed to see their patients most of the day. They resented being told how to run their practices.

Dr. A. W. MACARA (Junior Members' Forum) said that if general practitioners wished to end their evening surgeries they should be given the facilities to do so. The Meeting was not trying to dictate to those who in different circumstances in rural practices or for some other reason might wish to have an evening surgery.

Dr. J. MCGLONE (Glasgow) thought the doctors' obligation was simply to provide all necessary attention, and if that could be arranged before 4 p.m. then why not? As independent contractors doctors must retain the right to determine their own arrangements within their terms of service.

It was agreed that the question be now put.

Dr. ADDERLEY, in reply, said that the opinion of the Representative Body was the opinion of the profession as a whole. If the Meeting advised what it considered was desirable then that was not dictation.

The motion as amended was lost.

Group Practices

Dr. F. V. GRIFFITHS (Wandsworth) moved: "That this Meeting formally protests to the Government against the pressure applied to general practitioners to form group practices and protests against the concomitant financial and other discrimination against single-handed practitioners."

He said there was a danger of the single-handed general practitioner being squeezed out of existence. Over the last few years there had been a concentrated effort to discourage single-handed practice and encourage group practice, and even financial pressure had been used. To quote from paragraph 205 of the Review Body's Seventh Report: "The allowance for group practice is intended to provide a financial incentive to doctors to embark upon group practices from central surgery premises. The group practice interest-free loan has provided some incentive in the past . . . and, even though it is now to lapse, its place will be taken by the scheme for direct reimbursement of expenditure on practice premises, which will mean that the cost of raising capital for group practice will be directly reimbursed."

That meant that, though single-handed general practitioners had the basic practice allowance, they were denied the £200 per annum allowed to their colleagues in groups. They had to suffer a much higher percentage of their income going on expenses; when illness struck they were often lucky to get a locum—who in London in the summer might cost £80 per week—and there had also been an inference that single-handed general practitioners were in some way inferior.

Dr. Griffiths said he believed that patients of a first-class, single-handed general practitioner were equally well if not better served than those of a first-class group practice.

Dr. F. O. WELLS (East Suffolk) moved an amendment that the words "in rural areas" should be added at the end of the motion. He said that in urban areas it was possible for single-handed practitioners to work within a group and still retain the character of their single-handed practice. But rural practitioners geographically were less able to do that.

Dr. J. S. HAPPEL (Chairman of the Rural Practices Subcommittee) said he would be quite happy to support the motion as it stood, because it applied to single-handed doctors generally. His Subcommittee had set up a working group to study the whole future of practice in rural areas, and certainly the position of the single-handed doctor loomed large in these discussions.

The amendment adding the words "in rural areas" at the end of the motion was lost.

Dr. R. P. HENDRY (Rugby) suggested that if any group of practitioners was to be singled out for £200 a year it should be the single-handed practitioner and not the group. The single-handed doctors had the much harder job.

Dr. C. O. LISTER (Aldershot and Farnham) expressed much sympathy for the motion, but said that anybody engaged in group practice must know that far from reducing the work load it had increased it.

It was agreed that the question be now put.

The motion was carried.

Definition of Group Practice

Dr. J. H. MOIR (Guildford) moved: "That the G.M.S. Committee be asked to look again at the definition of group practice, in that many practices which provide the facilities of a group practice are unable for geographical reasons, and for the convenience of patients, to practise from one central surgery."

The definition of group practice, as "all members of a group must work in close association from a common main surgery, even if they sometimes were also working at branch surgeries," had led to some ridiculous situations where practices which had drawn group-practice loans were not eligible for group-practice allowance, because the members worked at two surgeries. A river or railway or, much more hazardous, something in the nature of a motorway might divide a practice in half.

Dr. J. D. SINSON (Leeds) spoke of the position in his own Division, where some doctors in receipt of a group-practice loan for six years no longer qualified for the group-practice allowance. The position was absurd and must be cleared up quickly.

Dr. CAMERON said that in the "Red Book" it was stated that "executive councils exercised discretion" in interpreting the terms of the definition. Many executive councils had used that discretion widely, but others had not. He would advise any representative who knew of a case of that kind that first of all it was essential to put pressure on the executive council through local representatives, and that there was a right of appeal to the Minister.

The motion was carried.

Direct Payment of Rent and Rates

Dr. S. C. C. SCOTT (West Essex) moved: "That this Meeting is of the opinion that the present system of reimbursement of rent, rates, and ancillary help is unsatisfactory."

He said that Dr. Cameron had already indicated some of the anomalies. Five shillings an hour was not nearly enough to cover the rate of pay of competent help at split and inconvenient hours, so he would say no more about that. Dr. Scott gave details of difficulties encountered in his Division in the interpretation of the regulations for reimbursement of rent and rates. He asked for more support in appeals to the Ministry.

Dr CAMERON said he hoped the Representative Body would not pass the motion in its present form: it was far too sweeping.

The motion was lost.

The Meeting adjourned at 6.30 p.m.

Second day: Friday, 7 July

The Meeting resumed at 9.00 a.m., with Dr. A. N. Mathias in the chair.

Payment for Rent and Rates (Continued)

Dr. G. C. Price (Bournemouth) moved, "That this Meeting congratulates the Chairmen of Council for acting with speed and vigour in leading a B.M.A. deputation to the Ministry of Health (*Supplement,* 22 October, p. 158) to protest about the fundamental changes contained in E.C.N. 569, para. 14, and E.C.N. 567, para. 2, from the basic principles outlined in the second and third reports of the joint discussions. It notes with pleasure that both matters have now been remedied."

Dr. Price referred to the report in the *B.M.J. Supplement,* dated 22 October 1966, and said that it was clear from it that the Chairman of Council considered the changes in the E.C.N. sufficiently important to warrant his personally leading a deputation to the Minister, thus putting the weight of the whole Association behind the protests against these fundamental changes. The changes in E.C.N. 569 had constituted a direct threat to private practice. It was quite inequitable that there should be a payment of rent and rates by principals not being paid at the universal rate. Dr. Price was sure that the Meeting would agree that the Chairman and deputation should be congratulated on the success they had achieved.

The motion was carried.

Dr. A. E. Loden (Tunbridge Wells) moved, "That this Meeting requests the Minister of Health to give written assurance that direct payments for rent and rates for surgery premises in no way implies a lease of these premises."

He said it was a worrying situation where there was a possibility of the Government considering leasing premises used for private practice. He hoped everyone had read in the *B.M.J.* that Headquarters had taken counsel's opinion on this matter. But counsel's opinion varied. He thought the Minister should be asked to give an assurance on this matter, because another issue was that the money was not going to be considered as part of practice expenses but as earned income. Until he was given such assurance he would have no part in taking rent and rates for his own private premises.

Dr. Cameron said counsel's opinion had been obtained and it stated that the danger regarding leases was non-existent. However, the Minister would be asked for his assurance on the question.

The motion was carried.

The Chairman formally moved a motion by Monmouthshire: "That the B.M.A. considers the present method of assessment of notional rent quite unjust and will discourage improvement of surgery premises. The notional rent should be assessed with regard to the capital value of the premises."

Dr. Cameron regretted that Monmouthshire's representatives were not present. He urged the Meeting not to pass the motion. He was prepared to accept it as a reference, because obviously the results of the scheme must be looked at all the time. It was too early to make a judgement. It was necessary to know what the "factor" (E.C.N. 569, para. 24) was and to see the final results of valuation of premises over the whole country. If individuals whose assessments had already been made felt aggrieved they should make local representations and use their right to appeal to the Minister.

The motion was lost.

Early Payment

Dr. M. Ross (City) moved: "That this A.R.M. considers that doctors should be entitled to submit a claim to the executive council for reimbursement of payments made on account of rent, rates, or ancillary help as soon as these payments are made, and that such reimbursement shall be made to the doctor within one month of receipt of his claim."

Dr. Ross said the motion dealt with a small but important subject. There was no reason why, having paid what might be quite large sums for rent and rates, a general practitioner should have to wait for repayments for anything up to 3½ months. Since the ancillary staff were paid weekly or monthly, the repayments to the general practitioner should be monthly. It was realized that monthly repayments for ancillary staff would give the executive council more work, but that would be balanced by the fact that the rent and rates payment would be spread over a quarter. If much of the doctor's income was to come through reimbursement repayments should be made within one month of the payment.

Dr. Cameron said it was true the executive councils had a lot of extra work at the moment, but these suggestions seemed reasonable, as one worked on monthly accounts in every other sphere.

The motion was carried.

Dr. W. F. de C. Veale (Brighton and Mid-Sussex) moved: "That this Representative Meeting urges an early settlement of the 'factor' referred to in paragraph 24 of E.C.N. 569 relating to direct payment for rent and rates."

Dr. Veale said it was no secret that the owner-occupier of a house in which he had his surgery got the worst deal under the repayment of rents and rates scheme. At present doctors were paid at the rate placed by the valuation officer on that part of the house used for the practice, with the promise that it would be multiplied by a factor later on. If that factor were greater than one, then the Government was withholding money owed to the doctor, but at the same time there was the threat that it could be less than one, and the doctor might have to repay some of it. He urged Dr. Cameron to treat this as an urgent matter.

Dr. Cameron accepted the motion, and it was carried.

Dr. J. D. Sinson (Leeds) moved: "That this meeting deplores the fact that no decision has been reached on the sum payable in reimbursement of rent and rates, which was to have come into operation on 1 October 1966."

Dr. Sinson submitted that the greater the time that elapsed before the factor was settled the greater would be the loss of confidence in the Minister's intention to make proper reimbursement of rent and rates. His Division deplored this.

The motion was carried.

Dr. D. Brown (Liverpool) moved: "That, in the event of non-agreement between a local executive council and a general practitioner in the matter of the proposed payments for rent and rates, recourse to independent arbitration shall be incumbent upon all parties concerned."

Dr. Brown said the concept of reimbursement of rent and rates was not a medical matter. It was known that the Association had sought counsel's opinion on the legal position and it was held that repayment did not come under the aegis of the landlord and tenant, nor was it governed by the Rent Act. It would appear that neither the law of property nor the law of equity applied to the situation. It was most probably related to administrative law. In Liverpool not only lawyers but also the Association of Chartered Surveyors and the Association of Estate Agents had been consulted. The one point on which all these organizations and lawyers were in agreement was the need for an independent appeals chairman.

Dr. Cameron, asking the Meeting to support the motion, said it was true that the negotiators had fought hard to obtain the Minister's agreement to the reference of appeals to an independent tribunal. They had been unable to obtain his agreement at that time, but it was increasingly clear that in time there would be an independent tribunal, and, more important, this would ensure justice was seen to be done.

Replying to a question from the floor, Dr. Cameron said that if any doctor submitted a case to a tribunal it was open to the other party as well to appeal. That was implicit in having an independent tribunal.

The motion was carried.

Dr. F. G. Tomlins (Waltham Forest) moved: "That, with reference to paragraph 19 of the Annual Report of Council, this Meeting requests that counsel's opinion on the risk of Government control of premises as a result of direct payments for rent and rates be made available in full to all members of the Association who desire it, or, alternatively, that it be published in full."

He said that it was difficult to get Government money without strings attached and it was the duty of Parliament to keep some control of the purse. Owning their own premises was the best assurance of independence for doctors, and the Government had an incentive to destroy that independence. The ownership of their premises was also their best security, and they would not want to become sitting tenants of the Government. Surely the best way to allay doctors' fears was to tell the full facts, and, unless there was some overriding reason why it should not be done, counsel's opinion should be made known.

Dr. Cameron said the Minister's assurance would be obtained and counsel's opinion would also be published.

The motion was carried.

Payments for Ancillary Staff

Dr. J. A. Rigby (Worcester and Bromsgrove) moved: "That this Representative Body is of the opinion that the present ceiling for the percentage reimbursement of payment for ancillary help is too low, and in order to recruit and retain staff of high quality this ceiling should be considerably raised."

He said that Dr. Cameron's comments yesterday on this subject had covered most of the things he wanted to say, but there were one or two points. The Association of Medical Secretaries recommended that the minimum starting salary should be £520 a year for a newly trained and newly qualified medical secretary. Those were completely inexperienced people. That was the maximum that the Ministry would offer. The Minister's offer worked out at 5s. an hour, which was just a little more than some of the cleaners earned. That sort of pay reflected on a system trying to attract and keep highly qualified staff.

Dr. E. H. J. COTTER (East Herts) moved an amendment to delete the words "should be considerably raised" and insert the words "should be removed."

He first examined the ceiling that the Exchequer put on indirectly comparable fields. A girl on a hospital appointments desk aged 21 or over was paid £849 a year; a staff nurse £850 a year. Did doctors want just a staff nurse? Should there not be someone comparable to a sister in the surgery? In the health department of a local authority the ceiling for the clerical Grade 1 and 2 was £1,020 a year; for the shorthand typist £820; and for the audio typist £780.

Dr. CAMERON said that the motion was sound and would put the Association in a very good negotiating position, but the terms of the amendment would put it back at square one, with all the difficulty about controls and so on.

Dr. COTTER, in reply, pointed out that there were three forms of control already, and he could see no reason why a fourth should be imposed which made the better doctor have to pay more.

The amendment was lost.

Dr. BROWN, in reply, pointed out that the Ministry had told doctors to use an appointments system and to employ qualified staff. How could they get suitably qualified ancillary staff for £500 a year?

The motion was carried.

Doctors' Wives

Dr. F. L. P. FOUIN (City of Aberdeen) moved: "That this Meeting considers that where the wife of a single-handed practitioner is wholly involved in her husband's practice in an ancillary capacity the allowance made in the basic practice allowance is inadequate."

The Meeting agreed to change the word "wholly" to "inevitably."

Dr. Fouin quoted from the Seventh Report of the Review Body: "We have also taken into account the fact that payment to wives and other dependants will not be included in the scheme for direct reimbursement of expenditure on ancillary help, and so will have to be made out of the remuneration from other payments."

He asked, "Which other payments and how much?" The situation might be acceptable for those in group practice, but for doctors in single-handed practice—especially rural districts—it was not.

Dr. JOYCE E. BROOKS (Southampton) regretted that the wording had been altered. The wife of a single-handed practitioner was not inevitably involved in her husband's practice in an ancillary capacity. It was quite possible to run a single-handed practice without a wife. "I have done it for 14 years," she said. (Laughter.)

Dr. FOUIN said that the word "inevitably," had been put in to overcome criticism that the ground was being cut under the feet of those moving later motions. It might have made more sense if it had been "if inevitably," but he thought the present version was basically correct.

The motion was lost.

Dr. A. E. LODEN (Tunbridge Wells) moved: "That this Meeting instructs our negotiating team to reopen negotiations immediately with the Ministry for the reimbursement of payments made to wives or dependants actually working as ancillary help, particularly in the case of those who have secretarial or nursing qualifications."

He pointed out that a motion of the Special Representative Meeting last year "instructed Council very urgently to find a solution." Six months had elapsed and nothing had been heard about it, so it must be assumed that it was now Association policy. Dr. Cameron had said two years ago that this was a matter "close to his heart." One had only to read the Review Body's Seventh Report to find that the negotiating team had got the subject muddled up with the general reimbursement for all wives. No member of the negotiating team seemed properly to understand the problem, otherwise they would not have made this mistake.

The CHAIRMAN said his attention had been drawn to Standing Order 25. The Representative Body was not competent to instruct the negotiating team. It was only possible for it to instruct the Council. He asked Dr. Loden if he was agreeable that the motion should be regarded as an instruction to Council.

Dr. LODEN agreed that it should be an instruction to the Council, but not a reference.

Dr. J. C. CAMERON said he did not want the Meeting to think that the Walls of Jericho would fall as easily as all that, and he assured Representatives that "we will try again."

The motion was carried.

A motion by Doncaster, "That, where existing staff have to work extra hours in order to cover the absence due to sickness or holidays of other existing staff, this extra payment involved should qualify for direct reimbursement of expenditure on ancillary help," was, by leave, withdrawn.

Dependent Relatives

Dr. D. J. P. GRAY (Exeter) moved: "That this Meeting instructs Council to inform the profession what were the checks and controls proposed by the Minister in relation to the employment of dependent relatives."

He quoted from the Annual Report of Council, that "the Ministry made it clear that it could not agree to direct reimbursement of a substantial proportion of payments made by doctors to their wives without considerable checking and control." Exeter believed that the profession had a right to know what those checks and controls were. If the Representative Body was to debate the problem of the relatives intelligently it needed to know the facts.

Dr. CAMERON said that in the case of a doctor's wife her qualifications would be examined, together with the hours she spent on duty, and the Ministry had in mind an inspectorate where the representative of the executive council could call at any time at the doctor's premises to see whether in fact his wife was employed on qualified duties. He could not see the profession agreeing to anything of this nature, and he asked the Meeting not to pass the motion. "You have given us instructions to negotiate. Let us go forth into battle and see what can be done."

Dr. GRAY, in reply, said that since Dr. Cameron had provided the Meeting with information about checks and controls he would withdraw the motion.

Permission to withdraw was granted.

Dr. GRAY (Exeter) moved: "That this Meeting instructs Council to determine and publish the commercial value of the work done in general practice by dependent relatives."

He said that Dr. Cameron had well summarized the present position in respect of dependent relatives—that the doctor should continue to pay his wife for the work which she did in the practice. It was important that the profession should continue this practice, for when the negotiators went back to the Review Body they must have a clear idea of practice expenses. His second point was that in formulating their recommendations the Review Body took into account practice expenses, including payments to dependent relatives. Thirdly, the Minister of Health had made it quite clear that the average payment in 1964 for all ancillary help in general practice had been a miserable £254 a year per doctor—this sum included nurses, secretaries, receptionists, dispensers, and dependent relatives. It was therefore perfectly clear that any payments made to relatives in the past had been purely of a nominal nature, since £254 could not have included a realistic payment for the services given.

Dr. Gray then outlined the work of a company in the Exeter Division consisting of management consultants and chartered accountants. It had, for the first time, professionally and independently evaluated the services of doctors' dependent relatives and had provided principles which would help the negotiators in arguing the doctors' case. The company had established that there was no limit to the amount a dependent relative should be paid, said Dr. Gray. Just as there was no upper limit to the work a doctor's wife had to do, so there was no upper limit to the payment. The principle of commercial evaluation would provide the negotiating team with the kind of evidence they had never been given before. "If you pass this motion," he said, "it will further this cause."

Dr. CAMERON said the issue was a highly technical one, and he was indebted to Dr. Gray for his close-knit argument. He agreed on the question of the commercial value of dependent relatives. He was prepared to accept the motion but was uneasy about committing himself about publication until he had a clearer view of the problem.

Dr. GRAY asked the Meeting's permission to delete the words "and published," and the Meeting agreed.

The motion, as amended, was carried.

Number of Dependants

Dr. GRAY (Exeter) moved: "That this Meeting instructs Council to determine immediately the number of dependent relatives working in general practice, their qualifications, and their geographical distribution."

He said that 13 months before the Representative Body had instructed Council urgently to seek a solution to the problem of dependent relatives. The motion was designed to obtain for the negotiators the facts they needed to press their case. It was important to find those dependent relatives who had special qualifications.

Dr. CAMERON said he considered the motion to be complementary to the previous motion. From the point of view of geographical distribution it was important to the problems of rural practice. He supported the motion.

The motion was carried.

It was agreed to amend a motion by Cumberland by the insertion of the word "partially." Dr. T. GARDNER (Cumberland) then moved: "That this Meeting considers that any pension contribution paid on behalf of ancillary staff should be partially reimbursed by the Government, and further that these pension rights should be transferable to any Government employment."

He said the present situation was that any doctor was obliged to carry the cost of providing for the pension rights of his employees. The matter had already been raised with the Ministry and there had been a reply, which was "typically parsimonious"—"We must treat the contributions on the same basis as contributions to National Insurance." It did not seem that National Insurance contributions were paid by all employers. They could be taken into account, and had been taken into account, when estimating doctors' expenses. Those doctors who paid superannuation paid into superannuation schemes for some of their employees. They had no kind of compensation for it and it seemed only right that what they paid in that way should be taken as part of the gross salary of the employee and that reimbursement should come from the Ministry on the same basis as the remainder of the employee's salary.

Dr. Gardner also argued that superannuation arrangements should be transferable.

Dr. B. L. ALEXANDER (Manchester) supported the motion. He said that ancillary staff were becoming a clearly defined group—specially trained, difficult to recruit, but without superannuation. Ancillary staff in the hospital service was superannuated, and if a member of the hospital staff should transfer to general practice then she lost her pension rights. Ancillary staff should be established as a superannuated class.

Dr. CAMERON said there had been discussions with the Ministry on the subject. The Ministry had given an assurance that it was going to consider this problem favourably. He thought these workers ought to have the benefit of a private pension scheme, and it should be treated as part of their remuneration. Dr. Cameron said that it ought to be possible to have a scheme whereby these girls could transfer from general practice to the hospital service or vice versa and retain their pension rights.

The motion was carried.

Payments for Special Experience and Service to General Practice

Dr. T. GARDNER (Cumberland) moved: "That this Meeting rejects 'payments for special experience and service to general practice.'"

He said that it would be hard to think of any matter that had come before the A.R.M. in recent years that had been more fully debated, canvassed, and investigated than this subject, almost to eventual boredom and irritation. Last year there had been 70 resolutions before the A.R.M. and three-quarters of them had been rejected unequivocally. The Representative Body had decided to give more time to the subject. There had been a working party and its report had been put before the general practitioners, almost 80% of whom firmly and, he hoped, finally had rejected the thing. In moving the motion he hoped that there would be a minimum of discussion, that the subject would be interred decently and quietly, and that by the size of the vote the Representative Body would indicate that it wanted to hear no more of the matter in the foreseeable future.

Dr. G. N. MARSH (Council), in opposing the motion, asked the Meeting to think for a moment of the position of a senior medical student or a junior hospital doctor. If they decided to enter hospital practice they no doubt dreamed that one day they would be at the pinnacle of the specialty they had chosen. If they entered general practice there were no pinnacles no matter how hard a family doctor applied himself to his practice. Family doctors were to some extent stultified by an egalitarian method of payment which made them all the same. What incentive was there if there were not some incentive payments? There must be some method of rewarding merit in general practice.

A motion that the question be now put was carried.

The motion was carried.

Postgraduate Education

Dr. R. P. HENDRY (Rugby) moved: "That the Review Body be pressed to recommend that an independent fund be set up for the furtherance of postgraduate education of general practitioners and for the encouragement of general-practitioner research."

Dr. Hendry said he was convinced there was a large reservoir of knowledge and expertise in various facets of general practice. It was already Association policy that adequate teaching facilities for general practice should be provided at undergraduate and postgraduate levels by practitioners actively engaged in general practice. Little progress had been made in that direction, through lack of money. The cost of such a fund would obviously be substantial, possibly in the region of £2½ million a year.

Dr. B. L. ALEXANDER (Manchester) said the motion was not an attempt to get the merit-award money under another heading but to express an opinion to the Review Body. "Let us use the money to train undergraduates in general practice, to train us in postgraduate work, and to help our research projects," said Dr. Alexander.

Dr. E. V. KUENSSBERG (City of Edinburgh) urged that there should be some clear thinking. While he agreed with the purpose of the motion, he felt the motion was not the way to go about it. Those responsible for the furtherance of general-practice education and research should have funds put into their hands through such organizations as the University Grants Committee and the Medical Research Council. The Review Body, on the other hand, was concerned with the payment of doctors for general medical services rendered to the population.

Dr. CAMERON reminded the Meeting that the money was Government money. The Review Body had set it apart and had said it was available if a suitable scheme could be found for its distribution. The Minister of Health could be approached with the suggestion that a fund might be set up along the lines of the motion.

Dr. HENDRY, in reply, said that he would be agreeable to the words "the Minister" being substituted for "the Review Body" if that were thought more appropriate.

The motion was carried.

Elections

It was announced that Dr. A. N. Mathias had been elected unopposed as Chairman of the Representative Body for 1967–8.

It was announced that Dr. J. G. M. Hamilton and Dr. J. Riddell had been returned unopposed by Scottish representatives as the two members of Council for 1967–8, and that Dr. T. W. Davies had been returned unopposed by Welsh representatives as a member of Council for 1967–8.

Other Items of N.H.S. Remuneration

Dr. E. H. J. COTTER (East Herts) moved: "That additional payments to practitioners in the case of sickness be raised to £50 per week."

Dr. Cotter said at present the sum to be paid in case of sickness had been agreed at £30. On consulting the advertisement columns he observed many figures of £65 a week plus accommodation for married couples as locum expenses likely to be incurred by a sick colleague.

Dr. CAMERON said the suggested target was a good one, and in that sense he was prepared to look at the matter again.

The motion was carried.

Dr. M. J. FORTH (Somerset) moved: "That additional payments during sickness should be the same for all general medical practitioners under the age of 70 providing unrestricted general medical services who are in receipt of a basic practice allowance."

Dr. Forth said that, though doctors were grateful to the negotiators for what they had so far achieved, it was still not enough. Only after 10 years' qualifying service did a doctor get the full rate. This penalized the young doctor entering practice who might have one or two years' qualifying service only but nevertheless a list of 2,500 patients. Admittedly it was much less likely for a younger doctor to go off sick, but if he did so he might be less able to withstand the financial strain than an older and more established doctor. Since the scheme was in its infancy still, Dr. Forth was prepared to accept the motion as a reference to Council for further consideration.

The motion was carried as a reference to the Council.

Dr. D. J. ADDERLEY (Lewisham) moved: "That the fee for emergency consultation where a patient is not resident for 24 hours should be at least that for a temporary resident, plus, if applicable, the night-call fee."

He said emergency consultations were probably the major cause of disturbance which occurred in a doctor's work. They usually occurred during a surgery or at night. In the Lewisham Division it was thought that consideration had already been given to the disturbance factor in that temporary residents were paid at the whole rate of a year's capitation fee. The fee of 12s. 6d. for emergency consultation was inadequate.

Dr. CAMERON accepted that the emergency treatment fee could well be increased. The negotiators had had great difficulty over this fee, which was an item-of-service payment. It was important that the item-of-service fees were watched and adjusted in the light of experience, but it seemed a little dangerous to tie the argument to the temporary-resident fee, because it implied other services. He preferred to keep the two issues separate.

The motion was carried as a reference to Council.

Family Planning

Dr. B. TAYLOR (Tower Hamlets) moved: "That this Meeting considers that when a patient attends a practitioner for family planning advice and examination this should attract a reasonable fee."

He said that with the advent of the pill and the coil more and more patients were going to their family doctors for family planning advice, and much time and energy was expended in this way. It could not be considered to be part of general medical services. The advice and examinations carried out should bring in a reasonable fee, and the fee should be paid by the patient. Ten shillings and sixpence was charged for a prescription to a patient for six months' supply of an oral contraceptive. This was a ridiculous fee.

Dr. CAMERON said there had been discussions on the question of providing a private prescription so that a patient might be able to purchase the pills and practise contraception on social grounds. This had been gone into thoroughly with the Minister, and the Private Practice Committee had set up a scale of fees. The difficulty was to determine whether contraception was on medical or social grounds. The view of the Minister was that he could not see how a doctor could determine that until he had examined the patient.

A motion to pass to the next business was carried.

Contraception for Social Purposes

Dr. S. J. CARNE (West London) moved: "That this Meeting is of the opinion that supervision of oral contraception for social purposes shall not be included in general practitioners' terms of service (Reference: Statutory Instrument 1966 No. 1210 Schedule 1, part 1, para. 10)."

Dr. Carne quoted the relevant regulation: "A practitioner shall not demand or accept any fee or other remuneration in respect of any treatment, whether under the terms of service or not, rendered to his patient, provided that nothing in this paragraph shall debar a practitioner from demanding or accepting a fee or other remuneration for (either) the prescribing of a contraceptive drug . . . where the drug . . . is not necessary to preserve the patient's physical or mental health, so, however, that no remuneration shall be demanded or accepted for an examination or advice connected with such prescribing and fitting."

It had been suggested that when doctors examined a woman to see if she needed an oral contraceptive they were determining whether or not there was a disease which, if present, would be treatable within their terms of service. If they prescribed an oral contraceptive and it produced side-effects those were treatable within those terms of service. He suggested it could be argued that that prescription too should be written on an N.H.S. prescription.

Dr. F. O. WELLS (East Suffolk) thought the motion a dangerous one. Supervision of oral contraception did not just include a prescription and an initial examination. If there were side-effects and complications he suggested that they would not be treated under the Health Service. Where was the line to be drawn?

Dr. CARNE, in reply, said that either the advice and the prescription were both within the terms of service or they were both outwith the terms of service. The Minister could not have it both ways.

The motion was lost.

Dr. J. A. BIRNIE (City of Aberdeen) moved: "That general practitioners should be able to give family planning advice and prescribe contraceptives as part of general medical services, and that remuneration of the practitioners should be on the basis of payment per item of service carried out for reasons of public policy." He explained the position in the City of Aberdeen, where the local authority clinic was not only giving advice on contraception but providing the pill and other contraceptives free. A general practitioner had to charge the patient, and the patient had to pay for the pills. Soon general practitioners would have no patients coming to them for family planning. The situation was illogical. It was therefore asked that general practitioners should be allowed to prescribe the pill under the N.H.S. without cost as a matter of public policy.

The motion was carried by 85 votes to 67.

Arranging Private Treatment

Mr. R. MYLES GIBSON (Leeds) moved: "That this Meeting deplores the failure of the Minister to correct what is a manifestly unjust and inequitable situation by refusing to agree to the alteration of the terms of service for general practitioners so that they may charge a fee of an N.H.S. patient when the patient insists on private referral for second opinion or treatment. The Meeting urges the profession's negotiators to persevere in this matter until justice is secured."

The Meeting agreed to an amendment: to delete everything after the words "general practitioners" and substitute "in accordance with the Resolution 311 of the Annual Representative Meeting, 1966, and urges the profession's negotiators to persevere in this matter."

Mr. MYLES GIBSON said that the motion simply registered the disappointment of doctors at their inability to put into effect the substance of last year's resolution, which read: "That paragraph 10, sub-paragraph 1, of the terms of service for medical practitioners as laid down in the National Health Service (General Medical and Pharmaceutical Services) Regulations, 1962, be amended, so that when a patient whose condition is such as to require treatment which is not within the scope of the practitioner's obligations, and who has been offered that treatment as available as part of the hospital and specialist services (Paragraph 7, sub-paragraph 1 of the terms of service refers), asks for private consultation and treatment by a specialist the general practitioner be allowed to charge a reasonable fee of the patient for making the arrangements and for attending the consultation(s) and treatment if requested to do so by the patient; and that to avoid abuse an appropriate declaration form be signed by the patient." This was in no way a censure of Dr. Cameron or his team but a request to the Meeting to endorse the motion.

Dr. CAMERON explained that the Minister had given an assurance that he would do nothing to discourage private practice. On the other hand, the Minister did not feel he should do anything to encourage it, and he had thought that proposal would encourage private practice. If the Meeting gave the motion its support the matter would be taken up again.

The motion, as amended, was carried.

Practice Premises

The CHAIRMAN formally moved: "That Council be instructed to review and report upon all aspects of general practice in health centres. (This motion has been drafted by the Agenda Committee under Standing Order 16 (iii))"

The motion was carried.

Dr. B. R. T. CARROLL (Croydon) moved: "That this Meeting asks the Council of the Association to safeguard the future independence of the profession by ensuring that health centre tenancy agreements are independent of executive council contracts."

He said his own local authority was itching to build health centres. The Minister had said that no more money would be forthcoming for infant welfare unless general practitioners could be persuaded to use the clinics as health centres. As a result, doctors in Croydon had made inquiries and had been concerned to discover that entry into health centres would entail surrender of the present contract and of the doctors' independence. As landlord, the Minister, through the executive council, would be able to exert total control over their practices.

Miss GLADYS M. SANDES (St. Marylebone) said that there were efforts to bring pressure to have the nominations of the appointments in these health centres made by the board of governors in the local teaching hospital, who wished to find a place to send clinical students, and, what was more serious, that the appointments should be made by the central board of governors and not by the local medical committee.

Dr. B. D. M. WILLIAMS (South Warwickshire) said that the key word was "independence." If enough doctors went into health centres the profession would be unable effectively to threaten resignation.

Dr. C. P. WALLACE (Council) thought that the G.M.S. Committee should issue a warning notice to all general practitioners about practice in health centres under existing conditions. In his opinion an amending Act was required and must be demanded, so that those practising in health centres could enjoy freedom and independence.

Remarking that there was a lot of muddled thinking on this subject, Dr. A. ELLIOTT (Redbridge) said the profession had to be careful when a new type of development was taking place, and he did not have to remind the Meeting that the type of medicine practised in the 1930s was, owing to economic and other influences, undergoing big changes. He knew that many doctors were not prepared, even with a finance corporation, to place themselves in a position of owing a lot of money. What worried him was there were doctors who were concerned more about being under the local health authority than they were under the executive council. The A.R.M. should not place rigid restrictions on its representatives.

Dr. CAMERON said that the previous day he had sketched out to the Meeting his feelings about health centres. He was pleased to accept the motions on the subject, though he was not entirely happy about the Croydon motion. "I have been quoted as being against health centres," said Dr. Cameron, "but this is not the case. I have already given you a balanced view of the situation, and those doctors who find it necessary to practise from health centres and undertake tenancies must be protected and their freedom and independence must be maintained. This is the basis of our thinking." He added that the G.M.S. Committee had set up a working party on the problem, and it hoped to issue a report as soon as possible. So long as the Meeting did not tie the Committee to motions like that from Croydon he was happy to accept the block of motions.

Replying to the debate, Dr. CARROLL said doctors in Croydon were not against health centres. They had, however, some experience of the way in which doctors were being pressurized.

The motion was carried.

Overseas

Dr. R. L. LUFFINGHAM, in the absence of the Chairman of the Committee on Overseas Affairs (Professor D. E. C. Mekie) moved: "That the Annual Report of Council under 'Overseas' be received."

He said that one-third of the members of the B.M.A. were overseas doctors and he would ask their representatives to speak for themselves.

Dr. J. ST. L. O'DEA (Republic of Ireland) said that Irish doctors also had their problems. Only about 35% of the population received a full comprehensive medical service. However, in various ways 93% of the population received some form of subvention or assistance from the State. The objective in Southern Ireland was to keep their own association active and alert so that it could deal with the problems that could arise. "I am glad of this opportunity," added Dr. O'Dea, "to acknowledge the debt which the Irish Medical Association owes to the British Medical Association. Over many years you have come to our assistance and you have always been available when we wanted advice."

Dr. LUFFINGHAM introduced the following representatives from overseas: Dr. E. A. MOSES (Trinidad and Tobago Medical Association); Dr. R. M. H. MALONE (Barbados); Dr. V. R. PATEL (Kenya Medical Association); Dr. J. ST. L. O'DEA, Dr. M. A. KEHOE, and Dr. N. REILLY (Republic of Ireland); and Dr. R. SCHRAM (Uganda Medical Association).

Constitution of Committee

Dr. LUFFINGHAM moved that the constitution of the Committee on Overseas Affairs be amended as follows to consist of: (1) The four Chief Officers of the Association. (2) Four members elected by the Representative Body. (3) Four members elected by the Council. (4) Nine members appointed by Council after consultation with Branches overseas. (5) Power to co-opt up to six additional members. (6) Cross-representation from other B.M.A. Committees where appropriate.

The motion was carried by the necessary majority.

Dr. LUFFINGHAM formally moved: "(1) That the policy laid down in 1919 on the inclusion of salary details in advertisements submitted for publication in the *British Medical Journal* be waived in respect of advertisements from overseas; (2) that a suitable notice should appear in the Overseas classified advertisements section of the *British Medical Journal* advising all applicants to make inquiry as to remuneration and terms of service before accepting any overseas appointment."

Dr. E. A. MOSES (Trinidad and Tobago) moved an amendment that after the word "overseas" in (1) should be added "but Council shall be authorized to reintroduce the requirement for any particular Commonwealth country if so requested by the Branch or national Medical Association directly concerned."

He said the doctors in Trinidad and Tobago viewed the decision to exclude the publication of salary details in advertisements submitted to the *B.M.J.* with some disappointment. Unlike some of the larger Commonwealth countries, the conditions of service and salaries in the Caribbean area were not as good as in the United Kingdom. Salaries differed from island to island. In some cases it depended on whether the applicant was of British birth or not. Many applicants might be misled into accepting posts which they found to be different from what they had originally bargained for. Until such time as their Governments offered conditions similar to those in the United Kingdom every effort should be made to acquaint every prospective applicant with as much detail on conditions of service, including salaries, as possible. To that end the Trinidad and Tobago Branch of the British Medical Association was prepared to supply prospective applicants with details of any posts advertised.

Dr. R. M. H. MALONE (Barbados) said that publication of salary scales in the *B.M.J.* was the only method of watching Government scales of pay. It would be disastrous if rates of pay in various countries were available only to applicants of posts in the countries concerned. Overseas rates of pay were bad, and the B.M.A. should maintain careful scrutiny both at home and abroad. He added that Barbados had decided to remain a Branch of the B.M.A.

Dr. LUFFINGHAM welcomed the fact that these representatives had taken the trouble to bring this matter before the Representative Body, and he accepted the amendment.

The motion was carried, as amended, with the necessary majority.

Dr. LUFFINGHAM reported that on 1 July the New Zealand Branch of the B.M.A. had become independent. He hoped that a telegram from the Representative Body would be sent congratulating the New Zealand Branch on achieving independent status and wishing it well.

This was agreed to.

Service by Retired Doctors

Dr. R. L. CORMIE (Glasgow) moved a motion: "That this Meeting proposes that Council inquires into the desirability of setting up a system whereby retired but fit doctors might give the benefit of their services, for a period, in the developing countries which are short of medical manpower, and report back to the A.R.M. in 1968, preferably with an already functioning scheme."

He said there were many countries where the number of doctors was inadequate. Malawi, for instance, had about one doctor per 50,000 persons. This was likely to continue for many years. Many medical schools had special links with areas of need—Glasgow with Nairobi and Edinburgh with Baroda (India), and so on. To those areas registrars and consultants had been seconded for varying periods, commonly up to one year. That, however, met with only a small part of the need.

There were many doctors in Britain who, when they retired from the N.H.S., were still fit and able. He believed some of them would be willing to give their services to necessitous areas for periods of three, six, or 12 months, or even longer, either as practising doctors or in an advisory capacity. Since they would be in receipt of a pension, they would not expect much more than their living and travelling expenses—presumably to be paid largely by the countries where they worked. "This would lessen the financial problem of the scheme," he said. The doctors would probably have to have insurance cover for illness, injury, and medical defence.

Not every underdeveloped country would wish to participate in such a scheme, and also there might be many initial difficulties to overcome. None the less, it was an idea worth investigating.

Dr. RONALD GIBSON said he would accept the motion on behalf of Council.

General Medical Services (Resumed Debate)

Practice Premises (Continued)

Dr. J. N. REDFERN (East Yorkshire) moved: "That, with reference to paragraph 25 of the Annual Report of Council, general practitioners who choose to practise from health centres should not be subject to pressures, direct or indirect, to receive remuneration by way of salary."

He said the point of the motion was to ensure that no general practitioner was forced to accept payment by salary because he was entering a health centre when other doctors in it had opted for payment by salary or because the Minister had chosen that health centre as one of the pilot areas for payment by salary. It was not a motion to discuss the advantages or disadvantages of payment by salary but a motion against the principle of coercion or pressure. This situation had occurred in his area, and doctors were unable to obtain a satisfactory answer from the Ministry.

Dr. CAMERON asked the Meeting to support the motion. It was true the Ministry was not in a position to give an answer, because the matter had not yet come under discussion with the representatives of the profession. The profession would never agree to any set-up which would deny the right of a doctor to choose the system of remuneration under which he wanted to work.

The motion was carried.

Service Committee Procedure

Dr. T. GARDNER (Cumberland) moved: "That this Meeting supports the G.M.S. Committee in its efforts to implement the proposals included in the third report on the reform of the service committee procedure."

He said that three years before, when the profession had determined to rid itself of some of the most oppressive aspects of the service, service committee procedure had been high on the list of items demanding urgent and radical reform. The system had engendered over a long period of time a sense of injustice and bitterness, for the Ministry had been unprepared to do anything about it.

The profession had won the right to renegotiate a new system. The profession had been presented with proposals which would, in the first place, abolish the multiplicity of badly constructed committees of amateur jurists and replace them by a small number of well-qualified chairmen of unquestionable competence and integrity appointed by the Minister. After consultation with the Lord Chancellor and the G.M.S. Committee doctors were now offered a system of conciliation which would leave in the hands of executive councils the job they could do best—to try to help patients, who wrongly imagined themselves to have a grievance, to understand the facts and to relieve their minds of the sense of bitterness or injustice which they might harbour. If this was impossible the service committee would become necessary.

In 1965 there had been over 700 complaints; half had been dismissed but half had gone to service committee hearings. In the end 38 doctors had had sums withheld from their remuneration. Fifty in a 100 had been brought before service committees.

Dr. F. E. GOULD (Birmingham) said that the G.M.S. Committee was moving in the right direction, but he did not support the details of the report. He was opposed to the conciliation procedure: it was unnecessary. It should continue, as now, to be done by the clerk of the executive council. The idea of appointing a lay person to assist the clerk was that he should be "a person of standing, with the requisite qualities of tact and sympathy." It might be very difficult to find a lay member of the executive council with those qualities. He hoped the G.M.S. Committee would continue on the lines of improving the procedure, but some details left much to be desired.

Dr. C. J. WELLS (Sheffield) reminded the Representative Body of the nursery rhyme: "When she was good she was very very good, but when she was bad she was horrid." This applied also to some medical service committees. It was an emotive subject. Those who were locally involved in the problem were perhaps unwilling to relinquish some of their authority. Their duty was to devise a scheme which would do the best for their colleagues. The proposals in the report were such that they would perhaps produce a uniformity and some form of control which would ensure that all doctors, and those patients who brought the complaints, had just and proper treatment.

Some Satisfied

Dr. M. R. SHERIDAN (North Middlesex) said it was of vital importance that the Representative Body should accept the motion. The previous speaker had spoken about overall uniformity that was required in service committee procedures in England and Wales. At the present time there were some executive councils and some service committees who said, "We have the finest service committee in the country and we do not want it interfered with." He compared this attitude with that of perhaps a magistrates' court, but there were many people who would rather take their chance at quarter sessions where they had a legally qualified chairman to dispense justice for them.

The Charter had called for an overhaul of the disciplinary committee. A magnificent scheme had been produced. Even if there were a prima facie case, a legally qualified chairman could give a doctor an absolute discharge without asking for a hearing because, though it might be a prima facie case, it was not enough to bring the doctor before what some might call the "star chamber," and cause him the anxiety of going through an inquiry only to be told it was a technical breach.

Dr. W. F. JONES (Liverpool) moved the following amendment: "That in any change in service committee procedure those areas who wish to keep the status quo should be permitted to do so."

He said that it was conceded that changes should be made, particularly in rural and semi-rural areas, and also in some minor matters, but in Liverpool and other large areas justice was already done to doctor and patient. That had been proved in practice, not in theory. Local experience was that in many cases the matter could be satisfactorily settled on a common-sense basis. A legally qualified chairman might be bound by his legal training and tend to make the hearing too formal. Three local medical men and three local laymen with their knowledge of conditions and people were more likely to arrive at a just solution for both sides. On the question of time, it was more convenient to travel a few miles than spend time travelling to a regional centre. Liverpool believed it was better to amend the existing method than support wholesale changes, and, where the existing method worked, it should continue.

Dr. N. G. NICHOLSON (South Middlesex) said that once again Liverpool had gone on record as trying to contract out of what was generally good for the country. The number of those unfortunate enough to be brought before the service committees went up every year, yet the number found to be in breach of service remained almost static—proving that the number of trivia brought before the service committees was going up. The Executive Councils Association had gone on record as saying that the existing system worked well and should be retained. That was not the profession's opinion.

Cases of Injustice

Dr. R. B. L. RIDGE (Council) said the object in the reform of service committee procedure was to secure the best procedure to ensure that no doctor was submitted to the ordeal even of the preliminary correspondence phase of service committee procedure, let alone the ordeal of the actual hearing, when it was not necessary. Even in some of the areas most outspoken in favour of retaining the status quo the saddest cases of miscarriage of injustice occurred. It was extremely difficult to judge the efficiency of one's own system when one was involved in it.

Dr. GOULD (Birmingham) said it was difficult to support the G.M.S. Committee in its effort to improve the medical service procedure and to agree entirely with the way it was going about it. He was not satisfied that the majority of local medical committees desired a change of procedure—on the contrary, he thought they would wish the present procedure to continue.

Dr. **OUTWIN** (Council) urged the Meeting, whatever its feeling on the motion, not to support the amendments if for no other reason than that they were badly phrased. As Dr. Gould had said, a large number of service committees were perfectly satisfied with the job they were doing, even if they were not doing a good job.

Dr. D. **BROWN** (Liverpool) said that from his own long experience of medical service cases he was certain reforms were necessary. Often the most satisfactory inquiries were those conducted in the smaller areas, where the local knowledge was greatest. If it was desirable the small areas could be retained, and if certain areas felt there had been an injustice they might want to go into bigger areas.

Dr. **GARDNER** said that, in spite of the satisfaction that had been expressed by several representatives with the present procedure, the system remained a pernicious one. If it was to be changed it must be changed for the whole country. After an uproar of protest throughout all the years of the National Health Service, with requests for reform of the Service, at last there was an opportunity to reform it. The reforms were sensible, good, and right. The reform suggested, although it might not be perfect, was an enormous step forward in the right direction.

Dr. J. W. **DIGNAN** (Stratford) asked what had been the conclusion at the Conference of Local Medical Committees ?

Dr. **CAMERON** replied that the Conference had referred that part of the report back for reconsideration by the G.M.S. Committee.

Dr. **JONES**, in reply, said that local medical committees must surely decide for themselves. Let the existing system be retained where it worked rather than make uniform arrangements for the whole country.

The amendment was lost.

Further Amendment

Dr. D. F. **HEATH** (Birmingham) moved the following amendment: " That this Meeting considers that medical service case procedure and method of appointment remain as at present, preferably with a legally qualified chairman."

Dr. Heath said the Birmingham Division did not wish to hinder the normal development of the medical service procedure, but it thought that regionalization would be a retrograde step. What support was there for regionalization ? The Executive Councils Association had circularized 119 areas asking them for the opinion of their local medical committees on regionalization. Of the 100 replies received 60 had been against regionalization, 12 for it, and 28 had expressed no opinion.

There was a tendency to blame service committee and tribunal regulations for not working well when the blame lay with the doctors for not seeing that it worked. Some said the lay members and chairmen were not well informed. It was the doctor's business to see that they were. Others said that a basic principle of justice was that those sitting in judgement should be completely independent and that a doctor should be able to count on getting justice. " What an indictment of the medical profession and all our friends who do this work for us," said Dr. Heath. The right of appointment of medical service committees and the right to appoint a chairman should be retained. Who wanted a chairman appointed by the Minister or the Lord Chancellor ?

In Birmingham in 1965–6 22 complaints had been dealt with by the medical service committee without a single hearing. In 1966–7 of 29 complaints 27 had been dismissed without a hearing, one had been withdrawn owing to retirement, and one appeared before the medical service committee and a suitable recommendation was made.

The informal handling of complaints took place already in many areas where doctors had taken an active part in working with and gaining the confidence of the lay members of the executive council and had chosen a chairman wisely. In that case Dr. Heath advocated if possible a legally qualified chairman. If the desire was to hand over control to the Minister or the legal profession the Meeting should accept the proposals in the third report and the recommendations of the Council and the G.M.S. Committee. But if the wish was to retain independence and look after the profession's own affairs the Meeting should reject regionalization and continue with the present regulations with amendments as necessary.

Dr. **RIDGE** (Council) told the Meeting of one area where the chairman of the service committee had decided that in every complaint where a death was concerned there would be a hearing. That was wrong. There were grounds for a hearing only when prima facie there was a breach of the terms of service. If the chairmen were to be of the quality and calibre to take the right decision it would be difficult enough to find the 16 who would be required for the proposed regionalization—men in the legal profession of such a stature that their abilities were well known to the Lord Chancellor.

Dr. N. G. **NICHOLSON** (South Middlesex) said that the amendment sought to throw out the whole conciliatory machinery, and all the amendments should therefore be firmly rejected. Dr. **OUTWIN** (Council) said that the Meeting, having already rejected the amendment whose design was to preserve the status quo, would be doing virtually the same thing if it passed the present amendment. The word " preferably " in the proposed amendment meant that there was no obligation on any local service committee to have a legally qualified chairman.

Dr. **GARDNER**, in reply, once more appealed to the Meeting to throw out the amendment, to support Cumberland's resolution, and to enable progress to be made with reforming of the system.

Dr. A. **ELLIOTT** (Redbridge) said that the amendment contained in substance what the Conference of Local Medical Committees had said, and Dr. Elliott warned that in his own and many other areas of the country there would be a terrible outcry if the A.R.M. came to a different decision.

Dr. **HEATH** expressed amazement at the number of representatives who had wanted all the machinery put into the hands of the Minister and the legal profession. " Surely we want to retain something of our individuality ? "

The amendment was lost.

The motion was carried.

Complaint in Writing

Dr. J. P. **GRIER** (Plymouth) moved: " With reference to the service committee procedure, this Meeting recommends that when conciliation has failed and the complainant persists in pressing his complaint he should be required to formulate his complaint in writing in the form of an affidavit or sworn declaration before it can be submitted to the chairman of the service committee."

Dr. Grier said the suggestion put forward by the Plymouth Division was intended to apply only to those instances where clerks of the executive councils had failed to achieve conciliation. The idea of a sworn statement by the complainant had three valuable purposes. The first was to discourage frivolous complaints ; the second was to prevent a change of ground by the complainant at the hearing; and the third was to ensure that the practitioner had an opportunity to seek advice before the hearing.

Dr. D. R. **COOK** (Camden) moved the following amendment: " To delete all the words after " complaint " in the fourth line of the motion and add " either at a service committee or on appeal no hearing should be held if the complainant does not himself appear."

Dr. Cook gave several instances of hearings at which complainants had not appeared to substantiate what they had said. He believed that was a monstrous practice.

Dr. **GRIER** said that the amendment was not in any way related to the purpose and intention of his Division's motion and he hoped the Meeting would throw it out. Dr. **COOK** replied that he wanted a reform in medical procedure and he wanted to do it in an effective way. The motion would be quite ineffective.

The amendment was carried, and the motion, as amended, was then approved.

Representation of Complainant

Dr. **HEATH** (Birmingham) moved: " That this Meeting agrees that at an oral hearing by the Ministry of an appeal from a service committee recommendation the complainant should not be represented by an employee of the defendant's executive council."

Dr. Heath said that when a complainant or respondent appealed against a medical service committee recommendation the Minister, if he considered fit, convened an oral hearing. He appointed a legally qualified chairman, a Ministry doctor, and a representative of the profession—usually a member of the G.M.S. Committee—to hear the appeal. The doctor could present his own case or be legally represented, as could the complainant, but in the Ministry notes on procedure at appeals it was stated that when the appeal was by a practitioner against a decision in the complainant's favour the clerk to the executive council might be prepared to arrange with the complainant to open the case on his behalf and to cross-examine.

" We feel that for the clerk of the executive council to represent the complainant is highly undesirable on two counts. The clerk is the only one at the hearing, besides the parties concerned and their witnesses, who was present at the service committee hearing. Not only that but he arranged the service hearing and was present when the case was discussed by the members and the recommendation decided upon. We feel that it would be difficult for the clerk to be impartial. This procedure could lead to very bad feeling between the local doctors and the clerk."

Dr. Ridge (Council) said that this was not a new point. While at first sight it would appear that the suggestion was a good one, when the subcommittee looked into it it found that the procedure worked to the doctor's advantage. He hoped the Meeting would not take a decision on the motion.

Dr. Heath, in reply, said he disagreed with Dr. Ridge. It was highly undesirable that the clerk to the executive council should act in this way, and he suggested that the clerk to an executive council from another area should be brought in on these appeals.

The motion was passed as a reference to Council.

Rural Practice Dispensing

A motion standing in the name of Hexham, "that this Meeting deplores any alteration in the present arrangements for rural dispensing," was, by leave, withdrawn.

Dr. Gardner (Cumberland) moved: "That this Meeting considers the right of prescribing doctors not to dispense should be safeguarded."

He explained that the motion simply asked that the Minister's proposals for the establishment of areas within which all patients would be dispensed for should not be accepted, because this would mean that large numbers of doctors who had been practising in an area for a generation or more would suddenly find themselves having to dispense. This development must be resisted.

Dr. A. M. Rankin (Council) supported the motion—which was a corollary of the preservation of the right of the dispensing doctor to continue to dispense. The new system would be that the executive council would decide, in the light of circumstance and of opinion, whether or not a doctor would be required to dispense. This mainly affected rural practices, but it might in certain circumstances affect urban practitioners.

Dr. J. S. Happel (Chairman, Rural Practices Subcommittee) accepted the motion.

The motion was carried.

Dr. A. M. Maiden took the chair.

Dr. Gardner (Cumberland) moved: "That this Meeting proposes that Tariff dispensing should be continued."

He pointed out that if the proposals of the Ministry were accepted the many doctors who had been dispensing on the Tariff all through the years would lose that right. It might be necessary to make minor adjustments of the way in which they had dispensed on Tariff up to now, but the enormous majority had dispensed to their own satisfaction and for the good of their patients. If there were difficulties in Tariff dispensing it was wrong that the whole system of Tariff dispensing should be abolished in order to deal with these marginal difficulties.

Dr. H. B. Muir (Council) supported the motion. The Tariff method was the only ethical method. The capitation system would depend on the continuation of the Tariff system for its viability. It was necessary to have continuation of the Tariff system for the capitation doctor who found his capitation fee did not cover his expenses, through no fault of his own. He must therefore have an alternative. The only one was the present Tariff system structure with minor amendments.

Dr. J. W. Bland (Nuneaton) pointed out that a small group of dispensing doctors working in the mining villages would be severely handicapped by the present proposals put forward by the Minister. In such areas the demand for the services of the Welfare State was high. Doctors' costs were high. There was a range of costs from 20s. up to about 80s. per patient per year. They were being offered a capitation fee of 49s. The alternative was a very uneconomic system. There must be some system, such as the Tariff system, that bore relationship to the demand on the Service.

Dr. Happel explained that if it were only a question of negotiating a new dispensing capitation system a reasonable agreement would quickly be reached on the basis of the third report and subject to certain safeguards for the future. However, the negotiators were not satisfied on the right of a doctor to dispense. The main stumbling block was the Drug Tariff system. Some points of clarification had been raised on the new proposals, and a further reply from the Ministry was being studied. A memorandum was being drafted setting out what dispensing doctors would be prepared to accept. The G.M.S. Committee had authorized a special meeting of rural doctors in 1967. There was no intention of calling rural practitioners together until there was some important decision for them to take. If the talks were very long the meeting would be deferred until the spring if necessary.

The motion was carried.

The Meeting agreed to the withdrawal of a motion standing in the name of Dorset: "That, having regard to the fact that profits from dispensing and rural practice payments constitute financial subsidies for rural practice, the G.M.S. Committee be urged to ensure, in its negotiations with the Minister, that any reduction in the former should be offset by an equivalent increase in the latter, and in any case remuneration under either of these headings should be considered in relation to the other."

No Detriment Clause

Dr. J. R. Edwards (Exeter) moved: "That this Meeting instructs the Council to insist on a "no detriment" clause in the event of any change being made in rural practice dispensing arrangements."

He pointed out that the so-called profits on dispensing were in fact payments for work done. They were an integral part of the income of rural dispensing doctors and helped in part to compensate for smaller lists. Exeter sought to ensure that no doctor was out of pocket as a result and was not further discouraged from providing an essential service in rural areas.

Dr. M. McKendrick (Hexham) said that the motion expressed the rural practitioner's justifiable fear of the unknown. He was greatly concerned that his future should be adequately safeguarded in negotiations with the Minister.

Dr. G. Cormack (Newcastle upon Tyne) explained what the effect of a "no detriment" clause might be. In certain circumstances rural patients would be deprived of an enormous convenience in being able to obtain medicines from the doctor, and the dispensing doctor would possibly as a result suffer a grievous drop in income. The facility should not be withdrawn from patients. But if the facility was withdrawn from country patients, and dispensing doctors suffered a drop in income, they must be compensated, and there were well-recognized means of estimating what that compensation should be. It had to be done on an actuarial basis. That was the way to do it rather than to insert a blanket "no detriment" clause which might give rise to complications not foreseen in the motion.

Dr. E. Townsend (Cornwall) supported the motion. Negotiations with the Ministry on the dispensing issue were difficult. There was a fundamental contradiction in the approach. On the one hand doctors were constantly saying to the Minister that they were overworked, and on the other hand they said they still wanted to do dispensing. In his part of the world there were many rural practices which had been built up over many years on the understanding that dispensing was part of the job. Many doctors had been dispensing for a great number of years. These people would be hard hit if the proposed system was introduced.

Dr. Happel advised the Representative Body not to accept the motion. The negotiators were trying to get a capitation payment to achieve a fair level with proper safeguards. They were also trying to negotiate a satisfactory Tariff, especially for the high-cost-per-patient areas. They were trying to secure protection for the right of every doctor to dispense, and, if that should be lost, to see that there was proper compensation. In view of these assurances, he wondered whether the motion might be withdrawn.

Dr. Edwards, in reply, said that he had been specifically instructed to speak on behalf of rural practitioners. They were providing a service and that service should not be lost. If their profits disappeared he suspected that so would many of the rural doctors.

The motion was carried.

Approach to Women's Institute

Dr. J. D. Shapland (Plymouth) moved: "That this Meeting deplores as both dangerous and unethical the approach by the secretary of the Central National Health Service Chemists Contractors Committee to the secretaries of the branches of the Women's Institute on the subject of rural dispensing, and requests Council to take appropriate action."

He said that in June the annual general meeting of the Women's Institutes had been due to debate the subject of dispensing in rural areas. Some time in April the secretary of the National Health Service Chemists Contractors Committee had circularized a letter to all secretaries of the Women's Institutes. The contents of the letter were in strong terms and against dispensing doctors. He had not before heard of a similar attack widely published to a lay audience by a man or committee, presumably fairly highly placed in his profession, about a group of practitioners in an allied profession.

A copy of the letter had not been sent to the B.M.A. but had been discovered accidentally. It was the sort of behaviour the Representative Body should ask the Council to deplore and to take whatever action it thought appropriate.

Dr. HAPPEL said that immediate action had been taken to circulate a dignified disclaimer; it had been sent to Women's Institute branches everywhere and to dispensing doctors. The W.I. branches had deplored the document even more heartily than had Council, and had shown their views in no uncertain manner at the Royal Albert Hall. The B.M.A. had received a letter of support from the W.I., who were the largest rural "patients' organization."

The B.M.A. had a Joint Committee with the Pharmaceutical Society, and had had a recent meeting. The B.M.A. members of it had taken the opportunity to make clear to their opposite numbers their view on the memorandum. But it was important to keep a sense of proportion. The chemists had their points of view and their problems.

The motion asked Council to take appropriate action. That had already been done.

The motion was carried.

General Practitioners and the Hospital Service

Dr. D. F. HEATH (Birmingham) moved: "That this Meeting agrees that in the discussions on hospital medical staffing between the profession and the Ministry on remuneration and terms of service attaching to part-time appointments in medical assistant and clinical assistant grades, the commencing level of payment per session should be not less than £5 6s., as at present."

He said that discussions were taking place between the G.M.S. Committee, the Joint Consultants Committee, and the Ministry on remuneration and terms of service for part-time appointments in the medical assistant and clinical assistant grades. The proposals for the remuneration of these new posts were disturbing. Those doctors who had been working in hospitals for four years or longer, under Section 10B, retained the present scale of remuneration of £5 6s. In the new medical assistant grade, in which most doctors would work, there were proposals for them to start at £3 4s. 6d. per session, increasing by 3s. 6d. per year per session to a maximum, in 15 years, of £5 14s. It meant that it would take 12 years for the new post to be paid at the present rate. That was an absurd situation.

In the words of the draft hospital memorandum on part-time appointments in the medical assistant grade: "The grade will be mainly for general practitioners and other doctors outside the hospital service." If the hospitals wanted the assistance of general practitioners they had to make it attractive and not offer less than they were now receiving.

Dr. C. J. WELLS (Sheffield) asked the Representative Body to support the motion. Negotiations on the subject were in progress. Some months before the G.M.S. Committee had found the Ministry proposals to be quite unacceptable because they stated that a general practitioner working at the present time in the hospital service should continue his work at a lower rate of remuneration. The G.M.S. Committee had produced further proposals. These had been agreed in the main by their hospital colleagues, and a tripartite meeting had been held with representatives of the Joint Consultants Committee, the G.M.S. Committee, and the Ministry. Unfortunately, the proposals had not been acceptable to the Ministry, but it had them in mind and would be sending a reply in the near future. These proposals were in complete agreement with the present motion from Birmingham.

Dr. H. GLYN JONES (Bromley) asked the Representative Body to reject the motion. There was a grade in the hospital service which was a career grade of medical assistant. If general practitioners wished to go into the hospital service to work as medical assistants it was an unthinkable proposition that, because they were general practitioners, they should be paid a higher rate of remuneration than someone who was in a career post as a medical assistant in the hospital.

Dr. CAMERON said that there was agreement with their hospital colleagues on certain proposals put to the Ministry. The Committee was aware of the difficulty in merging the two services in the hospital, but it was not for it to say that, because the career structure in the hospital was at a certain level, it should ask general practitioners to accept that scale of remuneration.

The motion was carried.

The following three motions were moved formally by the CHAIRMAN and approved:

"That this A.R.M. considers that there is now some urgency in defining the place and status of the general practitioner in the hospital service, with particular regard to level of remuneration and terms and conditions of service." (Medway and Gravesend.)

"That the fees paid to doctors working in hospital as clinical assistants should be more commensurate with their worth." (Dewsbury.)

"That in negotiations concerning general practitioners working in the hospital service a clear distinction be made between (*a*) education appointments, (*b*) stand-by duties, and (*c*) work requiring special skill and experience, and that for each category an appropriate grading and remuneration should be obtained." (East Herts.)

Dr. W. H. N. ANGUS (Southampton) formally moved the following motion: "That this Meeting instructs Council to ensure that general practitioners with special experience holding part-time posts which are an essential part of hospital staffing structure should have security of tenure in these posts."

The motion was approved.

General-practitioner Hospital Beds

The following three motions were formally moved by the CHAIRMAN and carried:

"That this Meeting considers that the Minister of Health should make greater efforts to encourage the provision of general-practitioner beds." (Camden.) "That all hospitals of district hospital status and above, currently planned or to be built in the future, shall include general-practitioner maternity beds." (West Suffolk.) "That this Meeting is of the opinion that there should be general-practitioner beds in all new hospitals, and that the establishment should be determined at the earliest possible moment in the planning project." (Redbridge.)

Prescribing

Dr. R. G. TROUP (Havering) moved: "That this Meeting considers that the regulations prohibiting a doctor from issuing a prescription for a substance for the treatment of several members of a family suffering from the same illness should be relaxed."

He said that no doubt medical practitioners had their own solutions for this problem, but nevertheless within the ranks of general practitioners there were a few sticklers for the rule book, and unfortunately a great many sticklers for the rule book were on executive councils.

Dr. B. L. ALEXANDER (Manchester) said doctors were treating individual patients and not issuing block prescriptions. A second point was that their chemist colleagues were being rather harshly treated at the moment, having accepted a cut in pay for prescriptions, and they as doctors must protect their interests as the chemists would protect the doctors' interests if the need arose.

Dr. CAMERON said he was opposed to accepting the motion as a reference to the Council. He was certain that doctors could not prescribe for a family as such with a bottle of medicine in the bathroom cupboard and someone dishing it out when it was required.

The motion was, by leave, withdrawn by Dr. Troup.

Dr. A. N. MATHIAS took the chair.

Election

The Secretary announced that Dr. A. M. MAIDEN had been elected unopposed as Deputy Chairman of the Representative Body.

President-elect

The Meeting welcomed Mr. R. V. COOKE, the President-elect of the British Medical Association.

Therapeutic Abortion

Dr. RONALD GIBSON (Chairman of Council) moved: "That the Annual Report of Council under 'Therapeutic Abortion' (Doc. A.R.M. 2, para. 200) be received." This was agreed.

Dr. R. H. SCOTT (Norwich) wished to speak against reception of this part of the report. He thought that any further discussion of therapeutic abortion would be only delaying action. Any further delay in legislation was not in the public interest. Discussions had taken place on therapeutic abortion in Parliament, in the Representative Body, in the Church, and in the legal profession. Nearly the whole of the discussion had been held by the male sex. Surely this was something which was predominantly of interest to the female sex. He felt it was wrong that the Meeting should be adjudicating in a matter which was of prior importance to the female sex.

Dr. RONALD GIBSON said that there would be wide interest in the debate, and he thought that representatives should speak to the debate rather than accept the motion. The Medical Women's Federation had reported on the subject, and so had the vice-chairman of the Association's committee.

The Annual Report under Therapeutic Abortion was received.

Request for Royal Commission

Dr. M. SIM (Birmingham) moved: "That this Meeting asks that Council, in support of its resolution passed unanimously at the Annual Representative Meeting, Swansea, in 1965, requests all members in both Houses of Parliament not to approve legislation of the Medical Termination of Pregnancy Bill until all relevant facts have been collected, scrutinized, and reported on by an independent tribunal, such as a Royal Commission."

He said that the private member's Bill on abortion at present before Parliament had been given unprecedented support by the Government in defiance of the medical profession's opposition to some of its fundamental aspects. He did not intend to divide the Meeting by putting forward a partisan attitude to the Bill or to the subject of abortion. He would like to unite the Meeting by putting before them a motion which was fair to all. Representatives should not be side-tracked by quibbles about the wording of the A.R.M. resolution in 1965—its meaning was perfectly clear. Nor should they be lulled into a false sense of security in the hope that the Association would obtain concessions which had been denied to opponents of the Bill in the House.

To be fair to all doctors, said Dr. Sim, there must be a thorough examination of all the evidence by an independent tribunal, such as a Royal Commission. That this had not yet been done was a serious criticism of the manner in which the Medical Termination of Pregnancy Bill was being pushed through Parliament. Doctors did not wish to delay or to obstruct enlightened legislation. If the facts warranted it they would welcome reform, but it must be based on sound evidence and not on the slanted propaganda of mass media. No single doctor could collect all the necessary information. Even the B.M.A.'s special committee could deal with only one aspect. A comprehensive inquiry by a tribunal which commanded the respect of doctors and laymen alike was desperately needed. The motion had added importance, for the Government had just announced that it would give as much extra time as was required to get the Bill through. A strong vote in favour of an independent tribunal would have a profound influence in the country and indirectly on Parliament, and it was a stand which would be eminently defensible. This was the last real chance the profession had to influence the Bill in the House of Commons. Dr. Sim concluded: "Let us leave the country in no doubt that we doctors do not accept fundamental changes in our clinical practice without the fullest inquiry into the facts. Our patients would not wish it otherwise."

Dr. J. L. MCCALLUM (Westminster and Holborn) said that the profession had asked that the Council should set up a special Committee. This had been done. The Committee had investigated the situation and no new legislation had been introduced until the Committee had reported. Asking for a Royal Commission at this stage, when for over 30 years the findings of the Birkett Committee had not been implemented—which were exactly the same as the recommendations in the present Bill before Parliament—was quite absurd, said Dr. McCallum.

Intention and Result

Dr. D. HOOKER (Cornwall) said that doctors must be clear on the difference between the intentions of the Bill and its final interpretation; final interpretation would be abortion on demand with all the relevant facts and figures that followed it. Dr. Hooker quoted statistics of mortality and morbidity in Scandinavia and Hungary, and suggested that there had not been enough discussion of the experience of other countries.

Dr. J. S. HAPPEL (Winchester) said that when motions had been discussed and drafted in his Division it had seemed that the Bill was being rushed through before the B.M.A.'s views, as set out in its Special Committee's report, had been discussed in Parliament. What his Division had wanted was breathing space to get the necessary amendments through. Things had since changed for the better. Further Parliamentary time had been made available. There were still a few changes in the Bill that the Association would like to see, but the report stage had not yet been completed, and the Bill would then have to go to the Lords. There now seemed a chance of the Bill going through in a fairly acceptable form. When so much of the Association's policy had been accepted why turn back the clock by asking for a Royal Commission?

Dr. E. TOWNSEND (Cornwall) explained why he was speaking against Dr. Hooker. Dr. Hooker had spoken at the request of a small meeting of the Division (which had a membership of 280) where the voting had been 11 to 3 for the B.M.A. policy as outlined in the report of the Special Committee. He was sure that did not really represent the view of his colleagues, and that it was the same in many Divisions. The motion demanded delay, and yet, as they all knew, the social evil of abortion existed and had done for a long time. If you had money you could get an abortion, if you had no money you could not, said Dr. Townsend. There were many parts of the country where abortion or termination of pregnancy could be obtained normally through the channels of the N.H.S. This was already done in Aberdeen. Scottish law was slightly different. All the Bill was doing was legalizing the position in the rest of the country. This should not be delayed. There were safety clauses in the Bill.

Element of Politics

Dr. JEAN E. LAWRIE (Dartford) reminded representatives that the B.M.A.'s Special Committee, together with the Royal College of Obstetricians and Gynaecologists, had taken a great deal of trouble to put before Members of Parliament the points they wished amended in the Bill. If Members of Parliament rejected this careful and thoughtful advice consideration would need to be given to forming some other kind of advisory body to try to get across to Parliament the wishes of the medical profession.

If it was likely that the amendments which the B.M.A. wished to see in the Bill would be accepted she thought her Division would not press for the setting up of a Royal Commission or another body. However, there was an element of pure politics in the Bill. Women doctors would be more satisfied if they could see some genuine attempt by the Ministry to improve gynaecological departments so that there were no waiting-lists of six months—because the passage of the Bill could be expected to increase the pressure on these departments.

Dr. D. R. WRIGHT (Thames Valley) said that abortion, together with sterilization and the use of contraceptives, was an integral part of family planning. Yet there were no provisions in the National Health or hospital service for a family planning service, although many hospitals leased their premises to the Family Planning Association. The Minister would be well advised to contemplate providing abortion and other family planning measures in a separate service. Gynaecologists with waiting lists would find their position intolerable. Sterilizations and abortions already occupied much of their time to the detriment of other routine and emergency work. The situation would worsen with the passing of the Bill. The Representative Body should encourage the House of Commons to stop and rethink.

Mr. E. COPE (Birmingham) said that as a gynaecologist he frequently performed therapeutic abortion on medical grounds under the protection of existing case law. He had been assured by senior members of the legal profession that it was very unlikely in the foreseeable future that the case law would be reversed. Mr. Cope told the Meeting about a thirteen-week abortion in his unit where the foetus had not been sectioned for several hours. When it was sectioned, the following morning, the heart was still beating. Was the baby to be registered or incinerated? In the near future it would be possible to hook up that sort of baby to an artificial placenta. The decision would then have to be made whether to drown it like a kitten or preserve its life. Until that and many allied matters had been discussed by an independent tribunal consisting of lay, legal, Church, and medical members, the law should not be ossified in its present form. (Applause.)

Extreme Views

Dr. D. L. WILLIAMS (Denbigh and East Flint) said the question of abortion had been bedevilled by the extreme views held both inside and outside the profession. Initially the Bill had been bad because it had been drafted by people with extreme views. It had then been extensively amended by people with opposite extreme views. That was not the way to go about such a serious piece of social legislation. The Government ought to have had the courage to consider and to introduce its own legislation. As a general practitioner he had never encountered any difficulty in referring a patient for abortion when he felt it was right.

He did not like the wording of the motion, but he did want further thought to be given to the Bill. He asked the Representative Body to support the motion.

Mr. T. F. Redman (Leeds) was also in favour of the Bill receiving further examination by a Royal Commission, because he thought that the Bill was going to be so watered-down that it would be useless. He could not understand why so many doctors were so adamant in clinging to medical indications for a termination instead of openly accepting a serious social dilemma as being a ground for therapeutic abortion. He had every respect for the doctor who said, "I will never perform an abortion," whether it be on religious or conscientious grounds, but once the Rubicon was crossed the argument was only on how strong the indication had to be. The majority of the so-called medical indications were social indications in disguise. He was not advocating abortion on request, but he wanted to get away from hypocrisy and humbug.

Dr. B. L. Alexander (Manchester) pleaded with the Meeting to try to divorce itself from the emotive side of the question. Representatives were in no doubt that the law required to be altered. They were trying to legalize the position, so that gynaecologists could perform an abortion without fear of prosecution. The Bill at present before Parliament should go through. The profession could then try to improve it in the future if it were necessary.

Mr. D. B. Brown (Mid Essex) said that in its present form the Bill provided that a pregnancy could be terminated if there was a risk to the patient's health or life. As Mr. Cope had said, that risk existed in every pregnancy and the wording should be altered to "substantial risk."

Dr. K. J. Sugden (St. Helens) said if the decision was put off this time he did not believe there would be any better proposals. Several speakers had said that when they felt there were medical reasons for an abortion they had no difficulty now in getting one done. On the basis of existing case law the chance of a doctor being prosecuted for an abortion on medical grounds was remote.

"Particularly what concerns me is this," said Dr. Sugden, "I have always held it to be one of the most important tenets of my medical practice that I should under no circumstances have the right to make a decision regarding life and death. This is clear in regard to euthanasia and I am equally certain it will apply if we have abortion on request or something of that sort. We must learn in this respect from Sweden, where in the past 10 years they have had three abortion Bills and they still have not got it right." Dr. Sugden concluded, "I do not think that we have this sorted out sufficiently to make a decision of this kind at this time."

Number of Modifications

Dr. Doris M. Odlum (Bournemouth) said she was a member of the special committee set up by the B.M.A. after the A.R.M. in Swansea in 1965. The decision of that meeting had not been as stated in the motion. It had been that a committee should be appointed by the B.M.A. to go into the matter and report. The special committee had held many meetings and had produced a report which had been published. It had taken an active part in trying to modify the original Bill and had succeeded in obtaining a number of modifications.

The special committee was unhappy about two points in the Bill being debated in the House of Commons. It thought that the practitioner who carries out the abortion should consult with somebody with special knowledge in the field and not just "another registered medical practitioner." It proposed to try to get this accepted.

The special committee also considered that the reference to "any existing children of the family" was unnecessary, because it was already covered, and as worded it was undesirable. With the rest the special committee was in general agreement. There was no question of any kind of abortion on demand. Discretion lay in the hands of the medical profession. The grounds specified could be determined only by medical men, and there could be no interference by politicians or anybody else. "We cannot see that the medical profession can have any objection to this Bill subject to one or two slight amendments," said Dr. Odlum. "The only ground on which we could object was that we did not want a Bill of any sort or kind. This is probably the best Bill that we shall ever get. We are hoping that you will agree and that you will permit us to go on with the negotiations."

If the motion was approved, Dr. Odlum went on, a tribunal would have to be established to discuss the matter at length and it would be some time before anything would be done. The profession had not the slightest idea what a Royal Commission would say. She had had sufficient knowledge of bodies of that kind to know that all sorts of evidence and opinions would be produced, so much so that the members would get more and more confused. Moreover, this would inevitably take two years at least. The position at the moment was as favourable as the profession could ever hope to have.

Fresh Points

Dr. E. E. Claxton (Dartford) said that it ought to be remembered that the B.M.A.'s special committee had not met since October 1966. Many fresh points had emerged in debate since that time. The matter was so serious that a Royal Commission should look into the motives of the many people who had supported the Bill and of those who opposed it.

Dr. C. P. Wallace (Council) said the question to be asked was whether what was before the House of Commons was a great social reform. "If it is, woe betide us if we stand in its way," said Dr. Wallace. Dr. Wallace said that if he could feel certain that the measure before the House would stop back-street abortions he would probably support it. However, he was not convinced that would be so. On the contrary, he believed they would go on and flourish with an increased demand for abortion.

Mr. J. Kyle (City of Aberdeen) said the main purpose of the motion seemed to be to ask for more time and more information—which, from time immemorial, had been favourite tactics for delaying reform. He reminded the A.R.M. that it was more than 30 years since Mr. Aleck Bourne had been prosecuted. "How much more time do we want," asked Mr. Kyle. Living, practising, and bringing up a teenage family in Aberdeen as he did, Mr. Kyle assured the Meeting that, even with its more liberal policy, Aberdeen had not become suicidal, it had not become deformed, delinquent, or depraved.

Miss Gladys M. Sandes (St. Marylebone) said she was convinced that the present measure would mean abortion virtually on demand. Her next point was that many doctors who had only 12 gynaecological beds would be left with an average of two beds for their ordinary patients when the abortions started to come in. Such doctors would then have to decide which patients were to be omitted from the list.

Dr. J. W. Dignan (Stratford) said the profession must make its voice heard on the principle of the right of the doctor to treat his patient how he or she thought fit. Parliament must not dictate to doctors how they should treat their patients. A Royal Commission would be welcomed by the majority of general practitioners. Many were frightened of the Bill because, like Dr. Dignan, they saw it would lead to abortion on demand. If a Royal Commission was set up tomorrow its findings could be published in 12 months' time.

Unworthy Imputations

Dr. A. W. Macara (Junior Members Forum) suggested that the arguments in support of the motion had in the main been emotional. Hard cases had been quoted. They made bad law. There had been unworthy imputations against the mover of the Bill in Parliament, which anyone who knew him could confidently refute. It had been suggested that the Bill would bring about abortion on demand. He suggested the reverse—that it would give an opportunity of proper selection of those cases where help ought to be offered. He suggested that a Royal Commission or any further investigation was not going to carry the subject one step further forward.

Mr. D. N. Menzies (Liverpool) said that many of those present believed that for abortion to be done safely it must be completed before the thirteenth week. This was incorrect. He personally had performed 54 abortions and expected to perform many more. He had seen the units in Prague where curettages were done before the thirteenth week. He assured representatives that abortion was safer from the 14th week onwards. It had been said that there was need for speed in passing the Bill. There was no need for speed.

Dr. Outwin (Council) commented on the great preponderance of men at the Meeting. If it had been the men who were having the babies a much more radical reform would have occurred many years ago.

Dr. Ronald Gibson said that he had a tremendous responsibility. He had not been a member of the special committee. Its chairman was not a member of the Representative Body, and therefore could not reply. Dr. Gibson said he did not propose to be emotional. He asked the Representative Body to be cold and calculating about this and to look at the facts.

In 1965 the A.R.M. had asked the B.M.A. to set up a special committee, which it had done. It had not asked for a Royal Commission. The A.R.M. had asked the Council to ask the Government not to introduce legislation, which it had not—the Bill was a private member's Bill—until the Committee had reported. The special committee's report had been published in the *British Medical Journal* on 2 July 1966. It had been available to members before the 1966 A.R.M. The Association had actively sought amendments to the present Bill on the basis of the special committee's report in consultation with the Royal College of Obstetricians and Gynaecologists. The Minister of Health and the Home Secretary had been seen on two occasions. Members of Parliament had been circularized and there had been press statements and letters in *The Times*. The B.M.A. had been active in supporting many amendments.

Firstly, the Association had played a part in securing that there should be two medical opinions. Secondly, in the elimination of social grounds for termination—the elimination of abortion on demand in fact. It had also helped to get eliminated the "well-being" ground for abortion and that concerned with environment, and that any nursing-home should serve as a place for abortion. What was left? What should the Association continue to press for? Dr. Gibson thought there were four things. Firstly, to ensure that the abortion was lawful only if carried out by or under the supervision of a registered medical practitioner of the required skill and status instead of any doctor. Secondly, to get removed the express indication in the Bill that pregnancy might be terminated if there was risk of injury to the health of any existing children of her family. Thirdly, to obtain a satisfactory amendment of the conscience clause. Fourthly, a satisfactory assurance that details of notifications required under the Act could be kept confidential.

Time Left

The Government had allowed extra time for the Bill to be debated. Therefore the Association had time for its extra work, and it could follow the Bill through the House of Lords if necessary.

What were the alternative courses before the Representative Body? Firstly, to continue to press for the remaining amendments that were needed. Secondly, to oppose the Bill completely and to apply for a Royal Commission. Dr. Sim had said when he opened the debate: "If we ask for an independent tribunal this will have a profound impact on Parliament." Indeed, he thought it would. The Representative Body was the parliament of the profession, and it was a responsible body. What would be the impact on Parliament if the profession asked it to abandon the Bill in favour of a Royal Commission? What would the image of the Association be? Would it not be thought to be showing lack of responsibility? That, he thought, was the impact such a decision would have on Parliament. He hoped that, having been responsible in the setting up of a special committee, the Representative Body would not vacillate now.

Dr. **Sim**, in reply, said that it was criminal to legislate or to encourage people to legislate when the answers were not known. Listening to the debate, it was obvious that there was much that representatives did not know. It was unfair for the special committee to claim that it had been successful in all these amendments. They had been fought tooth and nail, and the B.M.A. should not claim all the credit. If the motion was not passed by the Meeting those fighting the Bill would feel that the doctors did not want them to go on fighting any longer. It was an important issue. Most doctors wanted to know the truth. Those who were afraid to know the truth should declare their interest. Those who wanted to know the truth would say, "Let us get an independent inquiry into this."

The motion was lost by 274 votes to 98 votes.

The following motion, standing in the name of North Middlesex, was, by leave, withdrawn: "That this Meeting feels that the British Medical Association, in support of its resolution passed unanimously at the Annual Representative Meeting in Swansea, 1965, requests all members of both Houses of Parliament not to approve legislation on the medical termination of pregnancy until all relevant facts have been collected, scrutinized, and reported on by an independent tribunal."

The **Chairman of Council** moved: "That the remainder of the Annual Report of Council under 'Therapeutic Abortion' be approved."

The motion was carried.

General Medical Services Committee (Resumed)

Prescribing (Continued)

Dr. A. R. **Carmichael** (Guildford) moved: "That the form E.C.10A shall be introduced in England and Wales and should not be abolished in Scotland."

He explained that form E.C.10A, which existed in Scotland, gave the doctor the right to prescribe for himself a stock-list of items he required for use in his surgery.

Dr. Carmichael said that the form had encouraged good medicine in Scotland. It allowed a doctor to maintain at all times a properly equipped emergency bank.

Dr. J. S. **Ross** (Council) said he understood that the retention of E.C.10A in Scotland had meant a loss to doctors of 2d. on the capitation fee. If that happened to doctors in England and Wales he, as a Scotsman, would like to know the answer.

Dr. J. C. **Cameron**, Chairman of the G.M.S. Committee, paid tribute to Scottish colleagues for making a sacrifice of the 2d. fee, and congratulated them on keeping the door open on this matter. The G.M.S. Committee had been trying for years to get the Ministry to introduce E.C.10A in England. But it had been decided to do away with E.C.10A in Scotland and to introduce the system used in England and Wales. Dr. Cameron wondered whether the capitation fee would be reduced by 2d. if the form was introduced in England and Wales.

Dr. A. A. **Clark** (Dunbartonshire, Chairman of G.M.S. Committee, Scotland) asked the Representative Body to pass the motion unanimously. Scotland had had stock order forms since 1913. Doctors in England and Wales used to receive 5s. per 100 patients for the supply of drugs. On an average list that meant some £16 a year. How much of the new capitation fee was set aside by the Review Body for that purpose was unknown. But the sum of 5s. per 100 patients was quite inadequate, because in Scotland the average amount spent was not £16 but £55, and yet the prescribing in Scotland was more than in England. After prolonged negotiation the Department of Health in Edinburgh had agreed to retain form E.C.10A, but with a reduced capitation fee of 2d. The majority of Scottish general practitioners agreed with that decision. If the negotiators could persuade the Minstry that E.C.10A should be introduced throughout the country there would be no question of reduction.

The motion was carried.

Disposable Equipment

Dr. **Audrey M. F. Brook** (Liverpool) moved: "That as a means of improving the standard of general medical services the Ministry should make arrangements to supply a full range of disposable equipment for diagnosis and treatment."

Dr. Brook said that the Minister had offered to help general practitioners improve their standards of practice, and this was one field in which much could be done. Over the years the range of disposable equipment had increased enormously. There were now an increasing number of the more sophisticated slide tests. The use of disposable equipment was a great time-saver both for the doctor and for ancillary staff.

Dr. **Cameron** said the G.M.S. Committee had been to the Minister before about disposable equipment. The Ministry had agreed to distribute disposable syringes because it recognized that general practitioners had difficulties in sterilizing syringes. At present the Ministry's view on disposable equipment was that the doctor, as an independent contractor, should look after himself. But, said Dr. Cameron, the Ministry would pay for this in the end through the expenses part of general practitioners' remuneration, and he saw no reason why the Ministry should not supply a full range of disposable equipment.

The motion was carried.

Medical Records

It was agreed to add the following words to a motion by Havering: "and that there should be free distribution on request to doctors within the National Health Service."

Dr. R. G. **Troup** (Havering) then moved: "That this Meeting welcomes the discussions on medical record envelopes which are taking place and recommends that consideration should be given to the layout of the details on the front of the envelope. The Meeting welcomes the colour tagging system published by the Royal College of General Practitioners and considers that the envelope should be designed to accommodate this service, and that there should be free distribution on request to doctors within the National Health Service."

Dr. Troup said there had to be an improvement in the present record card in order to improve efficiency.

Dr. J. M. **Cane** (Dewsbury) said the work load would be easier as a result of the change-over to accurate and complete record-keeping. Reference to past records would be easier and it would improve the service to patients. He supported the motion, but it did not go far enough. Dr. Joyce E. Brooks (Southampton) also supported the motion.

The motion was carried.

Attachment of Nurses and Health Visitors to General Practices

Dr. E. H. J. Cotter (East Herts) moved: "That the terms 'district nurse attachment' and 'health visitor attachment' be restricted to full-time attachment only, and that part-time attachment be referred to as 'liaison.'"

He said that from time to time a trend developed which was welcomed by the majority but which appalled a few. Such a trend was the attachment of local authority district nurses and health visitors to general practitioners. This was a scheme that had to succeed, and though there were difficulties on both sides Dr. Cotter thought that it would be better to differentiate between full attachment schemes and less complete schemes put forward by some authorities.

Dr. C. D. L. Lycett (Public Health Service) agreed that the scheme had its difficulties. But he hoped the Meeting would reject the motion, because it was far too early to attempt to make fine distinctions and definitions. The best form of attachment might vary from area to area. The best criterion for attachment was that the health visitor or nurse should look after the same family as the general practitioner and work in close collaboration with him. He hoped rigid definitions would not be sought at the present time. "Liaison" was not an inappropriate term—it meant "part-time attachment" in a different context.

Dr. Cameron said the motion was the most light-hearted that had appeared on the order paper. He found it difficult to find out when an attachment became a liaison, or when a liaison became an attachment. There were all sorts of possibilities about these arrangements: "I wonder what is going on down in East Herts."

A motion that the question be now put was carried.

The motion was lost.

A motion standing in the name of Medway and Gravesend, "That this A.R.M. welcomes the increasing attachment of local authority paramedical personnel to general practitioners," was accepted, as was another by Medway and Gravesend, "That this A.R.M. considers there should be general practitioner representation, as of right, on all local health authority committees making these arrangements."

Fees for Dental Anaesthetics

A motion standing in the name of Winchester, "That this Meeting supports active efforts by the Council to increase the fees for dental anaesthetics," was accepted.

Dr. W. Ferguson (East Yorkshire) moved: "That, with reference to paragraph 41 of the Annual Report of Council, the minimum fee for dental anaesthesia is unrealistic and should be raised to two guineas, and that the cost of this should not be a charge on the dentist."

He said that in the recently published report by the Standing Medical and Dental Advisory Committee on Dental Anaesthesia it was emphasized that general anaesthesia for dentistry should not be undertaken lightly, and it classified the various groups of patients with dental conditions who were suitable for general anaesthesia. Dental surgery and anaesthesia could not be combined by one operator without some increased risk to the patient. Anaesthesia required the presence of either a consultant anaesthetist or a general practitioner. The present fee of 15s. as a minimum was grossly inadequate for the specialized work. East Yorkshire suggested that the fees should be raised to a minimum of two guineas, and the charge should not be on the dentist.

Dr. F. O. Wells (East Suffolk) moved an amendment that the words "at least" should be inserted before "two guineas."

The amendment was carried.

Dr. J. S. Noble (Council) supported the East Yorkshire motion. The importance of it lay not merely in the fee but in the superannuation attached to it.

Dr. Cameron said discussions were taking place with the Minister with the object of getting the fees paid through executive councils. They had been unable to agree a common policy with their dental colleagues, and dentists would make separate representations to the Ministry. Dr. Cameron asked the Representative Body to carry the motion.

The motion, as amended, was carried.

Survey of Practice Expenses

Dr. G. C. Price (Bournemouth) moved: "That this Body believes that the professional advisers to Council failed to understand the intentions of this Body in passing Resolution 260, A.R.M., 1965 (Annual Report of Council, 1967, para. 43) and instructs Council to seek the views of the Divisions concerned, Bournemouth and Morpeth."

He said the motion passed at the A.R.M., 1965, read: "That this A.R.M. considers it imperative that a suitable independent outside body conducts an impartial survey into the actual and concealed running costs of medical practice, both general and private consultant practice."

The motion had been rejected, but it was the view of his Division that the experts had failed to appreciate the purpose of it. That type of survey was not unique. He had with him a copy of a survey carried out for chartered accountants. An extract read: ". . . the information can be of immense value in promoting discussions as to practical steps to be taken by members to make their practice more efficient, to help them obtain proper remuneration for their services." A similar survey for the medical profession would help the negotiators by providing much-needed facts. The point of the motion was that it suggested that the Council should ask the Bournemouth Division to submit a memorandum which would explain in fuller detail the meaning and purpose of the motion.

Dr. Cameron said there had originally been an inaccuracy in the report the G.M.S. Committee had had from its advisers. Dr. Price had put his case moderately and he felt he would be churlish to advise rejection of the motion. He would be glad to have a memorandum on the subject from the two Divisions.

The motion was carried.

Work Load of General Practitioners

Dr. L. P. Grime (Junior Members Forum) moved: "That this Meeting instructs Council to negotiate simplified forms of a standard size, and at a uniform fee, not requiring the patient's signature, for use in all immunization procedures. A simplified form should also be introduced for cervical cytology."

Dr. Grime said the principle behind the motion was self-evident. It would improve efficiency by cutting out a lot of unnecessary paper work.

Dr. Cameron said he was prepared to accept the motion, but preferred that the fee should be one which measured up with the amount of work involved, rather than a uniform fee, as suggested in the motion.

Dr. A. M. Maiden took the Chair.

Dr. Cameron suggested that the words "realistic fee" should be substituted for the words "uniform fee," and the Meeting agreed.

The motion, as amended, was carried.

Dr. J. P. Fisher (Bournemouth) moved: "That a prescription on the form E.C.10 should be repeatable in the same way as any private prescription."

Dr. Fisher said that Bournemouth was attempting to reduce the work load.

Dr. Cameron said that what the motion proposed had been tried again and again, but there was great opposition from chemists because of the administrative work involved. Dr. Cameron promised to look into the matter again, but he did not hold out much hope of solving the difficulty.

The motion was carried.

Dr. J. C. Oakley (Medway and Gravesend) moved: "That this A.R.M. asks Council, in the light of the increasing work load in general practice, that list sizes be revised and lowered, without financial detriment, to figures beyond which no doctor be required to accept allocation of new patients."

Dr. Oakley said the time had now come to stipulate a maximum list beyond which doctors were not prepared to accept any further allocation, otherwise the standard of work would decrease.

The motion was carried.

Dr. M. Macleod (Wallasey) moved: "That, as the original aspirations of the Charter have not been achieved, an efficient service cannot be offered until the problems of work load, adequate time with the patient, and freedom from threats are solved."

The motion was carried.

A motion in the name of Cornwall, "That the Association seeks assurance from the Minister of Health that the agreement to accept responsibility for the general medical care of the population as a whole does not imply unlimited responsibility beyond what is practicable and possible," was, by leave, withdrawn.

Prescription Charge

Dr. N. Nelson (City of Dundee) moved: "That the Minister is mistaken in his view that a charge would not lessen the work load of the general practitioner, and this Meeting considers that a prescription charge is necessary to reduce the work load of the general practitioner."

Dr. Nelson said that a doctor in Dundee had done some research and produced figures to prove that the work load had increased. The results had indicated an increase of 0.6 items per patient owing to the withdrawal of the prescription charge and also a small increase in demand.

Dr. R. C. GREENBERG (Finchley) showed the Meeting a Yugoslav National Health Service prescription form which included a number of categories of patients—industrial workers, pensioners, holiday residents, and so on. The doctor indicated the appropriate category on the prescription form, and when the patient arrived at the chemist's the chemist referred to a book which told him the appropriate charge, if any, to make. That method had proved very effective.

The motion was carried.

Dr. F. G. TOMLINS (Waltham Forest) moved the following motion which had been reworded with the agreement of the Meeting: "That, with regard to paragraph 45 of the Annual Report of Council, this Meeting requests Council to devote further attention to the problem of work load in general practice."

Dr. Tomlins said that the matter of work load, particularly the lack of balance of supply and demand for medical services, was one of the most serious problems in medical practice today and one which was steadily worsening. He urged the Meeting to pass the motion so that the problem might be tackled with the urgency it deserved.

Dr. W. F. JONES (Liverpool) said he knew of no worth-while source of information on work load, and yet the Council still considered the time was not ripe for such a study. In his view the figures were essential now for evidence to the Review Body, and a start should be made in getting them.

Dr. C. C. LUTTON (East and Mid-Lothian) observed that the Annual Report of Council had stated that with the increasing shortage of medical manpower and a rising population which demanded more medical care, the profession faced a continuous increase in work. In his view the new remuneration structure had nothing to do with work load. The doctor's income was controlled, his work load was not. If that continued a new and terrible disease—"While I'm here, Doctor"—would be introduced, denying the really sick the treatment that they needed. It was therefore essential to employ work-study consultants to do a job analysis. It would cost money, but so did insurance policies. Doctors had nothing to hide.

Uttering "a word of warning" on the subject of work load, Dr. F. O. WELLS (East Suffolk) said that, whereas he was sure that all doctors thought their work load was excessive, the result of an investigation could be very misleading to the public. It would be better if the Meeting rejected the motion.

Dr. GILBERT R. SMITH (Council) said that two years ago he had resigned from the Health Service. Payments by patients did not influence work load at all. In fact, when patients were paying for their treatment there was even a tendency for the work load to increase. But the matter should be put in its proper perspective. There was no simple or easy way of reducing the work load of doctors. There was a population to care for and only a certain number of doctors. The work load had to be carried.

Dr. A. R. FOX (Waltham Forest) said in spite of a large number of suggestions to ease the work load the position had not changed materially. The Council should be asked to give further attention to this most important matter.

Dr. CAMERON said he was particularly interested in Liverpool's suggestion. The question of work load could not be considered until a final assessment of what it was had been made. There were no reliable statistics, but the Association was about to appoint an economist to its staff, and he would look into this question.

Replying to the debate, Dr. TOMLINS said Dr. Wells had said any investigation had to be done carefully, and for that reason he had suggested to the Meeting that it should vote against the motion. "We assume Council will do this carefully," added Dr. Tomlins.

The motion was carried.

Size of List

Dr. C. M. G. PEARSON (Tunbridge Wells) moved the following motion: "That this Representative Body believes that no general practitioner who has contracted to provide unrestricted medical services should be obliged or forced to accept a greater number of patients on his list than he feels he can provide an adequate medical service for in the light of his own health and the circumstances of his life and practice."

He said his Division was concerned with the changes that could take place in the nature of a doctor's practice without the doctor being able to control them. He was aware that the motion brought in echoes of the 100% issue discussed so thoroughly the previous day. With the decline in the general practitioners' strength, and the increase in the size of the population, general practitioners in some areas were allotted a large number of patients to them by the so-called block allocation. Whatever the reason, the doctor might find quite suddenly that the whole character of his practice, the size of his list, and the type of medicine he had been accustomed to practise had been changed overnight. The only person who could decide the amount of additional work he was able to do was the general practitioner himself, said Dr. Pearson.

Dr. CAMERON said that in recent years doctors had been increasingly anxious about block allocations. The G.M.S. Committee was negotiating with the Ministry on the subject. The motion gave guiding principles for these negotiations. Originally there had been considerable latitude in the kind of schemes to be operated over the country, and each executive council had had its particular scheme. By and large over the years there had not been great hardship to doctors. Block allocations were something that the G.M.S. Committee intended to resist.

The motion was carried.

Vocational Training and Continuing Education

The following two motions were adopted: "That the criteria for grants for prevocational training be less rigidly applied for those already in practice." (Mid-Glamorgan.) "That, while definite criteria may be applied to new general practitioners, those already established in practice should be considered on their merits, and a date in the future should be fixed for the full implementation of these criteria." (Salisbury.)

Dr. H. GLYN JONES (Bromley) moved: "That the scope of vocational training allowances be widened in order to encourage recruitment of women practitioners to general practice."

He said a number of suggestions on this subject had been made, and he suggested the motion should be accepted as a reference to the Council.

Dr. JOAN CHAPPELL (Council) said that the Vocational Training Subcommittee of the G.M.S. Committee thought that the problem was not confined to general practitioners. The criteria listed in the "Red Book" were such that there were very few doctors who had been successful in their claim for vocational training allowances. What was wanted was flexibility, so that those who were established in practice could take such hospital training as they thought they should to enable them to qualify for an allowance. The idea was to raise the status of general practice.

Dr. CAMERON said if it helped he would accept the motion as a reference to the Council, and write to the Medical Women's Federation to find out what was the position.

The motion was approved as a reference to the Council.

The following motion by Liverpool was approved: "That in the light of the Report of the Joint Subcommittee on Dental Anaesthesia immediate steps be taken to increase the number of refresher courses in dental aanesthesia."

Departments of General Practice

Dr. H. STOLL (Camden) moved: "That when departments of general practice are being formed in teaching hospitals, then as a first step consultation should take place with local B.M.A. Divisions and Branches, the respective faculty of the Royal College of General Practitioners, and the local medical committee concerned."

He said that it was important that in these departments tutors, teachers, and professors should be people who were acquainted with general practice. The last persons in the world competent to judge who was the best man to go out as a general practitioner were some of the hospital consultants.

Dr. JOAN CHAPPELL said some work was already being done on this. By next year it was hoped that a report would be available for the A.R.M. Meanwhile she would welcome any possible liaison between the interested bodies.

Dr. J. S. NOBLE (Council) said these bodies were not going to be set up everywhere. General practitioners would often have to push in where they were not invited.

The motion was carried.

The following motion by Southampton was approved: "That the vocational training allowance be increased."

Dr. B. TAYLOR (Tower Hamlets) moved: "That this Meeting considers that locum fees should be paid for a doctor attending intensive postgraduate courses and a similar fee if a partner or colleague looks after the practice during his absence. In order that there should be an incentive to attend such courses this money should not come out of the basic practice allowance."

He said that doctors going for an intensive course and those taking a week-end course were treated in the same way. Some fee should be paid so that doctors would be encouraged to take the intensive courses.

Dr. D. H. Jones (Mid-Glamorgan) said if the Minister honestly wanted general practitioners to have the benefit of regular postgraduate courses why did he not reimburse them for the locum fees necessary to enable them to attend such courses instead of making it a charge on the basic practice allowance ?

Dr. Cameron said that if the Meeting voted in favour of the motion then it would mean that the A.R.M. would have to change its policy and go back to the old system. That system had been completely changed by the basic practice allowance. He thought it would be better to wait until itemization of the basic practice allowance was available. If the scheme ran for a year the Committee could go back again to the Minister and ask for a fresh look at the question.

The motion was, by leave, withdrawn by Dr. Taylor.

General-practitioner Maternity Services

Dr. D. Burrell (Winchester) moved: "That the choice of obstetric care for the individual patient should rest with the patient's family doctor and not with the decrees of hospital or other authorities."

He said there was an increasing tendency for regional hospital boards and hospital management committees to lay down rules about which obstetric patients might or might not be dealt with by general-practitioner units. The same went to some extent for local authorities in connexion with home confinements. True, the 1958 perinatal mortality survey had been an extremely valuable exercise, and the recommendations of the Royal College of Obstetricians and Gynaecologists, based on that survey, were also helpful. But when these recommendations were used as absolute criteria that was quite a different thing. When patients corresponded to slide-rule or computer classifications many doctors would be able to take their pensions. But until then the only person who could decide what was best for the patient was her family doctor.

Dr. H. S. Howie Wood (Isle of Wight) said that the Meeting had already stressed the importance of general practitioners having maternity beds at their disposal. He was certain that the Meeting should press that there should be general-practitioner maternity beds in every district hospital.

Mr. D. B. Brown (Mid-Essex) said that he did not like the words in the motion "not with the decrees of hospital or other authorities." He proposed the substitution of "in close consultation and harmony with the consultant obstetrician."

The proposal was accepted. The amendment was carried, and the motion, as amended, was also approved.

A motion standing in the name of North Middlesex, "That this Meeting feels that the full fee for maternity medical services under the National Health Service Act should be in the region of £30," was adopted.

Certification

Dr. D. H. Jones (Mid-Glamorgan) moved: "That paragraph 49 of the Council's report is unsatisfactory, and that the B.M.A. should take immediate action to remove the responsibility of National Health Insurance certification for general practitioners."

He said that various solutions had been suggested, but a simple way would be the removal of the iniquitous National Insurance sickness certificate. This one stroke would eliminate a vast quantity of paperwork and enable the doctor to practise the art for which he had been trained. Patients should be able to declare the fact of their sickness. In the past misuse of certificates had been made, but he found it difficult to believe that a person would risk fine or imprisonment or both, as could be the case if the patient made such a declaration.

Dr. G. E. Crawford (Liverpool) said that this proposal was Association policy, passed at the A.R.M. in 1965. He maintained that if National Insurance certification were taken out of the general medical services the problem of the 100% issue and the work load would disappear rapidly. It would be of great benefit both to practitioners and to patients. It was time the Minister was told that the purpose of doctors was to care for the sick, not to be keepers of the public purse. That was the problem of the Ministry of Social Security, which should get on with it.

Dr. E. T. Griffiths (Monmouthshire) moved, as an amendment: "That Council be urged to continue pressure for removal of all National Health certification from the terms of service, but until this happens there should be a reasonable charge for each National Health insurance certificate to be paid by the Ministry and not by the patient."

Dr. E. C. E. Golden (York) opposed the amendment. The original motion was clear and unequivocal, he said.

Dr. Cameron hoped that the Meeting would reject the amendment and pass the motion. Dr. J. S. Noble also hoped the Meeting would reject the amendment. His only concern with the original motion was the question of the immediate steps. He liked the "continued pressure" in the amendment, but hoped that the Meeting would not settle for a fee.

The amendment was, by leave, withdrawn.

Declaration by Patient

Dr. W. R. King (North Glamorgan and Brecknock) moved, as an amendment: "That Form Med. 3 be abolished and replaced by a signed declaration of illness by the patient."

He pointed out that it was significant that the only three motions on certification on the agenda came from industrial South Wales, where the work load was the heaviest in the country and where certification played a large part in making it so. A signed declaration by the patient would do nothing to deter the genuinely ill from claiming what they were rightfully entitled to, but might work as a deterrent to the malingerer, who might think twice before he put his own name to a declaration that he was suffering from something he had not got.

Dr. M. Goodman (Liverpool) said that the Ministry of Social Security should be prepared to accept the word of the patient.

Dr. Cameron agreed that a form of affirmation seemed a sound alternative, but he would prefer to get on with the main motion.

Dr. King, in reply, pointed out that a case was always strengthened if a suitable alternative could be put. This scheme was already in use in certain countries in Europe.

The amendment was lost.

Dr. E. C. E. Golden (York) said that in Holland general practitioners were not allowed to issue certificates for their own patients, it being held that he could not be impartial. Certification was done by certifying doctors. He was not aware that there was more industrial absenteeism in Holland than in Britain.

Dr. Cameron said that some progress had been made in the last two years in the matter of certification. The Association's representatives had, after the Swansea meeting, seen the National Insurance Advisory Council. He thought that the time had come to be up and doing again. The motion asked for immediate action. He could give that assurance, but could not promise immediate results.

The motion was carried.

Renewal of Surgical Appliances

A motion standing in the name of North Devon, "That renewal of surgical appliances shall be permitted in any case where the patient has been using such a support for one year or more," was, by leave, withdrawn.

Dr. A. N. Mathias resumed the chair.

Remainder of Report under "General Medical Services"

Dr. Cameron moved: "That the remainder of the Annual Report of Council under 'General Medical Services' be approved."

He thanked Dr. Walter Hedgcock Dr. Peter Wilson, and Dr. A. Gilmour, who had just joined the team, and Mr. R. C. Barker and the clerical staff for their work for the G.M.S. Committee during the year.

Fee for Cervical Cytology

Dr. J. A. Sadler (Cambridge) moved: "That this Meeting considers that there should not be any lowest age limit at which a fee is payable for taking a cervical smear, and that a fee should be payable for repeated examinations every three years or earlier where there are clinical or pathological indications for doing so."

He said that the profession surely agreed that it was essential that cervical cytology must be available to all those at risk. Why, then, had the Minister of Health chosen an arbitrary age limit for payment of 35 years and over ? In Cambridge the University Department of Pathology, in association with the Cancer Research Bureau, kept a record of cervical smears done in the area. In 16 months between October 1965 and January 1967 10,878 smears had been taken. Of these, 4,755 (43%) related to women under 35 years of age. Of smears taken in the under-35-years group six showed carcinoma-in-situ present. An equal number was shown in the larger 57% over-35-years group. What was the reasoning for the Minister's figure of 35 years ?

Why was there no fee for the under-35-years group ? The figures he had quoted showed the under-35 group to be at equal, if not greater, risk. Did the Minister by paying for cervical smears for the over-35 group wish to discourage doctors from taking smears from the younger group? Maybe the answer lay in the *Supplement* of the *British Medical Journal* of 8 July. He saw in the reference to cervical cytology that further correspondence had taken place with the Ministry concerning lack of trained staff and technicians, which was preventing extension of the service. "But this arbitrary figure of 35 years is nonsense," concluded Dr. Sadler.

Dr. HARVEY GORDON (Kingston-upon-Thames) said it would be "a very reasonable and progressive motion" if it had age 25 instead of the "lowest age." There were limited resources available and they should be channelled to where they would achieve the maximum effect.

The motion was carried.

Transport of Patients

Dr. H. D. LEGGATT (Oxford) moved: "That the Minister be urged to review immediately the whole problem of transporting ambulant patients to their doctors' surgeries."

The CHAIRMAN said there was an amendment that the words "including the use of public ambulance services for this purpose" should be added after the last word of the motion.

Dr. J. H. MARKS (Barnet) spoke of the claim that doctors had insufficient time for their real work, and yet they wasted hours driving round the countryside doing unnecessary visits. Nowhere else in the world was this waste of a doctor's valuable time tolerated. In North America the average family had at least one car. In Britain those in the greatest need of medical care, such as the elderly and the poorest families, were least likely to have a car. That had already been shown by the number of elderly and chronic sick who would come to surgery provided they could have transport and would not be kept waiting. He believed that function should be taken over by the public ambulance service. The provision of transport for ambulant patients would improve the medical service for the public.

The amendment was agreed.

The motion, as amended, was carried.

Periodic Medical Examinations

Dr. C. M. G. PEARSON (Tunbridge Wells) moved: "That in view of the increasing public interest in periodic medical examinations the Representative Body proposes that a doctor should be at liberty to provide this, if requested by the patient, and to charge a fee for this additional service."

He said it was not uncommon for a patient to approach his general practitioner with the request that he be given a "check-up." There was often good reason for it, such as a proposed change of employment, marriage, or when the patient believed, or had been persuaded by reading a magazine to believe, that it was a wise and prudent precaution to have a periodic, routine medical examination.

His view was that such examinations did not come within the terms and conditions of general practitioners providing general medical services. The principle was already clearly established in examinations for life assurance, driving public service vehicles, and so on, where there was a separate fee.

Dr. CAMERON said the Association had been trying hard to get what was asked for. The Minister had not objected to an additional charge for check-ups, but he could not agree that the fee should be paid by the patient. It was difficult to differentiate between the kind of examination which the patient should have within the provisions of general medical services and the sort of check-up which was so fashionable today.

The motion was carried.

Motions on Other Subjects

A motion standing in the name of Plymouth, "That this Meeting urges that Selective Employment Tax for medically qualified and registered assistants and deputies in general practice should be reimbursed," was accepted.

A motion standing in the name of Camden, "That maternity allowances for principals and assistants of suitable seniority should be paid to women, as is the practice in the Civil Service and universities," was, by leave, withdrawn.

A motion standing in the name of South Bedfordshire, "That all postage paid by general practitioners for communications required by the Executive Council should be refunded, and this Meeting wishes Council to discuss this matter with the appropriate authority," was accepted.

A motion standing in the name of Exeter, "That this Meeting accepts the apology of the Chairman of the General Medical Services Committee for the mistake in the wording of E.C.N.569 and instructs Council to ensure that in future all E.C.N.s are checked in detail by the Association's professional advisers before being agreed," was, by leave, withdrawn.

Allocation Scheme

Dr. D. V. CASHMAN (Tyneside) moved: "That assignment of patients under the Allocation Scheme is not acceptable to the profession and that no doctor under his terms of service be required to accept a patient on his N.H.S. list except by free agreement between doctor and patient."

Dr. Cashman said that in a "National Health Service Note" of 1962 it had been stated: "Freedom of choice remains for both patient and doctor." That was not true. Freedom of choice remained for the patient but not for the doctor. There were patients who were ruining the family doctor service, and they were the patients whom the family doctor found that he was not free to refuse admission to his list. It had been said that to revoke that part of the allocation scheme would create difficulties for the Minister. That was wrong. The difficulties were there already.

A document had been circulated in March 1965 which had promised a revision of the terms of service and of the existing unsatisfactory allocation scheme. Doctors were still waiting for the negotiators to take an unyielding stand in demanding radical revision of the allocation scheme. The revision should include the unconditional right of any doctor to accept or decline to accept a patient in the same way as that patient had the right to select or reject a particular doctor. That freedom would be a tool with which to fashion a better family doctor service.

Dr. JOAN K. SUTHERLAND (City of Edinburgh) supported the motion because she felt very strongly that there was a most important principle involved. The possible injustices in the present position were highlighted in relation to the situation of the woman general practitioner. Many women who supplied general medical services wished to limit their responsibilities and number of patients to a load which they knew they could carry efficiently. The regulations relating to patterns for allocation schemes suggested that exemption could be sought by doctors, but the only grounds mentioned were age and ill-health. The Meeting had to establish an important principle—namely, that a professional person like a doctor should be in a position to limit his responsibility to what his conscience dictated.

Dr. B. D. MORGAN WILLIAMS (South Warwickshire) said that doctors had to be protected against objectionable patients.

Dr. CAMERON said he had touched on the subject earlier. It meant a revision of the allocation scheme. As a general rule, compulsory allocation was not used. He knew the difficulties of the troublesome patient, and in a rural area that could be most irksome. He had great sympathy with those doctors who encountered such difficulties.

He asked the Representative Body to leave things as they were. Provided the allocation scheme was worked with care then he thought the Association would finally reach a solution which would be satisfactory to the profession as a whole.

Dr. CASHMAN, in reply, said he knew it was a difficult problem. If the Meeting believed, as he did, that only a truly free profession could save family doctoring in the country it would say "yes" to the motion.

The motion was carried.

Finance

Dr. S. WAND (Treasurer) moved on behalf of the Council: "That the Annual Report of Council under 'Finance' (Doc. A.R.M. 2, paras. 166–170) and the Financial Statements (Appendix XIV and Doc. A.R.M. 3) be received."

He said that 1966, the subject of the balance sheet before the Meeting, was the first year of the increased subscription. The Association had expected that the increased subscription would produce £77,000. In the event it had proved to be £99,000. In addition increased rents and dividends, £9,000 net after tax, gave a total of £108,000 additional money.

The Meeting would want to know what had become of the money, because there had been mention of the economies that had had to be made in the light of decisions made this year and in the past.

In 1965 the Association had already overspent £40,000 on the secretarial account, and this continued in 1966. In addition, in 1966 there had been promised staff salary increases of £18,000; selective employment tax of £3,000; increased subsistence over part of the year of £2,000; increase in postage costs of £1,000; an increase of National Insurance of £1,000; and, after the Review Body's report, legal expenses, postage, printing, and extra editions of *B.M.A. News*, costing another £15,000. By the end of 1966

£80,000 had already been spent of the new money that had come from the increased rents, dividends, and subscriptions. The increases in subscriptions were expected to last a number of years. In 1967 the Association hoped to have a further increase in dividends and rents, but there would be a full year of selective employment tax, which was going to cost a further £7,000; staff salary increases would cost another £5,000; the forward planning unit would cost £9,000; and a full year of the increased subsistences another £6,000, making a total of £27,000.

Everyone knew and agreed that the Association had to advance and expand. It had been agreed that money should be spent on decentralization and regionalization. More money might have to be found, but the Association could not go on finding more money indefinitely at the existing subscription rate.

In 1966, and again this year, the Finance Committee had had to get the budget estimates revised, because the secretarial account showed an excess of income over expenditure of only £2,000 out of half a million pounds, without allowing for contingencies. The revision in the Budget had increased the £2,000 to only £6,000. Additional expenses were always occurring. A staff appointment had to be made recently. A few weeks before there had been an announcement about an increase in National Insurance stamps which would cost £2,000 a year, and there might be further increases.

Dr. Wand paid a tribute to the staff for the way in which they had co-operated in staying within the Budget. The Association was constantly looking for economies. It was moving much closer to computerization. It was a little difficult to arrange, but it would save money.

What were the financial objects? Clearly money had to be found and used to the best advantage, said Dr. Wand. Reserves had to be prepared to make provision for abnormal expenditure. A subscription increase had to be avoided as long as possible. With the present rate of expenditure and income there was a strong likelihood of a deficit on the secretarial account of anything up to £15,000 or £20,000 in 1968. The profits on the *British Medical Journal* publications must be used to build up a reserve. The *B.M.J.* was a successful commercial undertaking, but it was exposed to all the risks of commerce. It was competing in a competitive field.

A sinking-fund policy in respect of Tavistock House had come to an end in 1966. It appeared as a capital increase on paper because the money was shown as the premiums that had been paid from year to year over a long period, and the ultimate sum was greater. That had been invested as soon as it had come in. The value of the holdings in the balance sheet was now about £7,000 greater than as shown at 31 December, and was in excess of the cost.

One of the items debated at the Junior Members Forum had been the subscription. It had been made clear that it was the wish of junior members to pay as much as they were able to pay. A motion had been moved, and had received quite a lot of support, to add one guinea to the members' subscription for medico-political purposes.

Dr. Wand paid a tribute to the late Dr. Kate Harrower, who had been Deputy Treasurer of the General Medical Services Defence Trust, and to the Chief Accountant.

Revenue Budget for 1967

Dr. R. P. HENDRY (Rugby) moved: "That this Meeting notes the estates surplus for 1966 was £73,127 and the estimate for 1967 is only £47,520; it calls for an explanation of the anticipated reduction of over £25,000."

Dr. Hendry said that since the motion had been tabled he had received an explanation from the Treasurer of the reduction which was, apparently, merely the difference brought about after tax had been deducted.

The motion was, by leave, withdrawn.

On the motion of the Treasurer the remainder of the Annual Report of Council under "Finance" was approved.

Detailed Balance Sheet

Dr. D. C. ROBERTS (Hendon) moved: "That this Meeting requests that in future the detailed balance sheet annually available to the Representative Body shall be published in the Annual Report of Council."

Dr. Roberts said it would help in the compilation of motions if the detailed balance sheet was in future available to Divisions. However, it seemed undesirable for this information to appear in the Annual Report of Council where it could be read by everybody, and an undertaking had been given that it would in some way be made available to Divisions.

Dr. WAND said he was prepared to accept the motion as a reference to the Council.

The motion was carried as a reference to the Council.

Estates

Dr. WAND moved: "That the Annual Report of Council under "Estates" (Doc. A.R.M. 2, paras. 171–173) be received."

He reminded the Meeting firstly that the B.M.A. had a great deal of property to be maintained, and secondly that though the Association occupied a large part of B.M.A. House in Tavistock Square it also had a big property business. It was hoped the property income in the near future would be round £135,000. Contrary to some other types of office space, the accommodation in B.M.A. House was fully let.

The motion was carried.

The Annual Report of Council under "Estates" was approved.

Compensation and Superannuation

Dr. J. B. S. MORGAN (Chairman of Compensation and Superannuation Committee) moved: "That the Annual Report of Council under 'Compensation and Superannuation (Doc. A.R.C. 2, paras. 55–69) be received.'"

On 15 December 1966 new Regulations had come into force bringing a number of improvements to the National Health Service Superannuation Scheme, said Dr. Morgan. The improvements were the result of protracted negotiations over a number of years and now was an opportune moment to pay tribute to the hard and skilful work that Dr. Mathias had performed in his capacity as chairman of the Compensation and Superannuation Committee for 13 years.

The Editor of the *B.M.J.* had printed an account of the changes made in the new regulations and advice on their interpretation in the *British Medical Journal* of 10 December 1966. Dr. Morgan commended members to read that issue, but if further interpretation was required Dr. Peter Wilson, Assistant Secretary, would be pleased to help.

While an advance had been made on the superannuation front, much remained to be done for family doctors and also for hospital doctors and those in the public health service. Many doctors who had worked in general practice under the National Insurance Act and in voluntary hospitals for little or no pay had shouldered the responsibility and toil of those days and yet had no reckonable service to cover that period. That was an injustice that the State should be called on to repair, said Dr. Morgan. Doctors who had qualified and entered the Service after 1948 would ultimately have all their service reckonable. At a time of high taxation and inflationary spirals it was essential that the practice in other professional bodies in Britain and in other countries should be examined. If the Meeting expressed such views the Committee would be encouraged to soldier on to try to persuade the superannuation division of the Ministry of Health that further concessions must be granted. Finally, Dr. Morgan thanked Dr. Peter Wilson for all his help and guidance during the year.

Compensation

Dr. I. E. JAMESON (Salisbury) moved: "That this Meeting would like to see that the rate of interest on practice compensation is tied to the rate the Government sees fit to charge for loans through the Finance Corporation."

Dr. Jameson said that the time had come when the rate of interest received on the Association's compensation money should be related to the rate of interest the Association would have to pay for any money that it borrowed from the new Finance Corporation, and urged the Meeting to support the motion.

Dr. MORGAN said that the Committee had decided to include in its approach to the Ministry a request for an increase in the rate of interest, currently 2¾%. The rate of interest charged by the General Practice Finance Corporation was 7¼%.

The difficulties in negotiating an increase in the rate of interest were highlighted in the Third Report of Joint Discussions on the Family Doctor Service, in which the Government pointed out that the arrangements for interest at the rate of 2¾% (and no interest would have been earned by the goodwill had the right to sell it been retained) had formed part of a "once-for-all" settlement with the profession at the beginning of the National Health Service, and had been freely accepted at that time by both sides.

There was also the point made in 1964 by the then Minister of Health, Mr. A. Barber, that any increase in the rate of interest on medical practice compensation would have widespread repercussions on the rates of interest laid down for those shareholders who were compensated when various industries were nationalized.

Dr. JAMESON said that had doctors retained their right to compensation obviously the value of their capital over the years would have increased.

The motion was carried.

Superannuation Regulations

A motion standing in the name of Winchester, " That an independent trust be established to invest National Health Service Superannuation contributions on a realistic basis," was, by leave, withdrawn.

Dr. DAVID BROWN (Liverpool) moved: " That superannuated doctors' pensions should be continuously modified by a cost-of-living factor."

He said that superannuated doctors included those who had served Britain in two wars, who had practised during the decade of the worst depression the country had ever known, who had suffered the economic injustices of the early days of the National Health Service, who had been subjected to compensation with paltry interest, and had seen the capital value of the compensation sadly eroded. He urged the meeting to pass the motion, so that the B.M.A. could combine with other bodies in the public service to get the cost-of-living factor included in legislation. This was done in Common Market countries as well as Commonwealth countries.

Dr. MORGAN said he hoped the motion would be unanimously passed.

The motion was carried.

Dr. F. G. TOMLINS (Waltham Forest) moved: " That this Meeting, while recognizing the efforts of Council in this matter, regret the refusal of the Minister of Health to make satisfactory retrospective adjustment of superannuation contributions to compensate for the effects of inflation."

He said that it should be simple to rectify this by a factor which was fairly easily worked out.

Dr. MORGAN said that this motion was on the right lines and would be pressed.

The motion was carried.

Dr. W. P. LAMBIE (Sheffield) formally moved: " That this A.R.M. recognizes the real progress made by the Compensation and Superannuation Committee in the last year in wresting from the Ministry the concessions as laid out in the Report of Council. While justice to general practitioners had not yet been fully done, this A.R.M. acknowledges the advances made in that direction and congratulates the Chairman and his Committee on its interim success."

Dr. G. E. OWEN WILLIAMS (C.C. and S. Committee) supported the motion, and it was carried.

Superannuation on Part-time Appointments

Dr. E. T. GRIFFITHS (Monmouthshire) moved: " That Council be requested to ensure that all sources of income from Government departments be superannuable, comparable to the N.H.S."

He pointed out that for certain sources of income such as hospital sessions doctors did not get any superannuation. This was an injustice to single-handed practitioners with small lists who supplemented these by doing hospital sessions.

Dr. MORGAN said that the matter would be pressed with the Ministry but he was not hopeful.

The motion was carried.

The CHAIRMAN formally moved a motion standing in the name of Cardiff: " That doctors who had opted out of the superannuation scheme be now given the opportunity to opt in as from April 1967, such a step being fully in the spirit of the new forms of payment under the Family Doctor Charter."

Dr. MORGAN said that the matter was dealt with in the Annual Report.

A motion to pass to next business was carried by the necessary majority.

Dr. MORGAN moved: " That the remainder of the Annual Report of Council under ' Compensation and Superannuation ' be approved."

The motion was carried.

Superannuation Fund

Dr. GRIFFITHS (Monmouthshire) moved, "That Council be asked to press for the National Health Service Superannuation Scheme to be funded."

He said that £400m. of doctors' money was being held in a notional fund. There were 3,600 doctors over 65 years of age getting no pension and continuing to work. He therefore asked that the Council should press for this notional fund to become an actual fund.

Dr. MORGAN said that, unlike local government superannuation, the National Health Scheme was not funded. All contributions went to the Exchequer, which guaranteed to pay the benefits when they fell due out of general taxation. There were arguments for and against the question of investment. In 1953 the Government had appointed a Committee under the chairmanship of Sir Thomas Phillips to consider the " economic and financial problems of the provision for old age." Dr. Morgan quoted a passage from the report advocating funding for superannuation schemes.

Though this would seem to indicate that there was little or no objection to funding an investment of superannuation schemes, the Meeting must remember that the Ministry had pinpointed a number of difficulties when, in January 1966, the Committee had proposed the setting up of a separate, fully invested fund for practitioners' superannuation. The Committee's representatives had been informed that it was most unlikely that such a proposal could be accepted. At that time it had been said there were objections in principle to the proposal, and, moreover, there would be no guarantee—especially if there was a period of sharp inflation—that the fund would be adequate to meet benefits. Though local authority superannuation schemes were funded and many authorities invested their assets in equities and property, the benefits provided were no higher than those under the National Health Service Scheme, and indeed deficiencies arose which had to be met by the employer. If notional rates were realistic there was no practical difference between a notional fund and one that was actually invested.

Dr. BURRELL said that despite what Dr. Morgan had said it must be remembered that £400m. of doctors' money was invested with the Government. Why not have it for their own superannuation ?

The motion was carried.

Phased Retirement

Mr. MYLES GIBSON (Leeds) moved, " That as it seems likely the work load of doctors in the National Health Service will not appreciably diminish, and expecting the doctor's taking day-to-day responsibilities for his patients, while economic factors suggest large sections of the community may enjoy a shorter working week, the Superannuation Committee be asked to examine the possibility that doctors might in the future have the option to retire at a phased earlier age while retaining full pension rights."

Dr. MORGAN said that the National Association of Local Government Officers and the Conference of Local Medical Committees has passed motions on the lines of that proposed by Mr. Gibson, and if the Representative Body would do the same it would help in negotiations.

The motion was carried.

Occupational Health

Dr. J. C. MCMASTER, on behalf of the Chairman of the Occupational Health Committee (Dr. R. E. W. Fisher) moved: " That the Annual Report of Council under ' Occupational Health ' (Doc. A.R.M. 2, paras. 98–105) be received."

He said the Council had now to report that discussions had been concluded with the National Coal Board on the pay of doctors in its employ, and a joint approach had been made to the Ministry of Power. The implementation in this case involved the introduction of an increase on the old scales backdated to 1 October 1966, and the introduction of completely new scales to meet the total reorganization of the Coal Board medical service, which became effective on 26 March 1967. The new organization completely altered the relationship of medical officers to senior medical officers, who were now roughly on equality. That made considerable difference to career earnings. Discussions were still continuing with other nationalized industries.

The Association had completed its evidence to a committee on the care of the health of hospital staffs. It should be published within the next six months. The Royal College of Nursing had left the B.M.A. in no doubt that nurses were not at all satisfied with the existing provisions for the staff of hospitals.

The motion was passed.

Food Hygiene in Industrial Canteens

Dr. MCMASTER moved: " That all canteen staff should be examined from a hygiene point of view before employment, the type of examination to be determined by the medical officer in charge."

He said the motion was on something which had arisen in 1966. He was sure everyone would agree it was a sensible motion.

Dr. F. G. TOMLINS (Waltham Forest) moved the amendment that the words " handling food " should be inserted for the motion to read: " That all canteen staff handling food should be examined. . . ."

He said he was moving the amendment because it was thought the wording of the motion was too wide. It involved a certain waste of medical manpower in examining people who would never handle food.

The amendment was agreed.

The motion, as amended, was carried.

Dr. MCMASTER moved: " That the remainer of the Annual Report of Council under ' Occupational Health ' be approved."

The motion was carried.

The Meeting adjourned at 6.20 p.m.

Third Day: Saturday, 8 July

The Meeting resumed at 9 a.m., with Dr. A. N. MATHIAS in the chair.

Organization

Dr. J. S. NOBLE (Chairman of the Organization Committee) moved: "That the Annual Report of Council under "Organization Committee" (Doc. A.R.M. 2, paras. 206–224), the Amendments of Articles and By-laws (Appendix XIII), and the revised Report on the Constitution of the Association (Doc. A.R.M. 8) be received."

He said that a stiff increase in subscription, the troubles of junior hospital doctors—to say nothing of the wage freeze and the constant attacks of detractors of the B.M.A.—might have been expected to have had an adverse effect on membership. There had been a drop, but it was almost entirely accounted for by the loss of members to overseas Branches who had become independent and equal partners in the Commonwealth Medical Association.

The drop was nothing compared to previous falls in membership associated with rises in subscription. However, 70% was not enough and a membership drive was called for. Every non-member must be contacted personally, said Dr. Noble, and it was the duty of every member of the Representative Body to see that members in the Divisions did what they could to bring new members into the fold.

The B.M.A. was doing many new things for its members. It had had the offer of a comprehensive and efficient discount service from Independent Medical Services Ltd. There were also hire purchase arrangements that would help younger members. Another thing the B.M.A. had done for younger members was to introduce a personal careers advice service. Any young doctor could obtain a folder that dealt with career prospects, and so on. The introduction of other facilities, such as accountancy advice research and audio-visual and forward planning units, showed that last year the B.M.A. was neither wanting nor wasting.

Dr. Noble went on to say that the Representative Body should show it could respond to modern needs by enacting the constitutional changes agreed at Exeter. Last year it had been decided that the Association must have a smaller Representative Body, geographically and proportionately representative of the profession. This would lead to a rationalization of the relationship between the Representative Body and the Council on the one hand and the major sectional committees on the other. The latter would have domestic autonomy and the Representative Body would normally receive their reports and use the reference back in case of doubt and where there was dispute. That would free the Representative Body for more debating time on major issues and ensure that in matters of doubt those who were best informed decided. The individual doctor would have his say and any decision reached would be based on the full authority of the profession. The Representative Body would at all times retain the legal right to decide any issue on its merits.

In accepting the constitution report, the A.R.M. of 1966 had made certain amendments. It had expressed concern at the grouping of Divisions and at the inflation of the representation of minority groups. It had also been disturbed about proportional representation on the one hand—which it did not like—and at the same time it had called for proportional representation of hospital junior staff. It had accepted the idea of regional councils but had said (wisely, he thought) that they should be introduced only in a few years and on an experimental basis.

Previous Resolutions

The resolutions passed by the A.R.M. in relation to the Council (in respect of proportional representation and retaining regional representation) had led to a larger Council once more. It also meant the Council members attending the Representative Body—which made it more difficult to reduce its size. But that was in accordance with the wishes of the Association. The recommendations about the Representative Body had swung back the proposals a long way in favour of single constituencies. As had been suggested at Exeter, the recommendations loaded the more rural areas against the conurbations, but he believed that the electoral procedure for minority groups in the conurbations would to a large extent redress the balance. The Committee had gone as far as it could to achieve proportional representation. The document on the subject merely asked that members would be from each section of the profession, hospital, general practice, and others, according to the size of the constituency, with the exception of the large constituency and the allowance for the hospital junior staff.

There were many ways that those objectives could be achieved. The Organization Committee, by a large majority, believed that the present proposals were the best way to achieve them. Dr. R. P. Hendry, an invaluable member of the Committee, believed another way was equally good. Dr. Hendry would be putting his scheme to the Meeting.

"I come now to some matters on which I may be asked for an explanation," went on Dr. Noble. "Motion 310 requests us to explain the figures given in relation to the size of the new Representative Body. As we have said, these figures are only estimates, and they are subject to variation. The decision of the Representative Body to elect the Council on a regional basis has automatically made the reduction of that body in size more difficult, and the exact calculation of the members of the Council not being members of the Representative Body is equally variable. There is a further variable in that the retiring regional members of the Council are invited to the Representative Body, again enlarging it even more."

Another Variable

With the new constitution there was yet another variable. The non-voting committee chairmen on the Council would also be attending the Representative Body. They might be members of the Council, members of the Representative Body, or members of both. Any calculation about the size of the Representative Body must be an estimate. He believed that with all the variables taken into account East Yorkshire's figure [East Yorkshire Branch, movers of Motion 310] was a slight overestimate, and his forecast was that the reduction in size would be somewhere between the reduction in size forecast in the Constitution Report and that forecast by East Yorkshire.

In another motion, said Dr. Noble, he was asked to explain why the amendment to By-law 75 had been placed in the Appendix and not in the main Annual Report. The short answer was that there was no rule that laid down that recommendations for changes in the by-laws must appear in the main explanatory report. The Appendix was as much part of the Annual Report of Council as the main report itself.

Dr. Noble expressed his thanks to all those concerned with producing the report. The new constitution recognized the varying opinions within the Association. These had now been collated, and a flexible, fair method of representation produced ensuring that the minorities were heard, while the Divisions retained their place as the vital local unit. No constitution was perfect, and there would be anomalies, but the Committee had invited and received representations from Divisions on those. It had endeavoured to help every Division that had contacted them, said Dr. Noble, and he was satisfied with what had been done. The scheme was not sacrosanct, but he asked the Representative Body to give it a trial.

Dr. Noble concluded: "May I say that you have seen this meeting of the Representative Body labour under discussion of minutiae on matters that would have been better dealt with in committee. . . . We do not want to abolish debate in the Representative Body. We want to give the Representative Body the opportunity to speak for, and be seen to speak for, the whole profession on the weighty issues that face medicine in the future. Never has there been a greater need for co-ordinated leadership coupled with policy-making in strength. The Association ducked the challenge in 1957, and the task has been made the more difficult as a result. Failure to face the issues now may mean rejection for years, maybe for ever. I urge this Representative Body to take the decisions now that will enable us to go forward, acting for and leading the whole profession of medicine."

Subscription Rates

Mr. J. KYLE (City of Aberdeen) moved: "That the annual subscription of full-time lower-grade university medical teachers be reduced to 75% of the standard subscription."

Mr. Kyle said that the motion was put forward both to help non-professorial medical teachers and also to increase recruitment to the Association. The proposal was not a new idea; such rates had existed until about three years previously. The measure was not intended to be permanent, but to be effective until such time as the salary scales of the doctors involved were brought up to the level of clinical doctors. The non-professorial full-time university teachers were not a large group, though their numbers would probably increase more than those of any other section of the profession in the next few years if the Government's policy to increase the output of medical schools was implemented. Unfortunately, however, they were a bitterly disillusioned group. They felt that at a time when they were struggling, apparently hopelessly, to have their salary scales increased the Association had stabbed them in the back by withdrawing the concessional subscription rates. Acceptance of this motion would give back this concession.

Dr. J. S. Ross (Chairman of the Membership and Information Subcommittee of the Organization Committee) expressed sympathy with the full-time university teachers and other poorly paid doctors in their present financial difficulties. He said that it was most important that junior doctors should join the B.M.A. and stay in it. There was a tendency for doctors to leave the Association four or five years after qualification, though most doctors joined when they first qualified. It was too complicated to have a subscription ladder and a means test. All doctors must realize that they got value from membership of the Association, and no doctor could afford not to join. The Association could not afford to do its work properly without money, and would fail in its duty if it attempted to induce doctors into the Association by too low a subscription rate.

Dr. S. WAND (Treasurer) pointed out that the proposal would cost the Association £1,500 a year and there would certainly be repercussions in other fields. If subscriptions were lowered in one field, it meant that they had to be raised proportionally in others.

A motion that the question be now put was carried.

Mr. KYLE, in reply, said that he realized there were several privileged groups, but this was only reinstating a concession which was available up to a few years ago. He also realized that it might initially mean loss of income to the Association, but he did not think the Association could afford to fail to attract the many young graduates leaving medical schools.

The motion was carried as a reference to the Council.

Dr. J. M. CORALL (Medway and Gravesend) moved: "That on the payment of a fee of five guineas life membership of the British Medical Association should be granted to a member who had been a continuous subscriber for 40 years."

He said that his Division felt that after 40 years' continuous subscription one single, nominal sum should be accepted by the B.M.A. for life membership.

Dr. WAND said that this would cost the Association £8,000 a year. It could not afford it.

The motion was lost.

Constitution

Dr. W. F. DE C. VEALE (Brighton and Mid-Sussex) moved: "That immediate steps be taken to engage an independent firm of management consultants to examine and report on the whole structure of the B.M.A. before proceeding further with the proposed new constitution."

He said that his Division thought that the scheme at present before representatives had been prepared by people too near the trees to see the wood. The Division would like to know that the whole organization of the B.M.A. and its relation to the autonomous committees had been investigated, and would like the findings published in order to judge for itself. In 1953 a small committee led by Mr. H. H. Langston had drawn up a scheme which was virtually thrown out by the A.R.M. in 1957. The present scheme was only a rehash of the 1953 scheme. It had been prepared by the central hierarchy and put all the power into its hands. It put an extra barrier between the periphery and the centre. It put extra power into the hands of consultants, who would be able to veto general practitioners' wishes, and the A.R.M. would no longer be a policy-making body.

Dr. C. C. LUTTON (East and Mid-Lothian) opposed the resolution as being too late. If management consultants were brought in, it would probably be three to five years before the stage at which the Association was now was reached. The new constitution, if it went through, would have to be changed, and changed again. To stop at this stage would do harm.

Dr. WAND said that the Association had employed management consultants before, and that they had found few flaws in the manner in which the main Association's business was conducted.

Dr. H. L. LEAMING (Council) opposed the resolution because it would cost the Association a large number of members. Experts were needed on constitutional matters. He submitted that the Association had had them. The Solicitor, counsel when necessary, and the Board of Trade, all experts on constitutional matters, had advised the Association when necessary.

Dr. NOBLE asked the Meeting to reject the motion. The work of management consultants was management and consultation in business not in a free and voluntary organization representing a profession. Expert advice could be taken on internal administration but not in relation to the basic situation. Dr. Veale had inferred that consultants would be able to dominate the Representative Body; the constitution laid down that each section of the profession would have a fair say in the Representative Body. The constitution report stated that no section of the profession should dominate another by sheer numbers, and the Organization Committee stood by this statement.

Dr. VEALE, in reply, said outside advice should be taken. It would be money well spent. Referring to the proportion of consultants on the proposed new Representative Body, Dr. Veale said the scheme would allow for more than the original entitlement of 60.

The motion was lost.

Call for Reference Back

Dr. R. L. LUFFINGHAM (East Yorkshire) moved: "That, with reference to paragraph 208 of the Annual Report of Council, the Report on the Constitution of the B.M.A. (*Supplement*, 26 November 1966, p. 204) be referred back for further consideration in the light of the memorandum on the reform of the constitution of the Association, submitted for inclusion in the agenda for the A.R.M., 1967, by the East Yorkshire Branch, and that Council report back to the A.R.M. in 1968."

Dr. Luffingham said that the Constitution Committee had been set up in November 1963. East Yorkshire had set up its own subcommittee to look at the constitution of the Association a month later, and had informed the Association that it had been done. The Constitution Committee's report had then come before the Representative Body at Exeter. There had been no time or opportunity for East Yorkshire to be heard before that. The report had been discussed at Exeter, and, as a result of the proposals made at that meeting, a revised report had been published in November 1966. Once again it had been impossible for East Yorkshire to put anything forward, because the preamble to the document which had been published in the *B.M.J.* stated that "the Organization Committee would welcome comments, but the comments should be confined to constituency and boundary matters." Again general principles could not be discussed.

In February 1967 an offer had been made to all Divisions that the Chairman of the Organization Committee, or a deputy, should visit Divisions to explain the implications of the new constitution. East Yorkshire had written to the Association and had said, "We do not agree with the new scheme; may we put the opposite point of view?" The answer had been "No, you may not do that." Finally, East Yorkshire's views were made known through the *B.M.J.* on 3 June. It had been important that their proposals for reform should be published, so that, if there was debate and the revised constitution was turned down by the A.R.M., they would be in a position to say that here was a viable alternative which was worth investigating. Dr. Luffingham thought that if the resolution was passed discussion of the remainder of the motions on the Agenda dealing with changes in the constitution should be postponed. The last thing the East Yorkshire Branch wanted was that the constitution should not be discussed. What they wished to say was that here was a Branch who, four years before, had asked to be heard. If the promises that had been made to them then that they would be heard had been implemented the whole matter could have been settled. It was unfair that the Branch should be accused of delaying tactics and of wrecking the motions. They were not. The Representative Body had a further function over and above discussion, and that was its position as the last court of appeal for the aggrieved individual through his Division. East Yorkshire was an aggrieved Branch.

Previous Opportunities

Dr. J. S. ROSS (Council) said many had been disappointed when they had first seen the East Yorkshire memorandum appearing at such a late stage. Opportunities had been given to East Yorkshire representatives by the Organization Committee to meet and discuss the matter, but they had never been able to manage this. Criticism had been made the year before that there had not been time for discussion, but opportunities had been given to members to discuss the report in detail. The revised report had been published in the *B.M.J.* in November 1966. Further changes could be made to the constitution in future if necessary, but they could not afford to delay any longer if an efficient Association was to be formed.

Dr. C. C. LUTTON (East and Mid-Lothian) said time had been marked for long enough. The Association must go forward. There would never be complete agreement on the matter, but if a vote to proceed was passed the rest could come later.

Dr. H. L. LEAMING (Council) could see no advantages to be gained from the Council considering the memorandum. The urgency lay in implementing the revised Constitution. Until this happened the B.M.A. was in jeopardy. Another year's delay would be too long.

Dr. G. N. MARSH (Stockton), recalling past delays when the constitution was being considered, said that once more the motion, if carried, would stop progress. He welcomed the new constitution on two important matters of principles. Firstly, it embodied fair representation on the Representative Body and the Council so that those bodies would be composed of members of the whole profession from all areas, at all levels, and all ages; secondly, it avoided time-wasting duplication of medico-political affairs which had sapped the energies of the Association over the years.

Dr. R. L. LUFFINGHAM (East Yorkshire) asked what, if the motion were carried, the effect would be upon the discussion of the remaining business on the constitution. Would it not fall?

The CHAIRMAN did not share Dr. Luffingham's view. Other matters had been submitted by other Divisions for the Meeting's consideration and must be considered as well as E. Yorkshire's memorandum.

Dr. W. J. C. SCOTT (Dunbartonshire) regretted he could find no reference in the memorandum to regional councils or area health boards, which were, in his view, vital to the new constitution. Nor was there any mention of proportionate representation. Those were comparatively minor points. Others could be made more forcibly.

Mr. G. E. MOLONEY (Council) said that the Constitution Committee had gone to great trouble to arrive at its recommendations. There were things in the report that he himself did not like, but everyone could find something or other that was unpleasing. He urged the Meeting to give the new constitution a try and to modify it later if necessary.

Time Needed

Dr. A. V. RUSSELL (Council) strongly favoured East Yorkshire's motion. The doubts expressed in the East Yorkshire memorandum were also present in the minds of a good many of the Divisions. Though much time had been spent in considering the matter, even more time must be taken if necessary to reach as near perfection as possible.

Dr. G. R. OUTWIN (Council) said in his view the Association was trying to go far too fast in achieving the desired constitutional reforms. If the new constitution were put into full effect now the Association would be disrupted in every facet of its functioning at every level. That would be a grave mistake. It would be much better to do it by degrees.

Mr. H. H. LANGSTON (Council) urged the Meeting to reject the motion. The constitution now suggested was a vast improvement on what had previously been proposed. The Association could not afford to delay on the constitution any longer. He was constantly hearing from young consultants particularly, and not only hospital junior staff, that the Association did not fairly reflect the views of the body of the profession. If that continued, the divisive tendencies of which the Association was so afraid would mount and be difficult to contain.

East Yorkshire had put much work into its memorandum, but it was so different from the proposals of the Constitution Committee that he was certain that, even if the proposals were taken seriously, an answer would not be produced by next year.

Mr. M. J. GILKES (Brighton and Mid-Sussex) said Mr. Langston had stated that the Association could not afford to delay. In his view it could not afford not to delay. It was the duty of government to govern, but it was also the duty of government in a democracy, and the Association tried to be a democracy, to listen to opinion and to realize that there were an awful lot of people who were on the brink of departing from the Association. Nowhere in the debate so far had he heard any discussion of the merits of the East Yorkshire memorandum—merely that the Association must get on and could not afford to delay. He urged the Meeting to think about the matter very carefully indeed before taking a decision.

Heavy Weather

Dr. R. P. HENDRY (Rugby) suggested the Representative Body was making heavy weather of the matter. There were certain proposals it could get on with now, and during the year the East Yorkshire proposals could be studied. "Let us get on with some of the things we can get on with this year," he added.

Dr. R. COVE-SMITH (Council) said there were two points he wanted to make. Firstly, Mr. Langston had said that the dissatisfaction of hospital junior staff was due to the B.M.A., but it was mainly due to the defects in the constitution of the C.C. and S. Committee. Secondly, he thought the Association should proceed by evolution not revolution. Representatives knew only too well the effects produced on the medical profession by revolution from experience when Aneurin Bevan was bringing the N.H.S. into being. They were still suffering from that revolution. Evolution would have been much more effective.

Dr. RONALD GIBSON congratulated the Organization Committee and Dr. Noble in particular on the excellent report. He did not suggest that the new constitution was perfect. He could tear it to pieces and he could also add to it, but it had great merit, and Dr. Gibson asked the Representative Body not to block the scheme for a whole year.

Dr. NOBLE said that East Yorkshire should clear its own eyes before it asked the Representative Body to clear its eyes. He asked the Meeting to read through the East Yorkshire memorandum and the Constitution Committee's report at the same time. Who was guilty of glossing and who was being inaccurate? "They accuse us of wanting to abolish debate," declared Dr. Noble. "We are creating debate, and the anomalies in the Representative Body and the Council to which they have drawn our attention are largely the result of your own democratic decisions. I believe that if you will give this constitution a chance it will work. If you refer it back it will not work for years. I ask you to give this constitution a trial."

In replying, Dr. Luffingham said, "We may luff in East Yorkshire, but we do not huff and puff." (Laughter.) Some speakers had said, "Don't block the constitution," but he had not even begun to discuss the constitution. He was concerned with the reference back of the Constitution Committee's report and that only. An important constitutional issue was whether a Division or Branch had the right to make approaches to the Representative Body. East Yorkshire was asking the Representative Body to act as an appeal body.

Motion Defeated

The motion was lost, the vote being 159 in favour and 190 against.

A SPEAKER from the floor asked why the resolution required a two-thirds majority as it was not a change of policy of the Association.

The CHAIRMAN said it was a change of policy on the decision that the Meeting made last year. In any event, the motion had been lost on a simple majority.

Dr. K. W. BEETHAM (East Yorkshire) moved: "That, with reference to paragraph 208 of the Annual Report of Council, the Memorandum by the East Yorkshire Branch, entitled 'Proposals for Reform of the Constitution of the Association,' submitted for inclusion in the agenda of this Meeting, be referred to Council for consideration and report back at the A.R.M., 1968."

The motion, accepted by the Chairman of the Organization Committee, was carried with no dissentient votes.

Hospital Junior Doctors

At this point standing orders were, by leave of the Meeting, suspended to enable Mr. H. H. Langston to make what the CHAIRMAN described as an "important statement."

Mr. LANGSTON then read a statement about exchanges between the B.M.A. and the Junior Hospital Doctors' Association. This statement is printed at page 65.

President-Elect

The CHAIRMAN then introduced Mr. C. O. F. Rieger, of Adelaide, Australia, President-Elect for the year 1968–9. Mr. Rieger was accorded a standing ovation.

Mr. RIEGER said that he took it as a vote of confidence in the Australian Medical Association that his nomination had been approved. He pledged himself to follow the high tradition set by his predecessors and to uphold the dignity and honour of the profession, and promote the welfare of its members.

He urged as many members as possible to attend the Conjoint Meeting in Australia in 1968.

Organization: Constitution of the Association (Resumed Debate)

Sovereignty of Representative Body

Dr. C. P. WALLACE (Guildford) moved: "That notwithstanding any alterations made in the constitution, the Representative Body shall retain its sovereignty with regard to all matters concerning hospital, general practice, and the public health services, and will consider the reports from these bodies at each Annual Representative Meeting."

He said that if there were written into the constitution such statements as "the apparent conflict between the sovereignty of the Representative Body and the independence of the autonomous bodies," and "in all routine matters affecting sections of the profession we feel that the Representative Body would be satisfied if reports on the work of the autonomous bodies were submitted to it for information and not normally for detailed decisions," then it was essential that there should also be written into the constitution once and for all that if the Representative Body were to be worthy of its existence it must retain sovereignty in every section of the profession.

There would undoubtedly be cases which would seem to some people to be trivial and matters which should not be discussed at the A.R.M., but others that would appear to be matters of vital principle. It must not be made more difficult than it was at present to have such matters discussed at the A.R.M. He agreed that many of the motions which had been taken under the G.M.S. Committee report could adequately have been dealt with at the level of the G.M.S. Committee itself. On the other hand, there were innumerable matters concerning the three branches of the profession which concerned the profession as a whole and the great freedoms for which he hoped the Association still stood.

Dr. R. S. V. **Marshall** (South Staffs) agreed that the autonomous bodies should have a degree of autonomy in detail, but there was at present nothing to prevent them exercising their autonomy in matters of principle. The Representative Body must assert its position as the policy-making body. It would consult those bodies, but the present proposals put undue power into the hands of outside bodies.

Dr. G. N. **Marsh** (Stockton) said that the motion required the Representative Body to consider detailed reports from the Public Health, the C.C. and S., and the G.M.S. Committees so that it could reassure itself that all the right decisions had been made. That would be a scandalous waste of time, and would perpetuate the "crazy duplication" under the existing constitution.

Dr. J. C. **McMaster** (Council) said that splinter groups could not speak for the whole profession. The Representative Body was the only body which could speak for the whole profession, and it must at all times and in all circumstances retain that ultimate right.

Dr. C. **Shiers** (Council) pointed out that the greater power of the autonomous bodies in the Association might become a danger to the overall authority of the Representative Body. He believed that unity would come only by lack of sectionalism and could not be tripartite.

Dr. A. V. **Russell** (Council) emphasized that the most important single thing in the B.M.A. was that the Representative Body should be the sovereign body and the sole policy-making body in the Association. That it was to be written into the constitution that the Representative Body would be able merely to receive the reports of the two autonomous bodies and not to discuss them was appalling.

Will or Must?

Dr. D. C. **Roberts** (Hendon) asked if the speakers were interpreting the meaning of the word "will" in the motion in different ways. Did it mean "may at their will" or "must"? Dr. **Wallace**, in reply, said "will discuss" meant "will discuss." He was opposed to the detailed discussion of the trivia concerning general practice, but when it came to the principle of a report presented to the Representative Body, it had to be in a position to discuss that report before it was "rubber-stamped."

Dr. H. **Glyn Jones** (Bromley), on a point of order, said it was not what Dr. Wallace thought the words meant which was important, but what the words meant. "Will" gave power for something to happen. If it were mandatory it would have to be "shall." Since it was not "shall" or "must," it gave power to the Representative Body without necessarily compelling it.

Dr. **Ronald Gibson** (Chairman of Council) said advice had been taken from counsel and solicitors on the matter of the power of the Representative Body. It was clearly stated in the Constitution Report that the Representative Body was the sovereign ruling body of the Association, and in all circumstances it should have the last word on anything involving the honour and interests of the profession and on matters medico-scientific. There was no need for concern about the matter. He said he would regret, if through passing the motion in a mandatory sense, the Representative Body should have to go through every item of every report. What was intended was that the Representative Body should and must have the opportunity to be able to consider in detail every item concerning every member and group of the profession and have the final word.

Dr. J. S. **Noble** said the motion was one with which he was in complete agreement, provided it was made clear what the Meeting was being asked to decide on. It had been the wish of the profession that the work of the Representative Body should be reduced and that it should have a proper relationship with the standing committees. On the other hand, the Meeting should support the sovereignty of the Representative Body. It was stated "the Representative Body will normally receive the reports of the committees, but, if it wishes, it has the right to disagree. . . ." The report also stated "that the Representative Body can decide on any matter at any time that it wishes."

Provided the Guildford motion meant it was not mandatory on the Representative Body to consider everything, then the Organization Committee was wholeheartedly in agreement, but if the intent of Guildford was that it should be mandatory then he had to oppose the motion.

Dr. **Wallace**, in reply, said the Meeting was at one on the matter. He was satisfied that the motion should be passed. It meant the Representative Body would preserve its right to speak on matters concerning all branches of the profession.

The motion was carried.

Question on Statement to Press

Dr. E. **Townsend** (Cornwall) asked if it was a fact that the statement made by Mr. Langston about the Junior Hospital Doctors' Association had already been released to the press.

The **Chairman** said that it had. He had already stated that the whole question of the statement by the Chairman of the Central Committee for Hospital Services (Mr. Langston) and what action had been taken might be discussed on the Annual Report of Council on hospital and consultant services.

Constitution (Resumed)

Representative Body and Autonomous Bodies

Dr. I. M. **Jones** (Sunderland) moved: "That paragraph 28 of the Report on the Constitution of the B.M.A. (Doc. A.R.M. 8) be amended by the addition of the following words: 'provided such reference back is passed by at least a two-thirds majority of the Representative Body.'"

(Paragraph 28 read as follows: "We therefore propose that the Representative Body should normally receive and approve reports on the work of the autonomous bodies, but when it wishes to exercise its right to disagree in any respect it would normally refer the matter back to the autonomous body before reaching a final decision.")

Dr. Jones said it was important that the Representative Body should have the right to review any issue which had previously been determined by the autonomous committees. But it was not right to waste the time of the Representative Body unless there was an opinion contrary to that of a sectional interest. The need to get a two-thirds majority would ensure that there would be no unnecessary debates in Representative Body, yet its absolute sovereignty would be retained.

Dr. **Noble** said that it was entirely for the Representative Body to decide what sort of majority it would wish for the reference back of any motion. But he would ask one question: Supposing a motion was referred back by a simple majority of the Representative Body, what would be the attitude of the standing committee to that motion?

Dr. **Jones**, in reply, said he thought the sensible thing would be for the chairman of a standing committee to refer the matter as a proper reference to his committee. That was the procedure that had been adopted for many years. He did not think that invalidated the point that Dr. Noble had made.

The motion was carried.

Regional Councils

Dr. C. O. **Lister** (Aldershot and Farnham): moved: "That Regional Councils should be composed of B.M.A. members only."

He said that the Association must surely have learnt that unity was its strength. Anything that it had got from the Government in the last few years had been obtained by unified pressure. Yet in the new constitution it was proposed that one of the major debating chambers, the regional council, should operate with non-members. The fact that representatives were gathered together as members of the British Medical Association was a token that they had a common purpose in meeting and in joining the Association. If there were august persons who would like to sit on regional councils they should join the Association. Otherwise they were not like-minded and the B.M.A. could do without their counsels.

Dr. K. A. WOOD (Portsmouth) said he opposed the motion. He did not exclude the possibility of restricting membership of regional councils to the B.M.A. members only, but the new constitution must be got off the ground. It was the duty of the Association to ensure that regional councils were fully functioning and recognized throughout the regional area as a body that was unifying opinion.

Dr. W. D. GRAY (Liverpool) said it would be possible for all those appointed to regional councils from outside bodies to be non-members of the Association. Liverpool thought that was wrong.

Asserting that the B.M.A. did far too much for those who were not members, thereby devaluing the privilege of membership, Dr. J. H. MARKS (Barnet) said the Association's first duty was to protect and advance the interests of its members. If others benefited indirectly that was their good fortune. Non-members were already represented in negotiations, and it was unnecessary to make more arrangements for them at regional level.

Dr. W. H. N. ANGUS (Southampton) said if regional councils were to do the job they were meant to do—to collate opinion in the regions and to send informed opinion to the centre—they must, unfortunately, allow non-members to be on them.

Replying to the debate, Dr. LISTER said: " Let us take some measure of pride in our membership. It is difficult enough these days to give answers to the non-member who asks, 'What do I gain from joining the B.M.A. that I do not already have ? ' "

The motion was carried.

Divisional Secretaries

Dr. J. A. RIGBY (Worcester and Bromsgrove) moved: " That divisional secretaries should have a seat on the proposed regional council."

Dr. Rigby thought the divisional secretary was a person who might well benefit from being a member of the regional council, and the regional council might also benefit. It was of value for the secretary to discuss things with other secretaries and other people in such places as regional councils.

Dr. G. CORMACK (Newcastle upon Tyne) asked what, in view of the previous motion, the Chairman of the Organization Committee would propose as the make-up of a regional council, as in some areas it would be extremely difficult to make it up from members of the Association.

Dr. NOBLE replied that, looking at the specimen constitution of the regional council, he thought it could be managed. There might be areas where there would be difficulty. Replying to the debate, Dr. Noble said that in his view there was not a case for extending what was a fairly large regional council by adding divisional secretaries.

Dr. RIGBY, in reply, disagreed with Dr. Noble. According to the specimen constitution a Division would have to elect its secretary as its representative on the regional council.

The motion was lost.

Dr. D. S. STRACHAN (Cleveland and Middlesbrough) moved: " That this Representative Body reaffirms its decision of 1966 to establish a regional council in a few selected areas for an experimental period, and that no reorganization be implemented, contingent on and in anticipation of the success of such an experiment."

Dr. Strachan said that his Division wondered whether the regional hospital board area was the ideal one for the regional council. While accepting the need for experiment, it was anxious to ensure that no reorganization in other areas took place on the assumption that the present experiment was a success. That was prejudging the issue.

Dr. NOBLE accepted the motion, and it was carried.

Dr. R. L. LUFFINGHAM (East Yorkshire) moved: " That, with reference to paragraph 16 of the Annual Report of Council, no regional council shall be set up unless and until a majority of the Divisions it would serve call for this."

Dr. Luffingham said that the substance of the motion was the policy of the Council but had not appeared in its Annual Report. The aim of the motion was to secure the Representative Body's ratification of the Council's decision. It was ridiculous to have a regional council if the Divisions did not want it.

Mr. G. E. MOLONEY (Council), supporting the motion, said that the regional councils were likely to be highly expensive. A great deal of the local B.M.A. work was done for nothing by medical workers. There had been a suggestion that the full-time medical secretaries would help in the recruiting drive, but that was not the correct way to obtain new members. New members were obtained in the old way. " By your works ye shall be known," suggested Mr. Moloney.

Dr. RONALD GIBSON (Chairman of Council) emphasized the difference between a regional council and a regional office, one of which was administrative and the other organizational.

Dr. LUFFINGHAM, in reply, pointed out that the financial report received by the Council had made it plain that a regional office would be financially viable only if the medical secretary was also secretary of the regional council.

The motion was carried.

Representative Body

The following motion in the name of East Yorkshire, " That the proposed new By-law 30 (*a*) be amended by the deletion of the words 'in Great Britain and Northern Ireland,' " was, by leave, withdrawn.

Size of Representative Body

Dr. R. L. LUFFINGHAM (East Yorkshire) moved: " That, with reference to paragraph 208 of the Annual Report of Council, the Chairman of Council, or his nominee, be asked to explain to this Meeting why the figures contained in paragraph 51 of the Report on the Constitution (*B.M.J.*, 26 November 1966) relative to the size of the new Representative Body are so inaccurate."

Dr. Luffingham observed that Dr. Noble in his opening statement had said that the figures had been " guessed." It was criminal to make a change in the size of the Representative Body based on estimated figures.

Dr. NOBLE said that the figures he had quoted were based on an estimate over many previous years of the Representative Body. If they were underestimated, he took full responsibility and humbly apologized to the Meeting. By reason of all the variations he had himself already given the figures could not be more than an estimate, and it could not be known until next year how many of the future members of the Council and how many chairmen of standing committees would be elected representatives.

Dr. LUFFINGHAM said that the Chairman of the Organization Committee had now accepted that the figure was wrong. An estimate that was out on such an important issue must invalidate the conclusions upon which the figures were based. Was there to be a smaller Representative Body or not ? He submitted the answer was in the negative.

The motion was carried.

Dr. A. M. MAIDEN took the chair.

Dr. E. TOWNSEND (Cornwall) moved: " That under the new constitution of the Association the size of the Representative Body should not be greater than 400."

He said that so long ago as 1952 in Dublin there had been a motion that the Representative Body be reduced in size, which had not been accepted. There were three kinds of representative: the man who was knowledgeable, interested, and capable of putting a case ; the man who was willing and moderately competent ; and the man who was impressed to complete the quota. Good debates were important and good debates depended to a great extent on good representatives. They could well do without those who were impressed to complete the quota.

The argument against reducing the size of the Representative Body was that attending it had an educational value. The educational value would be greater if the turnover of members who attended the meetings was increased. The majority of members who had made maiden speeches in the last few days had made a valuable contribution.

Dr. G. N. MARSH (Stockton) said that under the existing constitution a large Representative Body was needed. Without regional councils the only place a Division could express its opinions was through its own representative. Many of those views could now be aired at regional council level. A smaller Representative Body, composed of enthusiastic and informed members who had had to compete for their place, would be a more effective and efficient mouthpiece of the Association. He supported the motion.

Dr. R. P. HENDRY (Rugby) said the Meeting should be aware of the implications of the motion. It proposed an overall strength of 400. That would allow for only 280 divisional representatives. Very few of the constituencies would have two representatives, so that they could not arrange proportional representation. He was against the motion.

Educational Value

Mr. H. H. LANGSTON (Council) said that Dr. Townsend was wrong in saying that the purpose of having a large Representative Body was merely educational. With proportional representation under the new constitution, the Representative Body would fulfil a useful function in providing a check on what committees did. Only a body of reasonable size could produce informed opinion from the periphery to provide that check. He therefore hoped that the arbitrary figure of 400 would not be accepted.

Dr. TOWNSEND, in reply, pointed out that he had said that an argument against reducing the Representative Body that was often produced was that it was of educational value. He had then said it would be of much more educational value if it consisted of representatives who were interested. It could only be a check if it consisted of informed members. He was asking for fewer but more informed and interested members. He emphasized that the motion was linked with other motions asking for a considerable reduction in Council, and this would affect the whole picture.

The motion was lost.

(The report will be concluded next week. Photographs by Photo Prints (Bristol) Ltd.)

Hospital Junior Doctors

On the morning of Saturday, 8 July, the Annual Representative Meeting at Bristol suspended its standing orders to enable Mr. H. H. LANGSTON to make the following statement.

Statement by Mr. Langston

"At the request of the Junior Hospital Doctors' Association, representatives of the British Medical Association met representatives of the J.H.D.A. on 29 June in order to hear the views of the J.H.D.A. about representative machinery for hospital junior doctors. A frank exchange of views took place, and the B.M.A. representatives undertook to examine the suggestions of the J.H.D.A. and to meet again in due course. On 30 June and on 6 July the Chairman of the J.H.D.A. wrote to the B.M.A. and expressed anxiety to continue the talks as soon as possible. In his second letter, the Chairman of the J.H.D.A. wrote:

"'Both sides realize that they must go back to their respective committees for a mandate to examine the problem jointly in more detail. We hope this will be done as a matter of urgency because, as we have stated in the press, unity within the profession is important in the long run. . . .

"'I would like to apologize in advance for the tone, but not the content, of some tendentious criticism in the second issue of *On-Call* about recent negotiations between the B.M.A.'s negotiating group of nine and the Ministry. I hope you will accept that because discussions may continue between our two associations, my executive would have toned down the presentation of this criticism had the newspaper not already been in press.'

"Notwithstanding these statements, a representative of the J.H.D.A. yesterday distributed copies, within this building in which the B.M.A. Representative Meeting is being held, of the second issue of the J.H.D.A. newspaper *On-Call*. This issue, like the first, contains statements and insinuations about the B.M.A., and about individual B.M.A. leaders, which go far beyond the bounds of what is acceptable or tolerable in public discussion and debate. In this atmosphere, we have regretfully come to the conclusion that no useful purpose would be served by continuing discussions with the J.H.D.A. and the Chairman of the J.H.D.A. has been so informed."

The Representative Body debated this statement, and a report of the debate will be printed next week. At its conclusion the Meeting resolved as follows:

"This Representative Body deprecates the continued attack on the B.M.A. leaders by the J.H.D.A., and offers its sympathy and support to all concerned. Nevertheless, this Meeting is of the opinion that talks should continue between the British Medical Association and the Junior Hospital Doctors' Association, provided that the Chairman of the Junior Hospital Doctors' Association disavows the actions of whoever distributed their publication."

The motion was carried by 224 votes to 61.

Unqualified Apology

During the afternoon the CHAIRMAN reported to the Representative Body that the Junior Hospital Doctors' Association had issued the following statement to the press:

"Today, after an emergency meeting of the officers of the Junior Hospital Doctors' Association Executive, Dr. Briggs, the Chairman, undertook to send to Dr. Gibson, Chairman of the B.M.A. Council, an unqualified apology for the distribution of copies of the second issue of *On-Call* at the B.M.A.'s Annual Representative Meeting at Bristol.

"He said that the J.H.D.A. Executive was in duty bound to send copies of the newspaper to its 4,200 members, but that its distribution at the B.M.A.'s A.R.M. was unfortunate and provocative, in view of the present discussions being held between the two Associations.

"He expressed the hope that meetings would continue between the two Associations in a friendly and open-minded atmosphere, and that the upset provoked by the criticisms in the second issue of *On-Call* would not obscure the major issue to be decided at present.

"Dr. Briggs said: 'It remains in the interests of the B.M.A. and the J.H.D.A. to continue negotiations on the matter of hospital junior doctor representation within one organization. Unity must come.'"

Dr. RONALD GIBSON announced that he had authorized the issue to the press of the following statement:

"The B.M.A. welcomes the spirit with which the J.H.D.A. has responded so quickly to the resolutions adopted by the R.B. this morning. The way is now clear for discussions to be resumed."

Representatives' Dinner

The Representatives' Dinner was held at Bristol on 6 July. Presiding over a company of some 500 representatives and their ladies at the Grand Hotel, Dr. A. N. MATHIAS, Chairman of the Representative Body, paid tribute to Dr. S. NOY SCOTT on his retirement from the Representative Body after 35 years continuously as a representative and as senior member of the A.R.M. Agenda Committee.

Dinner was followed by dancing until 1 a.m.

Hospitality

A German doctor living in Freiburg im Breisgau wants a girl of not less than 18 years old to stay *au pair* with his family from September for 6 to 12 months.

A French doctor living in Bayonne would like his daughter aged 22 years to stay *au pair* with a British medical family in or near London for three to four months from September or October.

A French doctor's son aged 17, living in Tiercé (Maine-et-Loire), would like to stay with a British medical family in August. In exchange the family would be pleased to receive a British boy of similar age in July or September.

An Italian doctor living in Rome would like his 14-year-old son to stay with a British medical family for four weeks in July or August. In exchange the doctor would be pleased to receive a British boy of similar age for four weeks at a convenient time.

An Austrian doctor living in Graz would be pleased to receive immediately a British doctor's daughter, aged about 14 years, to stay with her family for one month. In exchange the doctor would like her own daughter, aged 14, to stay with the British girl's family next summer.

Would anyone who is interested please get in touch with Dr. R. A. Pallister, Medical Director, International Medical Advisory Bureau, B.M.A. House, Tavistock Square, London W.C.1.

Central Consultants and Specialists Committee

The Central Consultants and Specialists Committee met on 29 June, with Mr. H. H. Langston in the chair. A report of the first part of the meeting, in which the Committee discussed its composition and that of the Joint Consultants Committee, was printed last week (Supplement, *8 July, p. 21*). *A report of the remainder of the proceedings is printed below.*

Distinction Awards

The Committee considered a letter from Mr. N. G. C. HENDRY about the distribution of distinction awards. The subject had been discussed with depressing frequency, he wrote. It had been taken to the Review Body, who indicated that it was a matter for the Distinction Awards Committee. The Distinction Awards Committee had indicated that it was a matter for the Review Body. In these circumstances it seemed reasonable to Mr. Hendry to bring facts to light as they became available, and he sent the following most recent figures from the Scottish Home and Health Department, showing the position of Scottish regional hospital board consultants relative to those with honorary contracts:

Category of Award	R.H.B.	Honorary	Total
A+	3 (11)	10 (2)	13
A	16 (34)	24 (6)	40
B	88 (108)	37 (17)	125
C	204 (215)	47 (36)	251
Total ..	311 (368)	118 (61)	429

The numbers in brackets indicated what the figures would be if distribution was proportional to the actual number of consultants in the two categories.

The Committee thought that this was an important matter and that it should be discussed at its next meeting, for which a memorandum could be prepared.

Ten-session Week

Dr. W. ESMOND REES spoke of a letter from the Welsh Regional Consultants and Specialists Committee expressing concern that abolition of the difference between part-time and whole-time service did not seem to have been considered by the C.C. and S. Committee. At a time when the Council of the B.M.A. was expressing its determination to expand private practice it seemed rather odd (the letter continued) that no steps were being taken to ensure the survival of private consultant practice. At many small centres it was not economically feasible for a young consultant to opt for maximum part-time practice, because the amount of private practice did not make up for the difference between part- and whole-time salary. The community in those areas was denied facilities for private consultation.

The Welsh Committee was convinced, the letter stated, that whole-time practice should be abolished in favour of a sessional contract and that preferably this should be on a "10/10ths basis." The essential point was that those who did the maximum number of sessions should not be precluded from private practice. The Welsh Committee saw no reason why this arrangement should not apply to all doctors in the hospital service except for those in preregistration posts.

Dr. Rees said there might be arguments about the 10/10ths method, but it seemed to the Welsh Committee that a whole-time doctor was employed 24 hours a day seven days a week, and he had no spare time. When the contracts were drawn up no allowance had been made for emergency work in calculating the matter of sessions.

The CHAIRMAN commented, on the last point, that emergency work should be taken into account. But if that was not the case, and no allowance had been made for emergency work in a substantial number of cases in Wales, the matter would be taken up.

Dr. T. D. CULBERT supported the proposals of the Welsh Committee. He hoped the matter would not be shelved. If adopted in their entirety the proposals would remove many of the anomalies in the employment of senior medical staff. Equally important, it would apply to the hospital junior staff, and he hoped that their representatives would speak on it. The sooner the change came the better it would be for the hospital service and for the medical staff.

No Strong Support

The CHAIRMAN explained that a scheme for dividing the whole-time week into 10 sessions, or half-days, had been circulated to regional committees in 1966, and there had been no strong support for a change. Mr. H. G. HANLEY believed that doctors did not understand the proposal. He hoped the Committee would discuss it and give a lead.

Mr. R. D. ROWLANDS was in favour of a 10-session week, but he could not support the scheme when the number of hours per week envisaged in the calculation was 40. Consultants were paid on an hourly not a sessional basis. If they now worked, say, 20 hours, that was divided by 3½. If the basis was a 40-hour week the payment would be reduced. He realized that that was compensated for in the draft scheme because there would be a rise in salary scale, but he did not think the Review Body would agree to any increase in salary scale, so in the long run consultants would lose. His regional committee supported the 10-session week and it thought the long-term aim should be a 35-hour week but in the short term it would be best to accept a 7½-hour day and 37½-hour week.

When the CHAIRMAN suggested that another document should be prepared and sent to regional committees, Dr. R. MAYON-WHITE said that it would probably prove fruitless. Many regional committees were not in favour of a change, and he was disappointed that they did not support the proposal more enthusiastically.

The Committee agreed that a document should be prepared and sent to the new Negotiating Committee.

Dr. I. G. JONES asked whether it was a matter for the Review Body or one that could be discussed in negotiations with the Ministry? The CHAIRMAN replied that he thought it was a matter which would go to the Review Body for pricing.

Inspection of Residential Accommodation

It was reported that, in response to resolutions of the A.R.M., 1965, regional committees had been asked whether they would arrange something like an annual inspection of residential accommodation in each of the hospitals in their region, with a view to reporting any in which the conditions were so bad that vacancies in them should not be advertised. Most of the committees had not been in favour of an annual inspection, but all had been prepared to look into any complaint from a member of the hospital junior staff.

The CHAIRMAN said that it was to everybody's advantage to know which accommodation was satisfactory and which was unsatisfactory accommodation. He hoped that regional committees would be prepared to undertake inspections.

Dr. CULBERT pointed out that in a region like Manchester it would be a full-time job. Dr. D. GUTTMANN was in favour of the matter being referred back to regional committees, and he asked that some guidance should be given on the sort of things that should be looked for in an inspection. There was a difference between listening to complaints from junior staff and actually inspecting.

Mr. H. A. KIDD said that an inspection of accommodation would not help the person occupying it. An approach should be made to the Ministry to discuss the matter. If the accommodation was substandard the charge for it should be substandard. That was the best way to bring influence to bear.

Hospital Medical Staffs Defence Trust

The Committee, meeting as the trustees of the Hospital Medical Staffs Defence Trust, received a report that, on a recommendation of the C.C. and S. Committee (Scotland), £600 had been donated from the Scottish Defence Trust funds to the Hospital Medical Staffs Defence Trust in respect of the year 1966.

Mr. L. DOUGAL CALLANDER, in presenting the Financial Statement, noted that the income had been slightly smaller last year. At the end of each year a good many bankers' orders were stopped owing to consultants retiring. Expenditure had exceeded income in the year 1966, and that was because of considerable expenses for the conference.

Report of Executive Subcommittee

The Committee considered a supplementary report from its Executive Subcommittee on constitutional matters affecting the Committee and associated bodies.

The Committee adopted certain recommendations of the Executive Subcommittee on the membership, administration, and standing orders of the Hospital Medical Staffs Conference.

Dealing with the Subcommittee's report on the Hospital Junior Staffs Group, the CHAIRMAN said that it had been thought to be important that the revised constitution of the H.J.S. Group (which the Committee had already approved in principle) should be before the Council for approval at its last meeting (*Supplement,* 8 July, p. 15). The Council had approved it.

The revised constitution of the H.J.S. Group was formally approved by the Committee.

The Committee also approved the following recommendations put forward by the S.H.M.O. Group's Executive Committee for the reform of the Group's constitution.

(1) That one S.H.M.O. Group Committee should replace the existing Group Council and Executive Committee.

(2) That the new committee should consist of 18 members, one from each region in England and Wales, two from Scotland, and one from Northern Ireland.

(3) That the Committee should normally meet before each regular meeting of the Central Consultants and Specialists Committee, but the chairman should cancel the meeting if there is insufficient business.

The Committee also approved the addition of a fourth item concerning the co-option of not more than two members, at the suggestion of Dr. E. GREY-TURNER, Deputy Secretary, speaking on behalf of the S.H.M.O. Group.

The Committee noted that the Executive Subcommittee had considered the revised report on the constitution of the B.M.A. (*Supplement,* 26 November 1966, p. 204), and that a motion had been included in the Agenda for the A.R.M. which, if carried, would ensure that both senior and junior hospital staff could be elected as representatives to the Representative Body.

Dr. E. A. HARVEY-SMITH thought that provision for the election of one representative from the H.J.S. Group from each region should be written into the constitution. Dr. H. GLYN JONES disagreed on the ground that it would make the constitution tremendously complex.

After a short discussion the Committee agreed to support the motion in the terms set out.

Work of Joint Consultants Committee

The CHAIRMAN reported on the work of the Joint Consultants Committee, the negotiating group, and of Whitley Committee B.

Dr. HARVEY-SMITH said that it seemed that the Ministry of Health was anxious to get away from any mention of the review of hospital medical staffing that came after the Platt report. It would, he thought, be foolhardy for the profession to allow the Platt review to be lost sight of. It was the only objective study that had been made.

Despite the excellent evidence given to the Review Body about the extra duty allowance, that had been turned down. It was said that work load had been taken fully into account in the last award.

The CHAIRMAN said that there was every intention of pursuing that matter so far as possible. He did not think it was true to say that the Ministry had thrown out the Platt review. It had recently admitted that there had been a failure to reach the median of the staffing requirements set out in the review. This was a matter which must be hammered at continually. Mr. Langston said his own feeling was that, particularly in some branches of medicine, not enough senior registrar posts were being created to enable the consultant vacancies to be filled. The tendency seemed to be to maintain the senior registrar establishment at a level required for the existing number of consultant posts and not to take into account sufficiently the requirements stated in the Platt report.

Mr. J. R. BLACKBURNE asked whether the instructions to hospital authorities contained in Ministry of Health circulars were mandatory.

The CHAIRMAN replied that hospital boards were asked to implement them straight away if they could. They were mandatory in the sense that where they could be implemented they had to be, and if they could not be the board had to explain why.

The Committee agreed to support a proposal that the new title for the medical assistant grade should be the "Assistant Grade," and that individual doctors should be known as "assistant surgeon," "assistant physician," etc.

At this point Mr. LANGSTON had to leave on urgent business, and Mr. W. S. LEWIN took the chair.

Interim Negotiating Subcommittee

The Committee received a report that the interim Negotiating Subcommittee had held its first meeting on 13 June, when the main items discussed were Categories I and II of the "Terms and Conditions of Service of Hospital Medical and Dental Staff." The Subcommittee, at a subsequent meeting with Ministry officials, had pressed strongly the view, which was set out in paragraph 50 of "An Appraisal of the Hospital Service" (*Supplement,* 17 July 1965, p. 70), that any services not directly concerned with the prevention, diagnosis, and treatment of illness should be regarded as outside the scope of the N.H.S. and transferred to Category II. A small working party of representatives of the Subcommittee and the Ministry were to meet to work out the details of any changes.

Medical Assistant Grade

The Committee considered a resolution from the S.H.M.O. Group Executive Committee stating its view that in the event of any future pay award to medical assistants the existing differential between the salary scales of the S.H.M.O. grade and the medical assistant grade should be maintained.

Dr. N. STRANG urged the Committee to support the resolution. He said there was no doubt that, with the close relationship between the salary scales of the medical assistant grade and the S.H.M.O. grade, S.H.M.O.s were becoming more and more associated with the medical assistant grade, despite previous assurances. There was a differential of only £125 at the top of the two scales.

The CHAIRMAN commented that the medical assistant grade was still in its formative years and it was likely changes would occur in the grade. Existing S.H.M.O.s had been given an undertaking that they could retain their name and seniority, and he did not think any Review Body would alter that. Dr. GREY-TURNER pointed out that the S.H.M.O. group wished to preserve the differential between S.H.M.O.s and medical assistants. The CHAIRMAN said that undoubtedly the committee would wish to support the resolution. But he had been rather nervous of talking about a differential in relation to a new group whose present salary scale might alter.

The Committee agreed to support the resolution.

New Consultant Posts

The Committee considered a report on new consultant posts. It pointed out that one of the major topics under discussion in the current "charter" negotiations was the profession's representations that immediate steps should be taken to attain the consultant establishment recommended as a result of the Platt reviews, and that there were many senior registrars, including some who had not yet completed the normal tenure of their posts, and also long-service registrars, who had the necessary experience to fill consultant vacancies immediately.

The profession had stated that there was a considerable number of well-trained registrars who had been held up in the grade by the bottleneck higher up. Discussions were taking place on the problems of time-expired senior registrars and of senior registrars who had only spent a short time in their present grade but had had long experience in the registrar grade.

The report stated that, as a first step towards alleviating this problem, hospital boards in England and Wales would, over the next few months, advertise additional consultant posts or readvertise unfilled consultant posts. Doctors with satisfactory training would not be excluded from consideration on the grounds that they had spent little or no time as senior registrars. Medical assistants would also be eligible to apply. There was no intention of lowering the standard of entry to the consultant grade, even temporarily, but it would allow every candidate to be judged by the advisory appointments committee on the length and quality of his training and experience, and on his other attributes, without being debarred by any rigid requirement about length of service in one particular grade. All the consultant vacancies that would be advertised were in posts requested in the Platt reviews.

The CHAIRMAN said that the negotiating group (the "Group of Nine") had been responsible for this interesting development.

Dr. GREY-TURNER emphasized that this was an important experiment.

Security of Tenure

The Committee considered a resolution referred to it by the Council from the Sutton Coldfield Division to the effect that the B.M.A. should press the Minister on the question of increased security of tenure for general-practitioner clinical assistants.

Dr. GREY-TURNER said that the proposal put to the Ministry had been that these doctors should be on a two-year contract in the first instance, and then renewable at seven-yearly intervals.

Mr. ROWLANDS thought that the doctors who warranted permanent tenure of office were those who had reached the medical assistant grade. Some of the clinical assistants were doing a short-term job for educational purposes. A number were earning high locum fees by filling casualty appointments and that type of post, which did not warrant permanent tenure of office.

Dr. H. L. LEAMING thought the Committee should be clear what was meant by a clinical assistant. He believed it was either a general practitioner who did two to three hospital sessions a week or a doctor who liked to help in hospitals and took the place of a house-officer on a part-time basis. In neither instance was security of tenure of more than six months necessary.

The CHAIRMAN said that general practitioners who wanted permanent posts would be likely in future to get part-time medical assistant posts.

Dr. A. N. MATHIAS (Chairman of the Representative Body) said that there were certain hospital jobs that had been graded for the last 18 years as clinical assistant posts.

Dr. BLACKBURNE said that if general practitioners gave up some of their practice commitments they wanted a more permanent contract. On the other hand, there were general practitioners who resented the fact that these posts were apparently held for any length of time by one doctor, and who wished them to be readvertised at frequent intervals. It was not always possible to make general practitioners medical assistants, since they might not have had the necessary training.

Mr. P. C. STEPTOE proposed, and Dr. J. W. WEDGWOOD seconded, a motion that the resolution should not be supported, and Dr. A. SKENE thought it would be wiser to note it. Dr. LEAMING said that the resolution could not be supported in its present form without further information.

The CHAIRMAN asked the Committee whether it would agree to a motion that, without further information, the Committee could not support a blanket increase in security of tenure for all general-practitioner clinical assistants.

The motion was carried.

Multiple Radiological Examinations

The C.C. and S. Committee decided to support the following resolution of the Radiologists Group Committee, and to refer it to the Negotiating Subcommittee:

> That the Central Consultants and Specialists Committee be informed that the Radiologists Group Committee considers that under the National Health Service (Pay-bed Accommodation in Hospitals, etc.) Regulations, 1953, the total of the charges levied by hospital authorities to Section 5 outpatients for multiple radiological examinations undertaken at the same visit are excessive. Multiple examinations undertaken at the same visit are by their very nature lower in cost to the hospital authority than if each examination were undertaken separately. The Radiologists Group Committee requests that the Ministry of Health be approached with a view to agreeing a formula for the compounding of charges for such multiple radiological examinations.

H.M. Forces

Major-General P. R. Wheatley, D.S.O., late R.A.M.C., has been appointed Honorary Surgeon to the Queen, in succession to Major-General R. A. Stephen, C.B., C.B.E., retired.

Appointments.—Wing Commander D. G. Jones (ear, nose, and throat duties, R.A.F. Hospital, Ely); Wing Commander J. D. Crowlesmith (senior medical officer, R.A.F. Wittering); Wing Commander H. D. Jones (anaesthetic duties, R.A.F. Hospital, Wegberg, Germany); Wing Commander J. P. McRory (deputy principal medical officer, Headquarters, Near East Air Force); Wing Commander L. K. Garstin (senior medical officer, R.A.F. Changi, Singapore).

ROYAL NAVY

ROYAL NAVAL RESERVE

Surgeon Lieutenant-Commander M. G. D. Davys, V.R.D., has been placed on the Retired List.

Surgeon Lieutenant H. G. K. Douglas to be Surgeon Lieutenant-Commander.

ARMY

Brigadier R. M. Johnstone, M.B.E., M.C., late R.A.M.C., to be Major-General.

ROYAL ARMY MEDICAL CORPS

Lieutenant-Colonel J. B. J. Mulvey has retired on retired pay.

Major E. R. Briant to be Lieutenant-Colonel.

Majors R. J. Givans and J. Monro have resigned their commissions.

TERRITORIAL AND ARMY VOLUNTEER RESERVE

ROYAL ARMY MEDICAL CORPS

Brigadier Sir John Bruce, Kt., C.B.E., T.D., has been appointed Honorary Colonel 205 (Scottish) General Hospital, R.A.M.C. (Volunteers) T. and A.V.R., in a new appointment.

Major G. Hall-Davies, Reserve of Officers, to be Major.

Association Notices

Diary of Central Meetings

JULY

19 Wed.	Joint Formulary Committee, 10.30 a.m.
20 Thurs.	Planning Unit, 5.30 p.m.
24 Mon.	North-west Metropolitan Regional Consultants and Specialists Committee, 5 p.m.
25 Tues.	Joint Consultants Committee, 10 a.m.
25 Tues.	Vocational Training Advisory Committee (G.M.S.C.), 2 p.m.
27 Thurs.	General Medical Services Committee, 10.30 a.m.

SEPTEMBER

22 Fri.	Planning Unit, 4.30 p.m.

Branch and Division Meetings to be Held

Members proposing to attend meetings marked ● are asked to notify in advance the honorary secretary concerned.

EASTBOURNE DIVISION.—At Beachy Head Hotel, Tuesday, 18 July, 7 p.m., dinner; 8 p.m., general meeting to receive report of representative to Annual Representative Meeting.●

KETTERING DIVISION.—At Hunting Lodge, Cottingham, Friday, 21 July, 8.15 p.m., buffet supper and cocktail party. Guests are invited.●

NORFOLK BRANCH.—At City Hall, Norwich, Thursday, 20 July, 4 p.m., annual general meeting followed by tea and tour of the City Hall. Ladies are invited.●

NOTTINGHAM DIVISION.—At 64 St. James's Street, Nottingham, Tuesday, 18 July, 8.30 p.m., ordinary meeting.

ROCHDALE DIVISION.—At Crimble Hotel, Monday, 17 July, 8.45 p.m., annual general meeting.

EAST ANGLIAN REGIONAL CONSULTANTS AND SPECIALISTS COMMITTEE.—At Bell Hotel, Thetford, Monday, 17 July, 8.30 p.m., meeting.

CONSULTANTS AND SPECIALISTS COMMITTEE: BIRMINGHAM REGION.—At Queen Elizabeth Hospital, Tuesday, 18 July, 5.15 p.m., meeting.

Meetings of Branches and Divisions

MORPETH AND BLYTH DIVISIONS.—Films presented by the Medical Insurance Agency were shown to members of the Morpeth and Blyth Divisions at a combined meeting on 28 June at Stannington, Northumberland. The programme consisted of travel documentaries on the Rhine and on Australia, and an informative film on insurance.

Branch and Division Officers Elected

PORTSMOUTH DIVISION.—Chairman, Dr. P. D. James. Vice-chairman, Mr. C. M. M. Murray. Honorary Secretary, Dr. J. A. Clark. Assistant Honorary Secretary and Treasurer, Dr. C. L. C. Arnold.

PRESTON DIVISION.—Chairman, Mr. R. S. Garden. Chairman-elect and Vice-chairman, Dr. J. G. Lord. Joint Honorary Secretaries and Treasurers, Dr. D. T. Irwin, Dr. W. M. Thomas.

READING DIVISION.—Chairman, Mr. C. Grimshaw. Vice-chairman, Dr. G. E. Mitchelmore. Honorary Secretary and Treasurer, Dr. T. J. Nokes. Assistant Honorary Secretary, Dr. O. Caiger Smith.

REIGATE DIVISION.—Chairman, Dr. T. H. Bingham. Chairman-elect and Vice-chairman, Dr. L. S. P. Divers. Honorary Secretary and Treasurer, Dr. K. R. Hughes. Assistant Honorary Secretary, Dr. R. G. Hornung.

ST. LUCIA BRANCH.—President, Dr. R. E. M. Lees. Honorary Secretary and Treasurer, Dr. B. K. Sil.

SUTTON COLDFIELD, LICHFIELD, AND TAMWORTH DIVISION.—Chairman, Mr. F. R. Hurford. Chairman-elect, Dr. A. R. Elsom. Vice-chairman, Dr. G. Hoyle. Honorary Secretary, Dr. E. C. Raybould. Honorary Treasurer, Dr. A. Parkes.

WAKEFIELD, PONTEFRACT, AND CASTLEFORD DIVISION.—Chairman, Dr. A. Reeves. Vice-chairman, Dr. J. McRobert. Honorary Secretary, Dr. H. Watson. Honorary Treasurer, Dr. L. J. Burns.

Correction

In the report of the meeting of the General Medical Services Committee (*Supplement*, 8 July) Dr. C. J. Wells was wrongly reported (p. 20) as speaking on the subject of information to hospitals.

British Medical Journal Supplement

LONDON SATURDAY 22 JULY 1967

CONTENTS

Annual Representative Meeting - - - - - - 69
Proceedings of Council - - - - - - - - 98
Annual General Meeting - - - - - - - - 98
Extraordinary General Meeting - - - - - - 98
Adjourned Annual General Meeting - - - - - 98
H.M. Forces - - - - - - - - - - 99
Annual Meeting Religious Services - - - - - 100
Association Notices - - - - - - - - - 100

British Medical Association

Annual Representative Meeting

The Annual Representative Meeting of the Association met at Bristol on 6, 7, 8, and 10 July, under the Chairmanship of Dr. A. N. Mathias. A report of the first part of the proceedings was printed last week. Printed below is an account of the remainder of the Meeting.

Third Day: Saturday, 8 July (Continued)

Junior Hospital Doctors' Association

Dr. H. GLYN JONES (Bromley) moved the suspension of Standing Orders.

He reminded members that earlier Mr. H. H. Langston had made a statement about negotiations with the Junior Hospital Doctors' Association (15 July, *Supplement*, p. 65). That statement had gone to the press. Unless anything arising out of it was discussed now, and urgently, what was said by the Representative Body on the matter would not reach the evening papers and would not reach the daily press until Monday.

There were those who deplored the statement. (Applause.) It had referred to "we"—"We have regretfully come to the conclusion that no useful purpose would be served by continuing discussions with the J.H.D.A. and the Chairman of the J.H.D.A. has been so informed." The statement did not even make clear who "we" meant, said Dr. Glyn Jones. He doubted whether "we" necessarily meant the Representative Body of the Association.

The motion to suspend Standing Orders was carried.

Dr. A. N. MATHIAS resumed the chair.

Dr. A. K. THOULD (Cornwall) regretted having to make his maiden speech to the Representative Body in disagreement with Mr. Langston, but he felt, as did the rest of the representatives of his constituency, that the matter was of considerable importance. They strongly disagreed with Mr. Langston's statement.

Dr. Thould said he spoke as a young consultant of some two years' standing. He was therefore well aware of the problems and frustrations of junior medical staff in hospitals. He thought that they had a case. The B.M.A. had not in the past been as thoughtful and considerate of their problems as it should have been. He thought that the Association was now reaping the rewards of past neglect, because the anger and frustration of these young people had boiled over and they were, in the manner of young people, a little more outspoken than they should be. Their rudeness was unforgivable and should not be allowed to continue, but he thought that for a senior body to break off negotiations with a young embryo group, who were angry because they were frustrated, was a mistake. (Applause.)

He asked Mr. Langston seriously to reconsider his statement. In particular, Dr. Thould said he thought it was unfortunate that it had been released to the press before the Representative Body, which was in session, had an opportunity to discuss it. (Applause.)

Debate on Statement

Dr. B. D. MORGAN WILLIAMS (South Warwickshire) proposed the following motion: "That this Meeting is of opinion that talks should continue between the British Medical Association and the Junior Hospital Doctors' Association."

Dr. R. L. LUFFINGHAM asked what majority would be required to pass the motion, and the CHAIRMAN ruled that a simple majority would be needed.

Dr. MORGAN WILLIAMS said that the statement issued to the press was a hasty, not very sensible reaction to a somewhat over-exuberant youthful organization. It was a shocking move, and he believed the Meeting should cancel it.

Dr. H. GLYN JONES (Bromley) said it was essential that the B.M.A. should continue these negotiations. A large body of junior doctors believed, rightly or wrongly, that the B.M.A. did not represent them. Great criticism had been made of what was in *On-Call*. Certainly there were points that were a little unfortunate; nevertheless there was nothing that was defamatory. There were rhetorical questions asking whether the negotiators could be trusted on behalf of the junior staff. That kind of comment was legitimate in a newspaper. There were references to amateur negotiators, but the question whether the profession should have professional negotiators had arisen before. It was quite true that the word "amateur" had not been used in a polite way, and there were rather snide remarks about "unelected representatives" who, in fact, were elected representatives but perhaps not elected by a very representative body of people. These were not very wise remarks to be made at a time when the Junior Hospital Doctors' Association was hoping for discussions with the B.M.A., but they were no more than that. There was nothing in the article to which the Association or the people referred to could take umbrage. He hoped the negotiations would continue.

Dr. D. HOOKER (Cornwall) said it was unfortunate that the B.M.A. should have taken such an undemocratic, sharp, sudden action. The youth in the medical profession had for a long time thought that Auntie B.M.A. moved slowly and was not very interested in them. It had been true, but nowadays in Divisions a really sterling effort was being made to contact the young members. He believed that the B.M.A. had begun to win the young men, but the action taken earlier that morning could spoil all that work.

Manner of Doing

Mr. M. J. GILKES (Brighton and Mid-Sussex) said he wanted the discussions with the junior doctors to continue. It would have been perfectly possible to have presented the motion with overtones of censure, but he did not wish to do that. Nevertheless it must be underlined that it was not what was done but the way in which it was done which was vitally important.

Remarking "that these young men were not bad chaps," Dr. A. ELLIOTT (Redbridge) said surely the B.M.A. was adult enough not to take offence about some silly remarks in a schoolboy sort of paper. Dr. G. S. R. LITTLE (Council) said he was quite sure that these young doctors did not want to perpetuate the mistakes that had been made. They had their professional life in front of them, and the Meeting should take into account the circumstances of their anger.

Speaking as Vice-Chairman of the B.M.A.'s Hospital Junior Staffs Group, Dr. J. R. Bennett (Council) said the Meeting must get some sense of proportion. Instead of taking another opportunity to have a go at the C.C. and S. Committee, the junior doctors should remember what the position was. The Hospital Junior Staffs Group contained many doctors who had laboured and battled for years within the democratic machinery of the B.M.A., with the backing of the Chairman of Council, the Organization Committee, and the C.C. and S. Committee. They had achieved a position in which they were able to play their part in the Association and in the negotiations on behalf of their colleagues. They were doing that now with the authorities.

"This has been achieved not because of splinter groups but despite them, and despite constant, unremitting attacks of an unpleasant kind which have continued for a space of nearly two years now," asserted Dr. Bennett. He went on to say there was an enormous amount of sympathy for this group of what some imagined were innocent young men. The fact was the B.M.A. had known about the Junior Hospital Doctors' Association for nearly a year, though most representatives had had very little contact with them, and few had even seen the edition of *On-Call* which had been distributed the day before. That distribution yesterday was "too much."

Chief Officers

The Chairman said he had received a communication asking Mr. Langston to interpret the word "we" in the statement.

Mr. H. H. Langston said the chief officers felt they had had to take urgent action about the document, and the "we" referred to the Chairman of Council, the Chairman of the Hospital Junior Staffs Group Council Executive Committee, and himself.

Dr. E. A. Harvey-Smith (Chairman of the Hospital Junior Staffs Group) said the last thing he wanted was to break relations with any hospital junior staff, but "one could not negotiate or discuss when, every time one left the room, another publication was made in which all one's work was thrown back into one's face." He wanted to see a strong Hospital Junior Staffs Group within the B.M.A. That was the only place for it. The Hospital Junior Staffs Group of the B.M.A. had increased its force in negotiation over the past three or four years. What the Junior Hospital Doctors' Association was asking was that junior staff should have an autonomous standing committee of the B.M.A. This might be an excellent idea, but if so it should be discussed and put forward to the Council and to the A.R.M. next year. There should not be fighting in the press. Negotiations should continue, but not in the prevailing atmosphere.

Dr. Joan Chappell (Council) said she admired the independence and energy of the Junior Hospital Doctors' Association, but those who had read the leaflet would agree that some of its publications had been over-enthusiastic and not professional. A junior member of the Council had been named in the last publication, and she thought an apology should be a preamble to renewed negotiations. It was difficult to negotiate and go forward to solve serious problems in an atmosphere of damaging and vituperative comments.

Dr. M. R. Sheridan (North Middlesex) moved an amendment: "That this Meeting asks for a retraction of the statement made by the Chairman of the C.C. and S. Committee, and that negotiations with the Junior Hospital Doctors' Association must be allowed to continue."

He said the Junior Hospital Doctors' Association had not the finesse or aplomb of the B.M.A., with whom it was negotiating. Mr. Langston and others had got together to produce a statement, forgetting that the Representative Body was the parliament of the Association.

Flimsy Excuse

Dr. A. Elliott (Redbridge) supported the amendment. He said the three chairmen had decided to make a statement and break off negotiations because of a publication. He thought it was a disastrous state of affairs for the young doctors of the country if such a flimsy excuse was used to break off negotiations.

Dr. Ronald Gibson said he had spent a major part of his career in the Association being concerned with the affairs of younger doctors. The B.M.A.'s Hospital Junior Staffs Group and Dr. Harvey-Smith worked extremely hard and had done very well. It was necessary only to consider the changes there had been in the constitution, and the fact that the B.M.A. was now negotiating on behalf of the young doctors with the Minister. The whole debate had centred on the fact that the Meeting should support a splinter group and not the B.M.A.'s own group. His thesis from the beginning had been that the B.M.A. should support its own group.

What had been done had not been a hasty decision. The B.M.A. had not taken any action on the first edition of *On-Call* because it wanted to do everything it could to help. The Junior Hospital Doctors' Association had asked for a meeting, and that had been agreed to. The B.M.A. had gone to great lengths to help. It had had discussions, and he had received a letter from Dr. Briggs, Chairman of the J.H.D.A., the day before saying that he had been happy with what had taken place. The B.M.A. had never abused the J.H.D.A. But facts might as well be faced: those innocent simple people had had everything beautifully timed for the Representative Body. The B.M.A. would go on talking provided the Junior Hospital Doctors' Association would act like gentlemen, as the Association had behaved.

Speaking to the amendment, Mr. H. H. Langston said that if it was suggested that he and his colleagues who had produced the press statement should be prepared to go on, without any retraction or any form of apology from the J.H.D.A., he could say unequivocally that the three of them would not be so prepared. "We are not closing the door to further discussions," he said. "But so long as this document is in existence, without any apology or any statement, we cannot go on."

Dr. G. R. Smith (Birmingham) said that the Chairman of Council and Mr. Langston were guilty of symptomatic treatment of the worst type. He added: "To make an issue over this document is to ignore the disease that has produced the document." He had looked at the document and had found nothing offensive in it to anyone of any stature. If the B.M.A. negotiators could not take criticism they should not be negotiating. The fact remained that had it not been for the young doctors forming their own association the British Medical Association would not have moved with the speed that it had moved in producing a hospital doctors' "Charter."

Greatest Asset

Dr. D. R. Cook (Camden) said he greatly regretted that the statement had been issued. "Here we were, doctors of all kinds in greatest peril, our greatest asset being unity, and we have issued a statement suddenly and arbitrarily which was bound to alienate the good will of a section of our youngest doctors." There was a tradition in this country of robust political argument.

What was the authority of the statements that had been made? Were they made with the authority of the J.H.D.A.'s negotiators? Might it not be that the Meeting would have to save those negotiating for the young hospital doctors from their friends? "Do not let us issue a statement which means the end of the road," he concluded.

Dr. M. R. Sheridan, in reply, said that everyone could understand the reasons that had produced the statement. It was still not good enough. Dr. Smith had mentioned membership. The B.M.A. could not afford just to drop off the Junior Hospital Doctors' Association and say, "We have regretfully come to the conclusion that no useful purpose would be served by continuing discussions. . . ."

The amendment was lost.

Dr. R. L. Luffingham (Council) moved as a rider: "provided that the Chairman of the J.H.D.A. disavows the actions of whoever distributed their publication."

This was the whole nub of the problem. On the one hand Dr. Briggs's letter contained an apology for what was going to be published, and then a representative of the J.H.D.A. had yesterday distributed copies of *On-Call* at the A.R.M. Nobody knew if that had been done with the knowledge and authority of its chairman. If it was, quite obviously it was in bad faith, because the chairman of the J.H.D.A. had written one thing and had authorized another. The question was how much the J.H.D.A. supported this scurrilous document.

Circulation Not Stopped

Dr. Ronald Gibson said that everyone knew that one could order a thing to be printed but stop its circulation. That could easily have been done.

Dr. G. R. Outwin (Council) agreed with all that Dr. Luffingham had said. It seemed to him that this been a carefully planned manœuvre to bring about the very explosion that had been produced. If so, the Meeting should support the rider.

Mr. Langston thought the rider made a substantial difference to the motion and might well make it acceptable. Dr. J. S. Happel (Council) hoped the Meeting would not pass the rider but vote on the motion. Whether to approve the statement or turn it down was a matter for debate. If the Meeting started to tell some person outside the hall what he must do it was making a mistake. A general opinion should be expressed and the action left to the individual concerned.

Dr. H. Glyn Jones (Bromley) said that the original motion was simple and did not condemn anyone. It expressed an opinion to the Representative Body that the negotiations should continue. He pleaded with representatives to be content with that. If the rider was added it would bring into the issue the pride of other people. He did not think the attack was such as to be intolerable to people who were of reasonable stature in their own profession. He asked representatives to leave the issue as a simple hope that negotiations would continue and that unity should be achieved.

Dr. A. K. Thould (Cornwall) supported the rider. The Meeting should not lose sight of the fact that justice must be done to Mr. Langston and to the Chairman of Council. (Applause.)

Dr. Luffingham (Council) echoed the words of Dr. Thould. The motion would repudiate the action properly taken by the Chairman of Council and his two senior colleagues. It had been the Chairman's duty to do that if he thought that it was in the Association's interests. If the motion was to be passed there must be the assurance that there was good faith on the other side.

The rider, "provided the Chairman of the J.H.D.A. disavows the actions of whoever distributed their publication," was carried.

Untrue Statement

Dr. D. Guttman (Council) said he did not wish to use the platform to reply to personal abuse. He wished merely to refute the statement that he had not been democratically elected to any of the positions in which he had served junior hospital staff. The statements were untrue and he could prove it at the proper time. Nevertheless, he would be in favour of continuing discussions with the J.H.D.A. if it disavowed the damaging statements, both particular and general, it had made about the B.M.A. and those members of the Association, both senior and junior, who had tried to serve hospital junior staff.

Dr. Arnold Brown (Public Health Committee) said that he felt most disturbed about the whole affair. Some of the young men in question could be, and he hoped would be, big men in the B.M.A. one day. They were bitter because they believed, wrongly, that the Association was not what they needed to gain improvement in their conditions of service. It was the business of the Association to raise the standard of the medical profession and the conditions of service in the various branches of the profession. Dr. Brown said he most sincerely hoped that the Meeting would decide that discussions should continue with the J.H.D.A.

Dr. L. P. Grime (Junior Members' Forum) said he supported Mr. Langston's statement. If various sections of the profession split off, as they were doing, its bargaining position was weakened.

Dr. W. A. H. Stevenson (St. Marylebone) said it was a question of mediation on the one hand and continued negotiation on the other. The B.M.A. should go on trying to negotiate, irrespective of whatever views were expressed by the J.H.D.A.'s leaders, but at the same time exacting from them due responsibility for their behaviour.

Extreme Provocation

Dr. G. E. Owen Williams (C.C. and S. Committee) said that the Meeting was facing the possibility of disunity not merely in the Association but in the profession. The need for unity was paramount. It was understandable that the Chairman of the C.C. and S. Committee, under extreme provocation, had spoken on behalf of the Meeting before the Meeting had decided upon the matter. It should be left at that. There were 3,000 avowed members of the Junior Hospital Doctors' Association. The Meeting risked splitting down the middle the main trunk in order to keep alive a twig at the other end. It was not inevitable that breaking off discussions made it impossible to resume them.

Mr. A. Lawrence Abel (St. Marylebone) moved an amendment to add the words: "and retract all scurrilous and offensive remarks." He said the word "disavowed" was not enough, and that all rude remarks should be retracted.

The amendment was lost.

Dr. A. W. Macara (Junior Members' Forum) suggested that the statement made by Mr. Langston did not compromise the Association in regard to further negotiations. Mr. Langston had stated that it was his view that in the prevailing atmosphere negotiations could not be continued. What had created the atmosphere were the scurrilous remarks which had been made. The standards by which the B.M.A. judged those with whom it should negotiate were those of decency, integrity, and accuracy. If the Meeting supported the motion it would be betraying those who had been working in the interests of hospital junior staff.

Dr. J. S. Happel (Council) moved an amendment to add the words, "That this Representative Body deprecates the continued attack on B.M.A. leaders by the Junior Hospital Doctors' Association and offers its sympathy and support to all concerned. Nevertheless," at the beginning of the motion.

He said the Representative Body should preface any resolution by an assurance of support, because passing the motion in its original form placed the chief officers in a difficult position.

The amendment was carried by 148 votes to 105.

Deliberately Circulated

Mr. Langston apologized to the Chairman and the Representative Body that the statement had inevitably occupied so much time. He thought it right that the statement had been debated so fully. The C.C. and S. Committee had been anxious to meet this organization, and in order not to prejudice the issue in advance, though the provocation had been strong, it had made no reply to the original issue of *On-Call* which had suggested such things as collusion between the C.C. and S. Committee and the Ministry. The meeting with this group on 29 June had been welcomed.

The issue of *On-Call* under debate must have been in preparation when it was known that the meeting on 29 June was to take place. It had been circulated—not only published but deliberately circulated—to the Association. It contained all sorts of tendentious remarks about some of the senior members, which they were prepared to take. What he was not prepared to take was the outright attack on the junior members who had been giving days and nights in the last six months to discussions at the Ministry—very often, he believed, to the jeopardy of their professional careers. It had been suggested in *On-Call* that the juniors had twisted things, that they had not represented things fairly and fully, that they had not been properly elected. "This makes it quite impossible," Mr. Langston said, "to go on

Lord Cohen of Birkenhead (left) being presented with the Gold Medal of the Association by Mr. R. V. Cooke, President, at the adjourned annual general meeting held at the University Great Hall. The citation and another picture of Lord Cohen appear at p. 99.

talking frankly and freely to these people until this sort of thing is retracted."

He had no desire to close the door to any group which had a real sense of grievance and which had a case it wanted to put up, but it must be quite clear to any such group that if discussions were to be fruitful there must be none of these tendentious smear attacks on the people who were trying to do the job for the junior members. The atmosphere of public attack made continued discussion impossible, but if there was a real, substantial withdrawal of all this, and a promise that it would not occur again while discussions went on something might be achieved.

Dr. Morgan Williams (South Warwickshire) said that Mr. Langston had reminded the Meeting that the second issue of *On-Call* had been prepared before the Central Consultants and Specialists Committee had met the Junior Hospital Doctors' Association. Something had been said about the J.H.D.A. being unable to stop or correct what appeared in *On-Call*. The Meeting was asking, in effect, that the Junior Hospital Doctors' Association should control its somewhat scurrilous publication.

The motion: "This Representative Body deprecates the continued attack on the British Medical Association leaders by the Junior Hospital Doctors' Association and offers its sympathy and support to all conconcerned. Nevertheless, this Meeting is of the opinion that talks should continue between the British Medical Association and the Junior Hospital Doctors' Association, provided that the Chairman of the Junior Hospital Doctors' Association disavows the actions of whoever distributed their publication."

The Chairman announced that the motion had been carried by 224 votes to 61.

The Representative Body returned to Standing Orders at 3 p.m.

Constitution (Debate Resumed)

Size of Representative Body

Dr. R. P. Hendry (Rugby) moved: "That the overall size of the Representative Body should be about 500 members."

He said that there were four essentials for a future Representative Body. They were: (1) proportional representation geographically and in the field of practice; (2) adequate representation of even minor groups; (3) increased representation of the hospital junior staff; and (4) that these things should be achieved without depriving any Division of its present rights of separate representation under By-law 40. Rugby believed all this could be achieved within a membership for the Representative Body of 538, and Dr. Hendry asked permission to alter the figure in the motion to 538.

Permission for the change was given.

Dr. J. S. Noble said that the Representative Body had already agreed that there was no virtue in an exact figure of 400, and he saw no great virtue in an exact figure of 538. The intention was to achieve a slightly smaller Representative Body. Bearing that in mind he suggested the rejection of the motion.

Dr. R. L. Luffingham (East Yorkshire) remarked that the whole business had gone wrong. There had been requests for the figures in the appendix to the Constitution Committee's report to be corrected, and Dr. Hendry, like others, had been deceived by them. The motion should be supported. A year ago the Council had been asked to come up with a scheme in which all the loose ends had been tied up, but rapidly it was becoming untied. He suspected the Council had not done its job.

Dr. Hendry said that the amended figure of 538 would give those supporting the Rugby proposals everything they wanted.

The motion was carried.

Dr. R. P. Hendry (Rugby) moved: "That the area of each regional hospital board shall be a constituency returning at least one representative, who shall be elected by the members employed as hospital junior staff (as defined in the proposed By-law 40(5)) by hospital authorities within each region."

He pointed out that even places as large as Manchester or Leeds would still be too puny to have a junior hospital staff representative in his own right. It was nonsense to regard a place as big as Manchester as being too small. He proposed that each regional hospital board should become a constituency.

Dr. Noble said that in view of the increased estimate in the size of the Representative Body it gave him the greatest pleasure to accept the resolution by Rugby, which would mean 21 more seats for the hospital junior staff. However, representatives must bear in mind that they must "watch how this goes." He was not convinced that the hospital junior staff would not themselves seize a number of seats in the Divisions.

Dr. E. A. Harvey-Smith (Hospital Junior Staffs Group) called for the Representative Body's support for the motion. Junior staff must attend the A.R.M. from the regions as of right. Their own Group was based on the regions. It was there they held their elections and it was from there they should come. Dr. J. R. B. Turner (Leeds) also supported the motion strongly.

The motion was carried.

Mr. C. O. F. Rieger, of Australia, President-elect.

Proportional Representation

Dr. Noble formally moved: "That the change of policy contained in paragraph 59 of the revised Report on the Constitution of the B.M.A. be approved."

Dr. R. L. Luffingham (East Yorkshire) said it was difficult to know who wanted proportional representation. The previous year the Representative Meeting had rejected it. In 1964 at the Representative Meeting in Manchester Mr. Langston had said that if anyone was proposing proportional representation it would not be accepted by Council. Dr. Noble on the same occasion had said that he hoped the motion under discussion would be accepted in the broadest sense, but "if the resolution sought proportional representation he would oppose it." Why had a change come about in 2½ years? Dr. Luffingham suggested that no one wanted proportional representation. He submitted that the proposals now before the Meeting did not provide for proportional representation. It was not satisfactory, therefore, for the Chairman of the Organization Committee to ask the Representative Body to make a change in policy. If what was wanted was proportional representation let Dr. Noble come before the Meeting with a proposal, which he had not done.

Dr. W. P. Lambie (Sheffield) said that the Meeting was being asked to reverse the policy of 1966. From a reference back to the debate on the constitution the previous year it would be seen that the Meeting had not considered mandatory quota representation to be desirable. It was unnecessary, inflexible, and meant that constituencies would be deprived of sending to the A.R.M. those they wanted to represent them and would have to elect instead certain people in order to fill places in a quota.

Dr. K. A. Wood (Portsmouth) said that the proportional representation proposed in the report of the Constitution Committee was the minimum necessary to ensure that the prestige of the Representative Body was maintained. Each section of the profession must be able to see that the B.M.A. represented all doctors if it was to be confident in the Association's management of their affairs.

Recognized Way

Dr. J. M. W. Sedgwick (East Herts) opposed the motion. He pointed out that proportional representation was a well-recognized way, used in many countries, of making more certain that those persons whom the electors most wanted to elect were actually elected. It had been argued that the method proposed by the Council was the only way by which proportional representation could be attained. He did not believe that was so. It could be done by separate groups electing their members in the right proportion.

Dr. C. O. Lister (Aldershot and Farnham) emphasized that it was desirable above all to have doctors on the Representative Body who were keen, who wished to come, who were representatives of quality. It was no good doctors coming because they were the only people who fitted the bill under the quota system.

Dr. F. G. Tomlins (Waltham Forest) related that in his Division all members of the Division were asked to attend meetings.

Local officers had gone out of their way to get hospital junior doctors to attend, and had held a special meeting for them. Meetings were held at the main hospital in the Division. Yet the meetings were hardly ever attended by a hospital junior doctor and rarely by a consultant. Nevertheless, the Division in two successive years had elected a hospital doctor and a general practitioner to represent it. Last year the hospital doctor had been unable to attend the A.R.M. This year, he had again been unable to come and his place had had to be filled by a general practitioner. It was important that representatives should be appointed who really represented the Division.

Dr. D. Burrell (Winchester) advised representatives to think carefully before voting against the motion. They had to remember that they had already decided that each regional hospital board should be a constituency to elect a junior member. The Meeting had to look at the whole new constitution. If the motion was defeated the Organization Committee would have great difficulty in putting any of the new constitution into operation.

Dr. D. C. Roberts (Hendon) suported the motion. The last A.R.M. had supported proportional representation. The Organization Committee had had to work out a way of doing what the Representative Body asked. He fully supported what it had done.

Give Confidence

Supporting the proposal, Dr. C. C. Lutton (East and Mid-Lothian) said if the proposal was agreed it would be the kind of reform which would give confidence to those who were often opposed to the B.M.A. and would make it a real fighting organization.

Mr. J. R. Blackburne (C.C. and S. Committee) said a speaker had asked who wanted proportional representation. The answer was those who thought they were not properly represented. One of the chief problems of the constitution of the Representative Body was that some doctors thought it was not representative of all the interests of the profession, and that was one of the objects in reforming the constitution.

"We are asking you as a body made up of some 75% of general practitioners to give up some of your rights in order that there will be adequate representation of some minorities," said Mr. Blackburne. "Those of you who have the interests of the Association at heart will be prepared to surrender some of those interests in order to have better proportional representation, including representation of minor groups."

Dr. W. J. C. Scott (Dunbartonshire), asking for the wholehearted support of the Representative Body for the motion, said a vacuum would be created unless it could be filled by doctors other than general practitioners, and that was the whole idea of the proposals. With such a constitution the Association would thrive.

Dr. D. T. Davies (South-west Wales) said a constituency should be in a position to choose its representatives whether they were general practitioners, consultants, or members of other branches of the profession. It was open now to any member of the Association to become the representative of his constituency, and if some doctors did not show an interest in their Divisional meetings, and therefore were not elected as representatives, no changes in the constitution would help them.

Dr. Noble said it had been decided the previous year that no single section of the profession should be allowed to dominate all other sections in the Representative Body. There had been a reference by Dr. Davies to Divisional meetings. It was regrettable that a section of the profession did not find Divisional meetings a channel through which it sought to find its home in the B.M.A., but for all that such doctors were members. Last year the Representative Body had approved the principle of proportional representation, but what had been objected to was the mandatory nature of it. He did not think the Committee's suggestion prevented the Meeting from giving an earnest of its intent to be truly representative of the whole profession.

The motion was carried by the necessary two-thirds majority.

Remain Void

Dr. R. M. Warren (Southampton) moved: "That if the proportional representation allowed in the Division becomes impossible to fill the seat remains void."

It was an honour and a responsibility to be elected to represent a Division, but it might become more so in future, said Dr. Warren. The Division should be sufficiently active and keen to attract interest from all branches of the profession. If the motion was carried there would be an additional incentive to fill places allocated to a Division. If it were found impossible to recruit representatives the seat should remain void.

Dr. S. E. Josse (Camden) moved the amendment: "That the words 'the seat becomes free and any member of that Division may be elected to fill it' be substituted for the words 'the seat remains void.'"

His Division was not against proportional representation. What Camden was saying was that where a seat could not be filled it should be declared free and any member should be elected to fill it. Camden had several hundred members and 200 who were on the staff of teaching hospitals. Meetings were rarely attended by any hospital staff. If the hospital staff wished to be elected as representatives they could go to the meetings.

The amendment was agreed.

Dr. B. L. Alexander (Manchester) asked the proposers to define the words "impossible to fill."

Dr. Warren said they applied if there were three categories and there were only two representatives available. He added that by voting for the amendment the Meeting had apparently negatived the motion. He hoped the Divisions would try very hard before they decided that a place was "impossible to fill."

The motion, as amended, was carried.

Two-year Review

Dr. R. M. Warren (Southampton) moved: "That the proportional representation in the Representative Body be reviewed every two years."

Dr. Noble suggested that the motion should be amended to read "in two years' time" instead of "every two years," and Dr. Warren said that would be acceptable.

The motion, as amended, was carried.

Dr. M. McKendrick (Hexham) moved: "That this Meeting demands that Divisions continue to enjoy the right of separate representation in the Representative Body contained in By-law 40."

He said perhaps it was no surprise that the motion came from one of the smaller Divisions, as did so many of the motions seeking to modify the new constitution. "By this might be seen the enthusiasm of the smaller Division, particularly, for the Representative Body and endorsement of the value which we see in it," he said. He based his argument on two principles. Firstly, the need to retain the viability of the Division as the basic unit of Association structure, and, secondly, the need to maintain the position of the Representative Body itself as the parliament of the profession. It was no good saying that it was to be hoped that the Division would continue to be the basic unit of the Association if at the same time its right to direct representation in the Representative Body was taken away. That prin-

At the President's Reception held at the City Museum are, left to right, Mrs. Golding, Dr. H. M. Golding, chairman, Local Organizing Committee, the President, Mr. R. V. Cooke, and Dr. Beryl D. Corner, from the Children's Hospital, Bristol.

ciple was most jealously guarded by smaller Divisions, and he would commend it to the Representative Body.

Dr. Noble said he had great sympathy for the resolution. He believed the Hexham Division was one of those cases that should be dealt with by the Organization Committee as a case for special representation of its own, because it was geographically isolated.

However, if the motion was passed it would upset the Council's efforts towards true representation, because it would increase the number of single constituencies. Every Division should have the right to apply to Council for separate representation.

A motion that the question be now put was carried by the necessary majority.

Dr. McKendrick said, in reply, that Dr. Noble had used precisely the arguments he expected against the motion, and he strongly asserted that they were in no respect valid. "We see it as a right that the individual member in the Division should have his say in the Representative Body through his own representative," he said. "This, I think, is incontrovertible."

The motion was carried.

Elections to Council

The election of the following 10 members of Council by the Representative Body was announced: Mr. A. Lawrence Abel, Dr. Joan Chappell, Dr. G. E. Crawford, Dr. J. S. Happel, Dr. R. P. Hendry, Dr. J. L. McCallum, Dr. G. N. Marsh, Dr. H. B. Muir, Dr. J. S. Noble, and Dr. C. M. Scott.

Dr. Ronald Gibson said that representatives might not have noticed that Mr. L. Dougal Callander had not offered himself for re-election this year. Mr. Callander was one of the B.M.A.'s elder statesmen. All members knew the debt of gratitude they owed him for his work as Treasurer and for the Estates Committee. He was a Gold Medallist of the Association. "He may be elderly in years," said Dr. Gibson, "but I do not think he is elderly in mind or in heart. We shall miss him on the Council." Dr. Gibson said he was sure the Representative Body would join him in thanking Mr. Callander for all he had done for the B.M.A.

The Meeting accorded Mr. Callander a standing ovation.

Mr. Callander thanked the Meeting.

Constitution (Resumed Debate)

A motion standing in the name of Rugby, "That where geographical isolation renders joint meetings impracticable any U.K. Division shall have the right to apply for separate representation as a constituency," was carried.

Dr. R. P. Hendry (Rugby) moved: "That greater flexibility should be given to allow members working in different minority fields of practice to be eligible for election as Divisional representatives."

Dr. Hendry said the motion, if carried, would allow any Division which had several keen minority representatives to elect more than one minority group representative. For example, if a Division had good public health and a good research representation it would be able to elect two representatives, one from public health and one from research. It would not often happen, but it was wrong to say to a Division that it should not elect too many from minority groups.

Dr. Noble said that though there was a great deal in what Dr. Hendry had said, he hoped the Meeting would not carry the motion as a mandatory one.

The motion was carried as a reference to the Council.

The motion standing in the name of East Yorkshire, "That the proposed new By-law 40(1) be amended by the insertion of the words 'amended by the substitution of the figure 3 for 2 in line 53 of the First 'Schedule' after the words 'First Schedule' in Paragraph 1," was, by leave, withdrawn.

Mr. H. H. Langston (Chairman of the Central Consultants and Specialists Committee) moved:

"That with reference to paragraph 57 of the revised report on the constitution (Doc. A.R.M. 8), clauses (5) and (6) of the proposed By-law 40 (Appendix XIII, Doc. A.R.M. 2) be further amended, to read:

> (5) Of the representatives elected by any constituency having the right to elect five or six representatives not more than three shall belong to the same category and at least two shall be engaged in hospital practice and of these one shall be a consultant or senior hospital medical officer and the other shall be a senior registrar, registrar, medical assistant, senior house officer, or house officer.
>
> (6) Of the representatives elected by any constituency having the right to elect seven representatives not more than four shall belong to the same category and at least two shall be engaged in hospital practice and of these one shall be a consultant or senior hospital medical officer and the other shall be a senior registrar, registrar, medical assistant, senior house officer, or house officer."

Mr. Langston said the motion incorporated a correction of an omission in the by-law which he imagined the Organization Committee would be prepared to accept.

Dr. Noble accepted the motion, and it was carried.

A motion standing in the name of East Yorkshire, "That the proposed new By-law 40 section (7) be referred back on the grounds that in its present form it is too difficult to interpret," was, by leave, withdrawn.

By-law 44 (Doc. A.R.M. 2, Appendix XIII)

Dr. R. P. Hendry (Rugby) moved, "That Council shall have discretion to appoint up to five additional spokesmen for minority groups."

Dr. Hendry said 5% of doctors were shown as "unclassified" in the report of Council. The Council had the right under the present constitution to give five seats to small minorities and groups not otherwise properly or adequately represented. Five did not seem adequate and the Council should have more within its discretion. If it was not found necessary to use the seats they need not be filled.

Dr. Noble said the operative word was "discretion," and he accepted the motion.

The motion was carried.

Dr. R. L. Luffingham (East Yorkshire) formally moved: "That the proposed new By-law 44A be amended: (1) by the addition of the words 'and Council in announcing the appointment of the said five representatives shall state the reasons for making these'; and (2) by the addition of a further paragraph to be numbered (4) reading: '(4) Provided that no representative appointed under the provisions of this By-law shall take his seat until his appointment has been approved by a simple majority of representatives elected from the Divisional constituencies.'"

Dr. Noble asked whether the Meeting wished the representatives to appear at the "bar of the house" until they had been voted for by a simple majority of the representatives elected by Divisional constituencies. Was that the way the Representative Meeting wished to welcome the new representatives? He asked the Meeting to reject the second part of the motion.

Dr. Luffingham, in reply, said that he saw Dr. Noble's point. However, the proposal was meant for the armed Forces representatives who had not taken their seats until the opening stages of the meeting. The motion would ensure that the Council was careful as to the representatives it selected.

The motion was carried.

Constituencies for Electing Representatives

Dr. J. S. Noble formally moved:

"That the proposals published in Appendix II of the revised Report on the Constitution of the B.M.A. be amended as follows:

> "(i) That A.R.M. constituency No. 19 be divided into two, that is, East and Midlothian (one representative) and West Lothian (one representative).
>
> "(ii) That A.R.M. constituency No. 23 be divided into two—viz., Fermanagh (1 representative) and Tyrone (1 representative).
>
> "(iii) That A.R.M. constituency No. 28 be divided into two—viz. East Denbigh and Flint (1 representative) and West Denbigh and Flint (1 representative).
>
> "(iv) That A.R.M. constituency No. 31 be divided into two—viz., Swansea (2 representatives) and Mid-Glamorgan (1 representative).
>
> "(v) That A.R.M. constituency No. 63 be divided into two, viz., Mid-Cheshire (2 representatives) and Crewe (1 representative).
>
> "(vi) That A.R.M. constituencies No. 80 and 82 be reconstituted, viz., 80—Sutton Coldfield and Walsall (2 representatives) and 82—Coventry and Nuneaton (2 representatives)."

An amendment standing in the name of Tees-side was accepted as a reference, as follows: "That constituency No. 45 should consist of three Divisions—namely, Cleveland and Middlesbrough, Hartlepools, and Stockton—returning three representatives, and constituency No. 46 should consist of the Darlington Division alone, returning one representative."

Dr. F. O. Wells (East Suffolk) moved as an amendment: "That A.R.M. constituency No. 89 be divided into North-east Suffolk (one representative) and East Suffolk (two representatives)."

He explained that the proposed new constituency was 55 miles from north to south and 35 miles from east to west. It was similar in size and distribution to constituencies such as Cornwall. It covered nearly 2,000 square miles.

Dr. Noble pointed out that the motion and the amendments were covered by the

Hexham motion carried earlier, and the Meeting agreed that it was so.

Dr. R. P. HENDRY (Rugby) moved: "That every U.K. Division having not less than 50 members may continue to form a constituency, but that the basis for the allocation of seats be changed to be one representative for the first 150 members and one additional representative for each additional 200 members or part thereof."

He said that the Meeting had agreed what the target should be for the size of the Representative Body. This was a matter of getting to the target. As far as he was aware, the Chairman of the Committee was prepared to accept the motion as a reasonable way to reach the target.

Dr. NOBLE said that by passing the Hexham motion the Representative Body had made it imperative that the "road to Rugby" should be taken. His only fear was that as a result representatives would find it more difficult to achieve proportional representation, especially on a geographical basis, but that was probably now the nearest the Meeting would get to a reasonable proportional representation married to the sacrosanct right of representation of the Divisions.

Substantial Change

Dr. R. L. LUFFINGHAM (East Yorkshire) pointed out that this proposal was a substantial change. It should be considered carefully because it made nonsense of the proposed constituencies. As guidance or as a reference to the Council it was fair enough, but as it stood it committed the Association.

Dr. HENDRY, in reply, said that if the constitution was not changed in this way presumably the five existing constituencies would be left, which would result in a very much bigger Representative Body.

Dr. J. S. ROSS (Council) agreed with Dr. Luffingham. This proposal would alter the whole situation and would throw the question of the division of constituencies back into the melting-pot. The Organization Committee had examined all sorts of different ways of achieving the correct proportional representation and had, with the exception of Dr. Hendry, agreed that there was much to be said for as many Divisions as possible having their representative. But there had to be a limit in order to get proportional representation. Bearing in mind the other motions already passed, he hoped the Meeting would not accept the motion.

Dr. C. C. LUTTON (East and Mid-Lothian) stated that under this proposal if the membership altered the number of representatives would alter as well. There could not be two yardsticks. The yardstick had been set at 538 members. That could not now be changed.

Dr. NOBLE repeated that the "road to Rugby" was now the road to take in view of the previous decisions taken by the Representative Body.

The motion was lost.

The following motions by East Yorkshire were, by leave, withdrawn:

"That the proposed new By-law 45 be amended by the addition after 'Research Workers Committee' in Section (1) of the words, 'Provided that no representative be appointed under this By-law who is not certified by his Divisional Executive to be an active member of his Division and that any such representative shall be subject to the provisions of By-law 47C, Section (4).'"

"That the proposed new By-law 45, paragraph (4), be amended by the addition after 'respectively obtained' of the words 'Provided that no deputy representative be appointed under this By-law who is not certified by his Divisional executive as being an active member of his Division and that any such deputy representative shall be subject to the provisions of By-law 47C, Section (4).'"

The following motion by Aberdeen was also, by leave, withdrawn: "That the Scottish representatives on the Representative Body should be nominated by the Scottish Council."

Nomination and Election of Representatives

Dr. JOYCE E. BROOKS (Southampton) moved: "That a postal vote be the sole method of election to the Representative Body."

She said that some members were disgruntled, accused the B.M.A. of not being democratic, and claimed that its representatives were not democratically elected. Doctors who could not attend Divisional meetings seemed particularly prone to that view. Under the new constitution there must be good standing between Divisions and the regional councils. The postal voting system would ensure that the representatives were properly elected.

Dr. D. C. ROBERTS (Hendon), opposing the motion, said that for many years it had been B.M.A. policy to have two alternative ways of electing representatives from Divisions; by voting or by a decision at the meetings. Last year it had been proposed by the Council that there should be a postal voting system, but this had been rejected by the Representative Body. It had decided that the appropriate method could be chosen locally. In the past, so far as he knew, the postal vote had never been used.

Dr. S. WAND (Treasurer) said the proposals for an increased membership of the Representative Body were going to cost a lot of money. The suggestion in the motion would cost £2,000 a year. There was no reason why the postal vote should not be used where it was considered necessary, but to make it the only method was going too far.

Dr. M. GOODMAN (Liverpool) reminded the Representative Body of the existing method of electing the Council. It was by postal ballot, and the results of the returns in those elections did not compare favourably with the ordinary system of electing representatives at Divisional meetings.

The motion was lost.

A motion standing in the name of Rugby, "That the present By-law 42(3) be renumbered By-law 47D and given a separate heading 'Constituency Meetings,'" was accepted.

Representative Body and Council

Dr. DORIS M. ODLUM (Bournemouth) moved: "That this Meeting instructs Council that proportionate representation on Council itself shall be voluntary."

Her Division had preferred the voluntary principle. Whether it worked in the long run depended on good will. No amount of orders would produce good will. If the proportional representation was made mandatory and it did not work the B.M.A. would look foolish.

Mr. J. R. BLACKBURNE (C.C. and S. Committee) said his chairman was anxious the motion should be defeated, because there had been many occasions in the Council when he had been the only representative to speak for the hospital services.

Dr. B. L. ALEXANDER (Manchester) said that if the Representative Body was to be proportionately represented on a mandatory system the same rule should apply to the Council. Dr. R. L. LUFFINGHAM (East Yorkshire) said that in his own experience the Council had never had fewer than a certain number of consultants as members.

Dr. NOBLE wanted further clarification, on a point of order. The Organization Committee had worked during the year on the assumption that proportional representation for the Council had been accepted by the Representative Body in 1966 by the necessary majority.

The CHAIRMAN said that was not so. Minute 45 of the 1966 Meeting had made it clear that that part of the motion had been defeated.

Dr. NOBLE hoped that, since the Representative Body had accepted proportional representation for itself, it would demand the same for the Council.

The motion was lost.

The motion standing in the name of Southampton, "That continuous steps be taken by Council to reduce the size of the Representative Body and of Council" was accepted.

Ex-officio and Co-opted Members of Council

Dr. T. O. LEWIS (Swansea) moved: "That under the proposed new constitution of the Association the Chairman of the Welsh Committee, as a member of the Council, shall have full voting rights."

The proposed new constitution would reduce the Welsh voting representation on the Council from three to two. Doctors in Wales were prepared to accept it, despite the difficulties that existed between North and South Wales, but the Chairman of the Welsh Committee should be given the courtesy of voting rights.

Dr. D. L. WILLIAMS (East Denbigh and Flint) said doctors in North Wales were represented in the Council by two voting representatives. Statistics and rules were fine, but it was "a dry and cold constitution" that allowed a Chairman of a Committee representing all Wales to attend the Council but refused him the vote.

Dr. D. L. W. CHAPMAN (Council) suggested that the Chairman of the Welsh Committee and of the other two regional standing committees should be treated differently from other chairmen.

Dr. NOBLE said the Organization Committee had devised a Council in accordance with instructions, and had thought the Council would benefit by having the guidance and advice of the chairmen of all the standing committees, but it had been thought proper that chairmen of standing committees should not vote. If the motion was carried it would open the floodgates.

Dr. T. O. Lewis (Swansea) said the Organization Committee had to accept the responsibility for the recommendation of reduction in voting and the effect it would have on the encouragement of new members.

The motion was lost.

Chairman of Journal Committee

Dr. Mary Esslemont (City of Aberdeen) moved: "That the Chairman of the Journal Committee should be *ex officio* a member of the Council of the British Medical Association."

The only Committee Chairmen suggested as *ex officio* members of the new Council were all persons concerned chiefly with medico-political matters. The income of the publishing department in the past year had been well over £1m. The image of British medicine abroad was in no small way determined by the quality of the *B.M.J.* and its associated special journals. It was a great responsibility for the Chairman of the Journal Committee. He should be in a position to be fully in touch with medical opinion in the country and, for that reason, be a full member of the Council.

Dr. Noble said that he opposed the motion. Chairmen of Committees could attend every Council meeting; the only bar was voting rights.

Dr. J. L. McCallum (Council) said it was no good saying the Chairman of the Journal Committee could attend on occasions when the *B.M.J.* was being discussed. How was he to know when to attend?

Dr. Esslemont, in reply, said that if it were possible for the Chairman of the Journal Committee to be present at every meeting it was equally possible to give him the importance of a vote, especially when points of policy came up in relation to the *Journal*.

The motion was lost.

Elected Members of Council

Dr. A. M. Maiden took the chair.

Dr. Noble moved: "That the provision for the election of one woman member of Council by the women members of the Association be retained, and that the appropriate addition be made to Appendix IV of the revised report on the constitution of the B.M.A."

Dr. E. Virginia Saunders-Jacobs (Woolwich) said women doctors had equal training and competition in their work. If they were to be appointed to the Council they would be appointed to represent their Division or their section of medicine. There were administrative problems which were different for women, and the Council should have the advice of someone who was there, watching the interests of women members.

Dr. Jean E. Lawrie (Dartford) said it was well understood that women doctors in the United Kingdom had career problems related to their family commitments. It would be a blow to many women members if their representative's place on the Council were lost.

Dr. Sanchia FitzMaurice (Westminster and Holborn) said that in 10 to 15 years' time 15% of the total medical manpower would be returning from motherhood to work. "Those of us who are fortunate and lucky enough to have emerged to the glorious freedom of middle age can look after their interests. We are the biggest trade union on the face of the earth. We will take care of our own interests as women, and the only respect in which we crave your indulgence as women is in this one special matter of helping medical women to get back to work."

The motion was carried.

An amendment by Mid-Glamorgan, "That the Council of the B.M.A. should always include a woman member of the B.M.A.," was approved.

Direct Vote

The following motion from East and Mid-Lothian was formally submitted: "That under the new constitution all the members of the Council to be elected by local constituencies of members in the United Kingdom should be elected by direct vote of individual members and by no other method."

Dr. W. W. Fulton (Glasgow) moved as an amendment to insert after "United Kingdom" the words "with the exception of Scotland."

He said there were a number of matters affecting Scotland on the agenda. The amendment would enable the Representative Body to consider those items and to take decisions at the right time.

Dr. E. R. C. Walker (City of Edinburgh) said there were occasions when Glasgow and Edinburgh saw eye to eye, and this was one of them. The report of the Constitution Committee stated that modification of the system of election to the Council would be required to provide for the filling of the five Scottish seats on the Council. It had been recommended that both matters should be referred to the Scottish Council and that it should be asked to submit recommendations. That had been done. Those recommendations had not been referred to in the Annual Report of the Council. It merely listed four different possibilities, and went on to state that it favoured a system which had not so far been considered by members in Scotland. What was proposed was that the whole of Scotland should be one single constituency. Edinburgh and Glasgow thought that the Representative Body should know what the Scottish Council had recommended and why it had done so, and so be given a chance to judge whether the Council had been right in rejecting the recommendations. That was the purpose of the amendment.

Dr. D. Buchanan (Council) said that the members in Scotland were far from unanimous on the issue under discussion. What had been carried the previous year was already the policy of the Representative Body—that 40 members of the Council should be elected by postal vote by members in the United Kingdom. "So far as I know, Scotland is still part of the United Kingdom," said Dr. Buchanan.

Dr. C. C. Lutton (East and Mid-Lothian) also denied that there was the overwhelming support for the amendment that had been alleged. Approximately half the Divisions were against it.

Negation of Free Speech

Dr. J. Riddell (Chairman of the Scottish Council) said that the principle contained in the motion was in many ways excellent, but everyone was anxious to preserve free speech. It was on that score that he was forced to oppose the motion. When the Scottish Council considered the new constitution it had put a proposal to the Organization Committee which that Committee had felt unable to consider in view of the terms of its remit. The Committee had said that the Scottish proposal would have to be put to the Representative Body. That was about to be done in two motions by Glasgow and Edinburgh. Dr. Riddell said he understood that if the motion under discussion was carried the motions by Glasgow and Edinburgh would fall. That would be the negation of free speech. Any representative who wished to support the principle of the individual voting directly could support the amendments to the next motion on the agenda.

Dr. C. J. Swanson (Council) also pointed out that if the Meeting passed the motion as it stood the Glasgow and Edinburgh motions would automatically fall. Dr. J. G. M. Hamilton (Edinburgh) supported the amendment merely in order to be able to speak to later motions. Dr. W. J. C. Scott (Dunbartonshire) said there was a cleavage right down the middle of Scotland and the Representative Body was being asked to act as an independent arbiter. After a lot of discussion it had been agreed at the A.R.M. in 1966 that every member should have a vote in the election of his member of Council. "If it is good enough for the rest of the United Kingdom, why not for Scotland?" asked Dr. Scott.

Dr. J. S. Ross (Council) said that he realized that there were special difficulties for Scotland, but in the case under discussion he could see no reason for special pleading. Why should Scotland depart from the general principle that members of Council should be elected by the periphery?

Dr. H. B. Muir (Council) asked whether Dr. Scott and Dr. Lutton had been speaking to the amendment or to other motions which might arise later. The Chairman replied that, since the amendment was a rather narrow one, the speakers had been permitted to show why Scotland should have a special procedure. Dr. J. E. Miller asked whether it would not be reasonable to give others who had contrary arguments to those adduced a chance to put them to the Meeting.

Dr. Noble reminded the Meeting that it had been a firm decision of the Representative Body that the elections of the regional members of Council should be by individual members. It was the existing policy.

Dr. Fulton, in reply, said he had deliberately not entered into the merits or demerits of the case as had most other speakers. The issue was complicated. Later the Meeting would be asked to decide certain matters for Scotland. Unless the amendment was accepted the Meeting would be denied that opportunity.

The amendment was lost.

Further Amendment

Dr. G. R. Outwin (Council) moved as an amendment: "That under the new constitution, members of Council shall continue to be elected by previous constituencies by direct vote of individual members and no other method."

He said he considered that the Representative Body was going too far too fast. A complex three-tier structure was to be built on foundations whose ability to support it was unpredictable. It was much better to preserve the present election of the Council from the periphery by the existing constituencies until the Association had had a chance of trying out the regional councils.

Dr. NOBLE pointed out that the Representative Body had approved proportional representation in respect of the Council in 1966 and had confirmed it at this Meeting. A schedule of constituencies had been prepared for the election of the Council, which provided a fair degree of proportional representation. With proportional representation and a return to the old constituencies it was difficult to know just what would happen.

Dr. OUTWIN, in reply, said he thought it would be wise to wait at least two years, until the regional councils had had a chance to prove themselves, before taking this drastic step.

The amendment was lost.

The motion, "That under the new constitution all the members of Council to be elected by local constituencies of members in the United Kingdom should be elected by direct vote of individual members and by no other method," was carried.

Chairman's Decision Challenged

Dr. H. B. MUIR and Dr. J. E. MILLER challenged the action of the Chairman (Dr. A. M. Maiden) in putting the East and Mid-Lothian motion to the Meeting so soon. Dr. Miller said there were three speakers on the platform wishing to speak to the motion, which was an extremely important one for Scotland.

The CHAIRMAN said that he had made an error. He said he would re-open the debate on the East and Mid-Lothian motion. It read: "That under the new constitution all the members of Council to be elected by local constituencies of members in the United Kingdom should be elected by direct vote of individual members and by no other method."

Standing Orders were suspended, and debate was resumed on the above motion.

Dr. C. C. LUTTON (East and Mid-Lothian) said that the direct vote of members must never be disenfranchised. Last year there was an overwhelming vote to this effect, and if this system was changed under the new constitution it would be possible to end up with four or five different ways of electing members to the Council.

Dr. JOAN K. SUTHERLAND (City of Edinburgh) said it had been stated that it was essential that members should all be elected in the same way. This statement needed careful thought, as totally different conditions existed in many parts of the country. As the population was distributed in Scotland, it would be almost impossible for smaller Divisions ever to get a member elected to Council.

Dr. J. E. MILLER (Council) said that the situation in Scotland, where there were vast areas covered by small Divisions, must be carefully analysed. There were "two big battalions" concentrated on Edinburgh and Glasgow, and it was possible that all five members elected to Council would come from these areas if elections to Council were by direct vote, taking Scotland as one constituency. Justice must be done to the smaller Divisions. He wished all areas in Scotland to have adequate representation, which could not be effected in that way. He asked the Meeting to reject the motion.

Dr. A. J. MACLEOD (Outer Islands) asked the Meeting not to disturb the status quo. Scotland wished to preserve the appointment of peripheral members in the rural areas. He asked the Meeting to support the motion.

Dr. NOBLE said that the East and Mid-Lothian motion was merely a reaffirmation of existing policy, and as it concerned the whole of the United Kingdom he advised the Meeting to pass it.

Dr. LUTTON, in reply, said that if the motion were lost the new constitution and everything it stood for would go back into the melting-pot. He asked them to support the motion as it stood.

The motion was carried.

Scottish Constituency

Dr. J. S. NOBLE then moved: "That the five members of Council elected by members in Scotland be returned from a single constituency embracing all these members of the Association."

Dr. R. T. CAMPBELL (Stirling) moved the following amendment: "That the five members of Council for Scotland should be elected by the five single-member constituencies as at present."

He said that the Stirling Branch had considered the matter fully and there was nothing to gain by taking Scotland as a single constituency. The geographical distribution would be in danger, as Glasgow and Edinburgh would out-vote the northern Divisions.

Dr. D. BUCHANAN (Council) said it was only in the past few years that satisfactory contact between the periphery and the centre had been achieved. The sacred cow—proportional representation—was now proposed, but that sacred cow could not survive in every area of the country. In the cold north geographical representation was more important in some cases than proportional representation.

Dr. W. J. C. SCOTT asked the Meeting to oppose the amendment, which would not ensure proportional representation, whereas if Scotland was regarded as one constituency it would ensure that one branch of the profession was not over-represented.

Dr. J. G. M. HAMILTON (City of Edinburgh) supported the amendment. He said that to treat Scotland as a single constituency was absolute nonsense. "You can do it in Belfast, Liverpool, and St. Marylebone, but you cannot do it in a country the size and shape of Scotland," he said. The political, geographical, and practical way was by the five single-member constituencies as at present.

Dr. W. W. FULTON (Glasgow) asked the Meeting to vote in favour of the amendment as "second best."

Dr. J. S. NOBLE said that he was sorry if some members of the Scottish Council thought that their advice had been spurned, but he could not support the amendment.

Dr. CAMPBELL, in reply, said he did not think Dr. Noble was correct. Proportional representation could be worked in by individual constituencies.

On a vote 91 voted for the amendment and 58 against.

Dr. A. N. MATHIAS resumed the chair.

Further Amendment

As a further amendment Dr. A. A. CLARK (Dunbartonshire) moved: "That this body proposes that if the five Scottish members in Council are elected by Scotland as a single constituency geographical representation should be maintained by there being not more than one member elected from each of the present five constituencies."

He submitted that this amendment was the only method of electing the Scottish members of Council and retaining proportional representation. The main point of the amendment was that geographical representation should be maintained. If the Organization Committee's proposal was accepted as it stood there would be a ridiculous position where the five members from Scotland elected to the Council in London could all be from one Division.

Dr. J. S. MCCRAE (Ayrshire (with Wigtownshire)) said that whatever method of election of the Council members was chosen it must, in accordance with the new constitution, be representative of the profession as a whole. That meant proportional representation, which had already been approved. Dr. McCrae said that so far as he was concerned there were three principles involved—namely, election by popular vote, regional representation, and proportional representation. He assessed them in that order of priority.

Dr. CLARK, in reply, asked the Representative Body if it realized the position if the motion from the Organization Committee was accepted. In fact, the City of Edinburgh and the City of Glasgow Division could elect all five members of the Council.

The amendment was carried.

The motion as amended was carried.

Dr. J. E. MILLER (Council) pointed out that a motion containing two incompatible amendments had been passed. It could not therefore be passed in that form.

Dr. W. W. FULTON (Glasgow), on a point of order, stated that if the amendment by Dunbartonshire was passed as an amendment to the amendment by Stirling it became the substantive motion. He hoped the Meeting would now pass it as the substantive motion.

The CHAIRMAN said he thought that the amendment by Dunbartonshire overruled the amendment by Stirling, and therefore the Organization Committee's motion could be passed as amended by Dunbartonshire's amendment as a substantive motion.

Dr. R. B. L. RIDGE (Council) pointed out that when the amendment by Stirling was declared carried by 91 to 58 votes it became the substantive motion, though this was not declared as the Chairman was taking advice about a two-thirds majority. Having become the substantive motion, the amendment by Dunbartonshire was then taken as an amendment to the new substantive motion.

The CHAIRMAN ruled that the amendment by Dunbartonshire was covered. He said that the Organization Committee's motion as amended by Stirling became the substantive motion. Stirling's amendment required a two-thirds majority. The vote on Stirling's amendment would be taken again. The vote on Stirling's amendment was taken again and carried by the necessary majority.

Advice on Procedure

The CHAIRMAN made a statement to the Meeting. He said that he had been advised by the Solicitor that if the Meeting had voted on a motion without appreciating the effect of the vote it was in order for him, as Chairman, to give the Meeting an opportunity of correcting what it had done.

The Meeting had passed the motion by Rugby "That the overall size of the Representative Body should be about 538 members." It had rejected the following two motions (as amended) by Rugby:

"That every U.K. Division having not less than 50 members may continue to form a constituency, but that the basis for the allocation of seats be changed to be one Representative for the first 175 members and one additional Representative for each additional 200 members or part thereof."

"That By-law 41 be *not* deleted but clause (2) be amended thus: delete the figure '150' and substitute '175'; delete words from '. . . for each complete . . .' to end of paragraph and add 'and one more for each complete number of 200 members in excess of one hundred and seventy-five members.'"

The effect was that the numerical right of representation of Divisions set out in the existing By-laws remained unchanged. In consequence, the Meeting's decision to add other members—for example, a motion by Rugby which added at least 21 junior hospital staff representatives—meant that the size of the Representative Body, it was now estimated, would be about 625. In view of the inconsistency of those decisions the Chairman said that the Meeting would have to consider whether it wished to reconsider the two motions by Rugby which had been rejected.

The Meeting adjourned at 6.15 p.m.

Fourth Day: Monday, 10 July

The Meeting resumed on Monday morning at 9 a.m., with Dr. A. N. MATHIAS in the chair.

The CHAIRMAN said he hoped representatives would bear in mind the need to avoid an adjourned meeting, primarily on the ground of expense. There were also constitutional difficulties.

The Agenda Committee recommended that at the end of the discussion on other motions from Divisions and Branches he would invite Dr. Noble, the Chairman of the Organization Committee, to make a statement on the present position of the constitutional proposals as a result of the decisions taken by the Meeting on Saturday. The Meeting had to finish by 5 p.m. If there had to be an adjournment he undertook that any motions withdrawn to facilitate business would be restored to the agenda for discussion at the adjourned meeting.

Motion of Thanks

Dr. D. P. STEVENSON (Secretary) moved a vote of thanks to all who had contributed to the success of the Bristol Meeting. Those concerned were:

The Lord Mayor and Corporation of Bristol; the Chancellor, Vice-Chancellor, and Court of the University of Bristol; the President, members, and staff of the University Union; the Dean and Chapter of Bristol Cathedral; the Chairman and Board of Governors of the United Bristol Hospitals; the Chairman and members of the South-western Regional Hospital Board; the Chairman of the Bristol Division and the President of the Bath, Bristol, and Somerset Branch, who had been the hosts for the Meeting; the Chairman and members of the Ladies Committee; the Chairman and members of the Hospital Management Committee of Southmead Hospital; all those who had kindly provided hospitality for the ladies.

Dr. Stevenson also thanked the British Broadcasting Corporation and Miss Marisa Robles, Mr. John Heddle Nash, Mr. Leonard Hirsch, and the New B.B.C. Orchestra for the concert on Sunday, and the Ciba Laboratories Limited, who made the concert possible; the President and members of the Bristol Medico-Chirurgical Society; the Librarian of the Medical School; Messrs. Frost and Reed; the Chief Constable of Bristol; Wessex Coaches Limited; the Automobile Association; Messrs. E. R. Squibb and Sons Limited; Messrs. Roneo Limited. Finally, he thanked those responsible for the floral decorations, particularly the Corporation Parks and Gardens Department, the students who had acted as stewards for the Meeting, and the staff of the West of England Regional Office of the B.M.A.

Dr. Stevenson said he was sure it would be the wish of the Representative Body that suitable letters of thanks be sent to all those who had made the success of the Meeting possible. (Applause.)

President of the American Medical Association

The CHAIRMAN introduced to the Meeting Dr. Milford O. Rouse, President of the American Medical Association, who before becoming President of the A.M.A. had been Chairman of its Board of Delegates, which corresponded to the British Medical Association's Representative Body. Dr. Rouse was given a standing ovation.

Dr. ROUSE said it was a privilege and a pleasure to bring to the Meeting the greetings and good wishes of the American Medical Association. The B.M.A. was the cousin of the A.M.A. not only in race but in service to mankind. It was comforting to know that the B.M.A. and the A.M.A. had common problems and the common objective of ever increasing the quality of medical care, while trying always to preserve the profession's freedom of judgement and freedom of action.

Other Motions by Divisions and Branches

Independence of the Review Body

Dr. J. R. B. TURNER (Leeds) moved: "That this Meeting records with dismay the recent attempt of the Government to undermine the independence of the Review Body, and urges Council to resist with all the means at its disposal any further similar attempt."

During the eight years of the Review Body's existence it had acted as a reasonable arbiter on remuneration. Its machinery had been more satisfactory to the profession than that of any of the previous methods of negotiation it had replaced. The profession had not always liked its decisions. Nevertheless the decisions had been accepted, and when the profession had felt wronged it had sought further evidence to support its claim. The profession had accepted those decisions because they had been made by a body of men of high individual and collective standing and of undoubted integrity, able to withstand pressure from one side or the other, a truly independent body.

In the recent White Paper on prices and incomes the Government had seemed to undermine that independence by bringing the Review Body either directly or indirectly under the remit of the Prices and Incomes Board. That would virtually bring the profession back to square one again, which must be strongly resisted. "The umpire is being got at, and the whole future of our pay negotiations is at stake," said Dr. Turner.

Dr. RONALD GIBSON (Chairman of Council) said that the Minister of Health had stated that paragraph 21 of the White Paper (Cmnd. 3235) implied no change in policy from similar statements used in previous White Papers, and the status of the Review Body was in no way affected by that paragraph. Accordingly, evidence had already been prepared and would be submitted to the Review Body in October on the assumption that the position of the Review Body remained unchanged. Dr. Gibson was prepared to accept the motion as a reference to the Council.

The motion was carried.

Remuneration

The CHAIRMAN moved formally a motion in the name of Medway and Gravesend: "That, in the opinion of this A.R.M., the overall level of remuneration contained in the 1966 Review Body award is too low to serve either as an incentive to recruitment or as a disincentive to emigration."

Dr. GIBSON said he was not against the motion, but was nevertheless a little worried by it. The Minister, in consultation with the profession's experts, was obtaining facts on both the points mentioned in the motion. It seemed unwise for the Representative Body to pass a motion in such terms knowing neither the effect of the award on general practitioners nor the rate of pay which the general practitioners would have under the new scheme. It would be better to obtain the facts first and then pass the motion, suggested Dr. Gibson.

A motion to pass to the next business was passed by the necessary majority.

The following motion by Bournemouth was, by leave, withdrawn: "That, mindful of the threat to all the professions that their fees may be referred to the Prices and Incomes Board, and being aware of the fact that the fees of architects have already been referred to that body, this Meeting instructs Council forthwith by all means at its command to obtain accurate up-to-date information on the realistic overheads of all forms of medical practice, private or N.H.S., in order to be able to justify before any Government body or to the public generally proper levels of gross fees required to provide a high standard of medical care to all patients."

A motion by Monmouthshire, "That the B.M.A. fully supports the public health medical officers and medical teachers in their present conflict over remuneration, and especially pledges its support in the event of their resignation," was accepted.

A motion by Tyneside, "That a contract entered into with a Government that has legalized the breaking of contracts is not worth the paper it is printed on," was accepted.

Profession's Leaders

Dr. C. C. LUTTON (East and Mid-Lothian) moved: "That in order that sufficient time may be spent by the profession's leaders on matters of importance in their negotiations and representations on behalf of the profession, adequate provision should be made for these leaders to absent themselves from their normal professional work; if necessary funds should be made available to provide for the employment of locums or deputies."

He said that earning daily bread in medicine was an onerous task, but earning other doctors' bread was more onerous. There were chairmen of committees who must be penalizing themselves in terms of promotion in hospital since they were so often away negotiating. The Health Service was going through a period of change and expansion, and therefore the work of the profession's negotiators was continually increasing and they were spending more and more time away from their work.

Any allowances that the profession's leaders received should not be charity but compensation for what they would have earned had they been working. He suggested that these doctors should be given official recognition for the work they did, and there should be a special fund available to which the leaders could apply if they were out of pocket.

Dr. GIBSON explained that there was already an *ad hoc* committee which looked into matters brought to its notice by officers or chairman of standing committees. He would be happy to accept this motion as a reference to the Council.

The motion was carried as a reference to the Council.

Public Opinion on N.H.S. Expenditure

Dr. A. W. MACARA (Junior Members Forum) moved: "That this Meeting has grave doubts whether the wishes of the public are being carried out in regard to the proportion of the national income spent on the N.H.S. That it be a recommendation to the Council of the Association to consider employing the modern techniques of sampling public opinion to obtain evidence of this question."

He said that politicians of all parties admitted that the finance available for the Health Service was inadequate. In the House of Commons on 9 June Members from both sides spoke of the need for an increase of as much as 40% in the National Health Service budget, which would bring this country into line with the United States in regard to the proportion of national wealth devoted to health. He suggested that it was time politicians and those responsible for dictating priorities did something about this. Dr. Macara said that he was confident that the public, given an opportunity to express its views, would demand that as national prosperity grew more money should be spent on the Health Service.

Dr. GIBSON said that the wording of the motion indicated that it should be a reference to Council. The proposal would have to be investigated from the point of view of expense and a report brought back to the Representative Body next year.

The motion was carried as a reference to the Council.

Medical Education

A motion standing in the name of Manchester, "That students receiving public money in the form of grants should be required to undertake to work in Great Britain for a period equal to the term of the grant or, in default, to repay a proportional amount of the grant," was, by leave, withdrawn.

Mr. D. B. BROWN (Mid-Essex) asked whether the motion he would put forward on behalf of Mid-Essex, asking for a central council for medical education, and the motion in the name of Morpeth and Blyth ("That in the view of the expansion and complexity of medical education, particularly in the postgraduate field, the Council of the B.M.A. is instructed to take steps to co-ordinate all bodies involved,") could be taken together.

Dr. GIBSON said it would be better to support the motion standing in the name of Morpeth and Blyth. A central committee had already been set up and the B.M.A. had been excluded. But the Association should not weaken in its determination to be represented on any bodies concerned with medical education.

Mr. D. B. BROWN (Mid-Essex) then moved the Mid-Essex motion: "That there should be set up a central council for medical education as a forum for discussion and negotiation on all matters relating to both undergraduate and postgraduate education."

Mr. Brown said that as medical education developed it had been urged increasingly that its further progress should be controlled by a central council. It was not surprising that undergraduate hospitals had dominated the thinking on medical education in the past, because it had been concerned mainly with students. However, opinion was changing, and it was now considered that greater emphasis should be placed on postgraduate education. There was inadequate co-ordination in the schemes that had developed and little liaison between postgraduate and undergraduate teaching. Mr. Brown said that the B.M.A. should now set up a central committee for co-ordinating postgraduate and undergraduate education. This would be a major step towards unity.

Dr. S. WAND (Treasurer) said that it sounded a very simple exercise, but in the words of the motion it could be a large and expensive undertaking. The motion standing in the name of Morpeth and Blyth indicated the kind of policy that the Association had been trying to carry out. He hoped that the Meeting would persuade the mover of the Mid-Essex motion either to withdraw it or to refer it to the Council in general terms, and pass the motion standing in the name of Morpeth and Blyth.

A motion to pass to the next business was carried.

The motion standing in the name of Morpeth and Blyth was carried.

Road Accident Service

Dr. E. L. R. MCCALLUM (Darlington) moved: "That this Meeting urges the Government to take responsibility in organizing a more efficient road accident service." Dr. McCallum said that last year the total number of road casualties in the country had been in excess of 392,000, of whom 100,000 had been seriously injured and 8,000 fatally injured. Twenty-two people were killed on the roads each day. It had become increasingly obvious that there should be a major controlling body of police, fire, ambulance services, and the rest which could act at once on matters of improved efficiency. Ambulances should be provided with positive-pressure oxygen-giving equipment, suction apparatus, various dressings of all sizes, portable floodlighting, and blood transfusion sets. If such ambulances attended at accidents any passing doctor could fulfil a vital role. All general practitioners should be trained to use such equipment. The important time was the period between the accident and the time of hospital admission. The injured should receive the best possible attention, but the equipment, and proper control of the equipment, was needed.

Mr. A. LAWRENCE ABEL (St. Marylebone) said that the number of serious injuries would be cut down and the death-rate reduced if the road accident services were better organized. "A larger number of those who are mutilated and murdered on the roads could be saved," said Mr. Lawrence Abel.

Dr. G. CORMACK (Newcastle upon Tyne) said he was in an area where it was twelve miles to the smallest cottage hospital, which was not adequately equipped to deal with local casualties. As a result, doctors were frequently asked to deal with road-accident casualties. The amount of help that could be offered was usually limited to little more than first aid. An improvement in the facilities immediately available to doctors at the scene of the accident would make a substantial improvement in the number of fatal casualties.

Dr. GIBSON agreed that the motion was important, and he had hoped there would be time for a debate. However, the Association would urge the Government to take action in the matter, and he thought it would be the wish of the Representative Body to invite the help of other bodies such as the Royal Colleges.

The motion was carried.

Dr. A. M. MAIDEN took the chair.

Notification by Police of Patient's Death

Dr. H. STOLL (Camden) moved: "That where the police are called following the discovery of a dead person then that person's doctor should be notified of the death by the police as soon as possible."

He said there were areas in the country, and perhaps more of them in the Metropolis, where it was possible to inquire about a person only to be greeted with the embarrassing reply, " Didn't you know she had been dead for the last three months ? Didn't the police surgeon tell you ? " Dr. Stoll thought that if the Association was to negotiate with the Home Office or with the Police Surgeons' Association to make sure that every death about which the police were called in resulted in a notification to the general practitioner a lot of embarrassing situations would be avoided.

The motion was carried.

Boxing

A motion moved by Dr. D. Buchanan (Dundee), " That this meeting deplores the continuing of professional boxing in this country and its resultant mental and physical damage," was, by leave, withdrawn.

Sterilization

Dr. B. Taylor (Tower Hamlets) moved: " That, as all methods of contraception appear to have their drawbacks, this Meeting considers that the time is due for the medical profession to consider the question of the legality of sterilization and help to form the law by deciding its view of what the law ought to be."

He stated that in the past, and before the reformers got to work, the medical profession had given insufficient consideration to the question of what ought to be the law on abortion. The profession had given even less thought to the law relating to sterilization for either sex.

Dr. Doris M. Odlum (Bournemouth) could not support the motion and hoped that the Meeting would pass to the next business. No issue had been raised on this point and she thought it unfortunate to create laws which also created offences. If in future there was a charge of a criminal nature brought against a doctor for performing a sterilization, then there would be a case for considering whether it should be legalized. " But as the situation is completely fluid," she said, " and nobody has ever suffered from the absence of such a law, I deprecate the raising of the issue at all."

Dr. Gibson said that the Representative Body must have the last word on this matter. He could accept it as a subject that the Medical Science, Education, and Research Committee and the Central Ethical Committee should examine and on which a report could be made to the Representative Body in 1968.

The motion was carried as a reference to the Council.

Professional Independence and Freedom of Choice

Dr. G. R. Smith (Birmingham) moved: " That this Meeting agrees that the policy of the Association shall be: (i) freedom of the doctor to choose his patient ; (ii) freedom for the patient to choose his doctor ; (iii) freedom for the doctor in his clinical assessment and therapy ; (iv) that the doctor be entitled to a fee from his patient where the payment made by the State is considered by the profession to be inadequate for the services rendered ; (v) freedom for the patient to avail himself of all or any relevant services available within the framework of the welfare state."

Dr. Gibson said that he accepted items (i), (ii), and (iii). They were already Association policy.

Dr. Smith explained that, though doctors in this country accepted many of these things as " just one of those things " and nothing to worry about, these were the very points that doctors in Europe at present were coming under pressure about from their own Governments.

Item (iv) was important. " It is time the profession in this country stood up and said, ' We are professional men. These are our fees. If the State will only pay this proportion of our fees then the patient pays the remainder.' " The profession in this country had failed for too long to stand on principles. This was a principle on which it could no longer afford not to stand.

With regard to the fifth item, time and again representatives came to the A.R.M. and discussed drugs for private patients. He preferred to talk about drugs for all patients.

The spirit in which he put these items was " The B.M.A. shall not enter into any negotiations nor conclude any agreements that are in any way contrary to these freedoms."

Dr. K. S. Maurice-Smith (Isle of Ely) said he hoped that, if nothing else, a young man coming for the first time to the A.R.M. would learn that the one precious thing the medical profession must never give up was freedom.

Dr. Gibson said that the principle that a doctor was entitled to a fee from the patient was already B.M.A. policy. A resolution to this effect had been passed at the Annual Representative Meeting in Swansea. If Dr. Smith would accept that the second part of the motion meant that the Council should bring pressure to bear on the Government to ensure that the profession was paid adequately for the services it rendered he had no objection. However, it was difficult to interpret the second half of the motion as presently worded.

Dr. Smith, in reply, asked how long doctors were to go on putting pressure on the Government. When would they start saying, " These are the terms, these are the conditions, this is the medical profession you are talking to, and these are our fees. If you pay this proportion, the other proportion has to be paid by someone else." The spirit of the motion was that the B.M.A. should not enter into any negotiations nor conclude any agreements that were in any way against such freedom. He said that he accepted Dr. Gibson's interpretation of the motion.

The motion was carried.

A motion by N.E. Suffolk, " That this Representative Body reaffirms its utter opposition to an encroachment on a doctor's traditional freedom to prescribe for his patients as he sees fit," was carried without debate.

Index of Drugs in Hospitals

A motion by Finchley, " That the British Pharmaceutical Society index of drugs should be readily available in all hospitals to hospital medical staff and visiting general and specialist practitioners," was also carried without debate.

Publication of Annual Report of Council

Dr. J. M. W. Sedgwick (East Herts) moved: " That in view of the increasing length and complexity of the Annual Report of Council, Council be requested to issue the report in such time so as to provide at least one more week for its consideration."

He said that there had been some difficulty lately in persuading members of his Division who were not members of the executive committee to attend a meeting when the Annual Report of Council was being discussed. This was partly owing to the daunting prospect of trying to digest the whole of the report of 80,000 words. He suggested that the report should first be discussed by the local divisional executive committees, which would draft some motions. Those could then be given prominence in the letter sent round to members, with the proviso that other resolutions could be discussed. That would be impossible in 17 days, but it could be done in 24 days. The Council might have to compress some business, but the change would produce dividends in an increased peripheral participation in medical affairs.

Dr. Gibson said the problem was not so much compressing the work of the Council as of staffing and clerking. The Council would have to compress the timetable by an extra week or fortnight.

The motion was carried.

Duration of Special Representative Meetings

Mr. R. J. Williams (North Glamorgan and Brecknock) formally moved: " That the duration of a Special Representative Meeting should not be decided until the number of motions to be discussed is known."

The motion was carried.

Information Services

Dr. C. C. Lutton (East and Mid-Lothian) moved: " That in the interests of strengthening the services of communication and information the " B.M.A. News " should be developed and published regularly as a professional medical newspaper."

He said that the Association's information services must surely be developed further and brought really up to date. If they had been, there would not have been the incident of the Junior Hospital Doctors' Association on Saturday. The *British Medical Journal* was a wonderful publication for selective readership, but not all its subscribers were members of the British Medical Association. Other organizations provided " medical fringe publications." Surely the B.M.A. should do the same, said Dr. Lutton. Newspapers often made slanderous attacks on the Association and what did the B.M.A. do about it? It turned the other cheek. Many of those publications would go out of business if the B.M.A. had a good publication. They had had a few irregular issues of "B.M.A. News," but he thought the B.M.A. should go further. He did not ask its leaders to run a newspaper, but there would have to be a new voice that would deliver stimulating views. A revolution was taking place in the medical newspaper world, and the Association should get advice on how to produce a news sheet, with advertising, so that there would be little expense to the Association.

Dr. B. D. Morgan Williams (South Warwickshire), endorsing what Dr. Lutton had said, said it might look as though the B.M.A. was trying to keep up with the "Joneses—the fringe journals." Those journals had got a long start, but he thought the B.M.A. could beat them.

Dr. S. Wand said that "B.M.A. News" was costing the Association £1,100 an issue. If the number of issues exceeded six a year the advertising would be likely to fall off, and the cost would be proportionately greater.

Dr. J. L. McCallum (Council) said he thought the matter should be looked at carefully. The cost of a newspaper published regularly would be "pretty high." It would need a lot of work to produce. It had been done by the American Medical Association, but it would cost a lot of money, would need extra staff, and might even clash with the *British Medical Journal.*

Dr. Ronald Gibson said the subject was worrying. Clearly the information services must be strengthened and developed, but there were snags, not only from the point of view of money but also of advertising. Another snag was that, even with a professional editor, the Secretary must have effectual control of material put out.

Dr. Lutton said in reply that the quality of the newspaper depended on its editorial comment, and that meant "journalistic art." He thought the B.M.A. must have something that came out regularly. If the motion was accepted as a reference to the Council no doubt his Division would put it up again next year.

A motion to pass to next business was carried.

The following two motions by Bournemouth were by leave withdrawn:

"That this Meeting believes that the reports of Council proceedings appearing in the *Journal* are unduly limited by space. In view of the fact that, while all members of the Association may attend Council meetings, few have time to do so, this body instructs the Council to maintain for the inspection of members at all times a verbatim report of the proceedings of Council and to arrange for copies of such reports to be made available to any member of the Association on payment of a suitable fee to cover duplicating and postage."

"That this Meeting asks whether agreed minutes are kept of all discussions between representatives of standing committees or of Council and any Minister of the Crown or representatives of his department. If such minutes are not kept this Representative Body instructs Council forthwith to see that this is done and that such minutes are made available to members of Council."

Decisions of Representative Body

A motion by Bournemouth, "That this Representative Body notes with approval the statement by the Chairman of Council that 'the decisions of the Representative Body are sacrosanct' [*Supplement,* 29 October, p. 167], and believes that this body has an important part to play in ensuring that the views of all members of the Association are kept constantly before Council," was carried without debate.

A motion by Exeter, "That this Meeting requests Council to explain why the Resolution No. 330, 'That this Meeting wishes to draw the attention of B.M.A. members to Medical Management Services Ltd.,' passed overwhelmingly by the Representative Body in July 1966 does not appear in the Annual Report of Council," was withdrawn.

Dr. Ronald Gibson thanked Dr. Derek Stevenson and his staff for all that they had done during the past year.

Dr. A. N. Mathias resumed the chair.

Organization Committee: Constitution (Resumed)

The Chairman said that the Agenda Committee had gone into the details of the various motions on the constitution carried on Saturday. There was some conflict in the decisions taken and a complex position had arisen. The Chairman of the Organization Committee would speak to the Meeting in order to present the facts of the position. After that the Meeting would go back to complete the debate on organization.

Statement on Position

Dr. J. S. Noble (Chairman of the Organization Committee) said the motion in the name of East Yorkshire, asking that its memorandum should be referred to the Council, had been passed. It had been agreed not to refer back the report of the Organization Committee. The Representative Body had said that its sovereignty and its power to consider any matters reported to it were paramount, but at the same time it had approved the rationalization of the relationships between the Representative Body and the Council on the one hand and the autonomous committees on the other. The Representative Body had decided that its total size should be about 538 persons. The Meeting had also decided that in future at least 21 elected representatives should come from the hospital junior staff elected from the areas of the regional hospital boards. The Representative Body had approved of the mandatory scheme for flexible allocation to achieve proportional representation in elections. This would be given effect and reviewed at the end of two years. The Meeting had revised By-law 40 in the matter of the Representative Body and also the proposed schedule of the constituencies of the Representative Body. The motion by the Central Consultants and Specialists Committee had been agreed, which laid down that where large constituencies had second and reserved hospital seats on the Representative Body they would be reserved in respect of both senior and junior hospital staff.

The nub of the matter was in the two motions by Rugby on the size of the Representative Body. A further motion (312) by Rugby, which had been carried, had fixed the size at 538—and that figure was to include representatives from the hospital junior staff, 10 appointed by the Council to represent small minorities, and further minority representatives to represent public health, teachers, and so on. The figure of 538 had been intended to be the overall figure, a figure close to the existing Representative Body. An arithmetical formula which controlled the numbers which each Division elected could reduce their total number by the number of new members representing the minorities. The Representative Body wished the size to be 538, but the by-laws which it had amended would produce a Representative Body of between 625 and 629 members. The Solicitor had advised that the by-laws were the overriding factor.

Consequences of Decisions

The present scale was one representative for 50–150 members, plus one more for each full 100 thereafter, said Dr. Noble. The motions in the name of Rugby, as amended, proposed to raise the latter figure of 100 to 200. A further consequential amendment had been tabled to the remainder of the report to extend the schedule governing the proportional representation system to include the larger constituencies. That was consequential on the Representative Body's decision not to accept the system, but there would already be constituencies with eight, nine, or ten members.

So the positive decision taken on the motion in the name of Rugby, "That the overall size of the Representative Body should be about 538 members," and the negative ones taken on the later motions by Rugby were in conflict. The Representative Body must decide.

If the Representative Body thought that it had inadvertently made a decision that was in conflict with that which it had tried to achieve it could reconsider that decision.

The Chairman asked the Meeting if it wished to reconsider its decision, and pointed out that if it did there must first be a motion properly proposed and seconded to suspend the standing orders.

A motion to suspend standing orders was carried.

Size of Constituencies

Dr. R. P. Hendry (Rugby) moved: "That every U.K. Division having not less than 50 members may continue to form a constituency, but that the basis for the allocation of seats be changed to be one representative for the first 150 members and one additional representative for each additional 200 members or part thereof."

It had been agreed, he said, that the Representative Body should be genuinely representative of all fields of practice. There had to be various special electoral groups to elect the representatives of minorities. But that decision had increased the size of the Representative Body by 48.

Dr. Hendry said he had suggested that by varying the number of members that qualified a Division to appoint a certain number of representatives it was possible to get a Representative Body of whatever size was wished. The motion therefore suggested that if all constituencies retained their existing rights to one representative any Division having 151 or more members would be entitled to a second member. Instead of having one member per 100 seats, a Division would have to have 200 extra members to get an additional seat. Dr. Hendry said it would be hard, on small Divisions to be knocked down from one representative to none. It would not be a terrible hardship for large Divisions to be knocked down from five to four.

Figures in Dispute

Dr. R. L. Luffingham (East Yorkshire) maintained that it was the figures that were in dispute. The first part of the motion was that each United Kingdom Division having not fewer than 50 members should continue to form a constituency, which seemed right. It was agreed the approximate figure on which to work was that the basis for calculation should be changed to one representative. However, to achieve the overall figure of 538 the figure of 150 might have to be altered to 148 or 175. The Organization Committee would have to do that during the coming year. If the Meeting passed on to the motion immediately after in the name of Rugby, which made the motion under discussion mandatory, it would be possible for the Organization Committee to come back the coming year with the figures corrected. "This is what we are suggesting might well be done," said Dr. Luffingham.

Dr. H. B. Muir (Council) said he had no doubt that the Representative Body had grown far too big, a tendency which had continued from year to year. The formula contained in the motion under discussion was in his view a reasonable one.

Dr. W. P. Lambie (Sheffield) said that the Meeting had agreed to accept, somewhat reluctantly, mandatory proportional representation from Divisions. The Meeting had been told that one section, the hospital junior staff, would be in a position to appoint 21 representatives. That must be at least a factor in producing the excessive size of the Body. In his view the Meeting was at present going too far in appeasing certain sections of the profession to the detriment of Divisions, which would lose representation.

Dr. Noble pointed out that the approach to this matter from the start had been to obtain fairness for everyone in achieving a structure truly representative of the whole profession within a reasonable size. As a result of Dr. Hendry's motion there would probably be a tendency for the number of single constituencies to increase, and that would give greater representation from one section of the profession. That would to a certain extent be balanced by the direct representation of hospital junior staff. The formula would be reviewed in two years.

Dr. Hendry explained again that if the motion was not accepted a mathematical impasse would be produced.

The motion was carried by the necessary two-thirds majority.

Amended Clause

Dr. Hendry (Rugby) moved: "That By-law 41 be not deleted but clause (2) be amended thus: Delete words from '. . . for each complete . . .' to end of paragraph and add 'and one more for each complete number of 200 members in excess of 150 members.'"

Dr. Luffingham (East Yorkshire) asked if that was not the amendment of a by-law, for which four weeks' notice was required.

Dr. Hendry (Rugby) said that it would be perfectly simple to say that the motion should be voted on in two parts. He begged leave to withdraw part 1, that the figure be 175 instead of 150. The second part then became a consequential amendment. That made it perfectly legal, because the second part became a consequential amendment which would comply with the decision already made.

Mr. N. Leigh Taylor (Solicitor to the Association) said that it was in order for the proposed amendment to the by-law to be amended in the way it had.

The Chairman ruled that the motion could legally be amended in the sense that it had been moved by Dr. Hendry.

Dr. Noble hoped that the Representative Body would pass the motion.

The motion, as amended, was carried.

The Chairman announced that the suspension of standing orders had now ended.

Elected Members of Council (Continued)

Dr. Doris M. Odlum (Bournemouth) moved: "That this Meeting resolves that 10 members of Council shall be elected annually, as heretofore, by the Representative Body."

This proposal gave an opportunity, she said, to elect members of standing and experience who otherwise would not be on the Representative Body.

Dr. Noble accepted the motion.

Dr. H. S. Howie Wood (Isle of Wight) said that the Representative Body had always been jealous of its right to elect to the Council members who had not been elected by the constituencies and who it thought were deserving to continue to serve. The right should be preserved.

Dr. C. C. Lutton (East and Mid-Lothian) moved as an amendment: "That under the new constitution the members of Council directly elected by the Representative Body be increased from five to ten, of whom not more than seven shall be representatives of constituencies in England, and of these seven not more than four shall be from the same category as defined in the proposed By-law 40 (2)."

He said that if there were to be proportional representation, so that the smaller areas might not be too swamped, it would be reasonable to have seven elected from England, presumably two from Scotland and one from Wales. Northern Ireland should not be forgotten, but it could speak for itself.

Dr. Noble said that two for Scotland out of the ten was a high proportion, but, subject to the ruling of the Representative Body, he would accept the motion.

Dr. D. L. W. Chapman (Northern Ireland) said that if the representation was to be raised to ten Northern Ireland should have one representative. Dr. J. S. Happel (Council) asked if the motion were not intended to apply to England and Wales only. Dr. Lutton replied that there was obviously doubt about the detail. The intention was that the Representative Body should continue to have the right to elect, and those it elected should come from various parts of the United Kingdom. Dr. B. L. Alexander (Manchester) said that "ten members as heretofore" meant ten members from England and Wales as heretofore.

Dr. R. H. Scott (Norwich) thought that the ten members elected by the Representative Body had nothing to do with geographical areas.

Dr. Doris M. Odlum (Bournemouth) was not in favour of the amendment. The ten were elected on a free vote of the Representative Body as a whole. It was a new idea to introduce proportional representation. Dr. D. J. P. Gray (Exeter) supported the original motion. It was impossible to apply the slide rule to a number as small as ten. Dr. G. R. Outwin (Council) opposed the amendment on the ground that Scotland would be able to have its own representaiton.

The amendment was lost.

Geographical Representation

Dr. W. R. King (North Glamorgan and Brecknock) moved as an amendment: "That, of the five members of Council proposed under the new constitution to be elected at the Annual Representative Meeting, three should be elected by the Representative Body as a whole and one each by the Scottish and Welsh representatives respectively."

He said he presumed that the reduction had been suggested on a basis of the number of the doctors in Wales. That was false reasoning. He pointed out that the geographical conditions in Wales and Scotland made it impossible to maintain efficient contact. Hard rules could not apply where unusual circumstances and terrain prevailed.

Dr. J. S. Ross (Council) said he had seen a lot of Wales and been told much about its difficulties. The Council went all the way with Welsh doctors on this. The B.M.A. was trying to make arrangements for vast improvements in the office in Cardiff and was providing a regional medical secretary to do all the things Wales was asking for.

Dr. Outwin (Council) supported Dr. Ross, and pointed out that the amendment was not a valid one to the motion.

Dr. Doris M. Odlum (Bournemouth) pointed out that if the matter was left to a free vote outstanding doctors in Wales would have an equal chance of election with those in England. The matter must not be treated sectionally.

Dr. Noble said that the Organization Committee would be watching every anomaly.

Dr. W. R. King, in reply, said that in Wales doctors appreciated the fact that Headquarters was taking more interest in them. It had influenced doctors who were nonmembers of the Association. "Having gained this ground," he said, "why voluntarily surrender some of it by removing one member of Council from Wales, thereby weakening the communication between the periphery and Headquarters instead of further strengthening it?"

The amendment was lost.

Dr. B. L. Alexander (Manchester) opposed the motion and hoped that the Representative Body would carry on as it had been doing.

Dr. Doris M. Odlum, in reply, pointed out that the ten members elected by the Representative Body had always been appointed on a free vote, never on a proportional basis. The individuals were chosen entirely on their merits.

The motion, "That this Meeting resolves that ten members of Council shall be elected annually, as heretofore, by the Representative Body," was carried.

President-Elect

The Meeting received Dr. John W. Howie (President-Elect for 1968–9), who was accorded a standing ovation.

Dr. Howie thanked the Meeting for electing him and said: "It will be with great pleasure that I will try to discharge the duties of President in Aberdeen in 1969."

Constitution (Continued)

Constituencies for Election of Members of Council

Dr. Noble formally moved: "That the proposals published in Appendix III of the revised Report on the Constitution of the B.M.A. be amended as follows: (i) The East Herts Division be transferred from Council constituency No. 6 (N.E. Metropolitan) to constituency No. 5 (N.W. Metropolitan), and that an additional member of Council be allocated to Council constituency No. 5. (ii) The Council constituency No. 11 be divided into two—namely, South-western Branch (one representative), Bath, Bristol, and Somerset Branch, and Gloucestershire Branch (two representatives)."

Dr. J. A. Jamieson (West Herts) moved an amendment: "To add, following 'No. 5' in line 7 at the end of the second paragraph, 'and that it be divided into two, namely, (*a*) Bedfordshire, Hertfordshire and Thames Valley (one representative); and (*b*) the remainder (four representatives).'"

The amendment was accepted.

Dr. C. D. L. Lycett (Public Health Committee) moved an amendment: "After the words 'Gloucestershire Branch' add 'Trowbridge Division.'"

Dr. Lycett said the effect of the amendment would be to include the Trowbridge Division in the new constituency for the regional council with Bath and Bristol. It was now the policy to relate B.M.A. regional organization with that of the hospital service. Wiltshire was unusual in being split between three regional hospital boards, each of the B.M.A. Divisions being in a different hospital Division. The Trowbridge Division, which covered West Wiltshire, was firmly linked with Bath and Bristol for hospital and other purposes, and ought to be included in the suggested regional council constituency.

The amendment was carried.

The motion as amended was carried.

Dr. A. E. Loden (Tunbridge Wells) formally moved: "That, with reference to paragraph 213 of the Annual Report of Council, the proposals published in Appendix III of the revised report on the Constitution of the B.M.A. be further amended as follows: That Council constituency No. 7 (South-east Metropolitan) be allocated three members of Council."

The motion was carried.

Dr. Charlotte C. Arnold (Belfast) moved: "That in the proposed new constitution of Council Northern Ireland should have two elected members of Council as hitherto."

Dr. Arnold said that there was concern that the representation of Northern Ireland would be reduced by 50%, from two to one elected member of Council. "How could one representative effectively represent the interests of general practice and the hospital service," asked Dr. Arnold. Northern Ireland was not asking for an extra member but that the Northern Ireland constituency should have two members of Council with full voting rights.

Dr. Noble said Northern Ireland had 1,400 members. They had one representative on the Council. They also had a chairman of the Northern Ireland Committee who as a chairman of a standing committee would be a non-voting member of Council.

Mr. W. Mathews (North-east Ulster) asked the Meeting to compare the Council member ratio in two areas. Area 11, South-western region, with a B.M.A. population of 2,700, had three representatives; Northern Ireland, with 1,400 members, had a representation of one.

The motion was lost.

Chairman of Council

The motion standing in the name of East Yorkshire, "That, with reference to the proposed alteration of By-law 75, the Chairman of Council, or his nominee, be asked to explain to this Meeting why it is proposed that By-law 75 shall be amended when no reference to this change is to be found in the Annual Report of Council, on in the 'Report on the Constitution,'" was, by leave, withdrawn.

A motion standing in the name of East Yorkshire, "That no alteration to By-law 75 along the lines proposed in Appendix XIII of the Annual Report of Council shall be made until this proposal has been fully discussed in Divisions and Council itself, and reaffirms present policy that 'The Chairman of Council shall be elected by the Council from its own number,'" was carried.

Term of Office

Dr. R. L. Luffingham (East Yorkshire) moved: "That the proposed new By-law 65 paragraph 2 be amended by the deletion of the words 'elected under paragraphs (*c*) and (*h*) of By-law 56' in lines 2 and 3; and that the new paragraph 3 be deleted in its entirety; and that the amendment to By-law 65 (*a*) (i) be withdrawn; and that the amendment to By-law 65 (*a*) (iii) be withdrawn."

The motion, said Dr. Luffingham, was a request to the Representative Body to reverse its decision last year, and it dealt with the question of the length of time a member of Council might serve and how often he might be re-elected. It was proposed that a member of the Council should serve for two three-year terms. He would have to be re-elected, and his Division might not be able to "get rid of him for three years." It might have to elect second-best or, if it did not get anybody to stand because nobody wanted to accept the seat, the seat would remain empty for three years. The constituency should have the right to elect its best candidate and to get rid of him if it did not like him at least yearly.

Dr. Noble said it had been approved by the Representative Body that in future elected members of the Council should serve a three-year term, and that after six years' service a member should be ineligible for election for one year. Two terms were considered to be a reasonable time. On the other hand, if a member was really good and contributing to the Association in an outstanding way he could then stand for election by the Representative Body.

Mr. Robert V. Cooke (left), President of the B.M.A., Professor Hamid Ali M. Khan (centre), and Mr. A. Lawrence Abel before they received their honorary degrees at the University of Bristol.

Dr. LUFFINGHAM, in reply, said the policy was a mistake in the sense that the needs, desires, and wishes of the candidate were being put before those of the constituency. He urged the Representative Body to reject the proposals made at Exeter and asked them to support the motion.

The motion failed to achieve the necessary two-thirds majority and was therefore lost.

Dr. LUFFINGHAM (East Yorkshire) moved: "That the proposed new By-law 65A be amended by the deletion of all the words after 'term of office' in line 3."

The motion was lost.

A motion standing in the name of Worcester and Bromsgrove, "That the maximum number of consecutive years' service on the Council for any constituency member should be nine years," was, by leave, withdrawn.

Brains Not Age

Dr. A. M. SPENCER (Worcester and Bromsgrove) moved: "That this Representative Body is of the opinion that membership of Council should cease at the age of 70."

He said that in the interests of the Representative Body as a whole, there should be some upper age limit for the members of Council. Without it the progress of the younger members to the Council might be limited.

Describing it as "an eminently sensible motion," Dr. M. SIM (Birmingham) said the only criticism he had to make of it was that the age should not be 70 but 65. However, 70 had been included in the motion and a start must be made somewhere. In industry, commerce, the health service, and even among the B.M.A.'s excellent officials, the retirement age was 65; but there were some people who seemed to think a certain grace was gained when people attained Council status and that they could go on for ever. What he had said was not to be taken as any criticism of the present Council members; they were extremely good, but what he would like to have would be Council members in their prime.

Dr. J. C. MCCALLUM (Council) said members should be elected on their merits.

Dr. DAVID BROWN (Liverpool) said he had been a member of the Council, and well before the age of 70 he had found his powers failing, his hearing going, and his sight getting poor, and he had found that when he made a speech the Council were bored with him, and when they made speeches he was bored with them. The journey to London became more hazardous, and he felt in his bones that it was time to go, because his colleagues would throw him out anyway. While he was on the Council two of the best members serving with him were Guy Dain and Thomas Horder, and each was over 70. It did not depend on age but on brains.

Dr. A. W. MACARA (Junior Members Forum) moved as an amendment to insert the word "normally" between "should" and "cease."

Dr. NOBLE said if the word "normally" was inserted who was to decide the issue?

The amendment was lost.

Dr. NOBLE said that the motion had great attractions. He believed the Council attained its greatest strength when it combined both young and old in its membership and when it represented the whole profession. He agreed with what Dr. David Brown said.

The motion was lost.

Two Consecutive Terms

Dr. J. B. MACFARLANE (Halifax (with Todmorden)) moved: "That after serving two consecutive terms a member of a central committee (including the Council) or an honorary officer should be ineligible for re-election during a further term."

He said the object of the motion was to fix a limit to the period of service in any office or on any committee and, in fact, as a representative. His Division had been asked to submit its ideas to B.M.A. House, but unfortunately the correspondence took longer than expected and the Division was unable to substitute a motion which appeared as an amendment, which read: "That with the aim of combining the benefits both of reasonable continuity and infusion of new ideas, the Council be requested to investigate the question of terms of office and eligibility for re-election as they affect officers, representatives, and committee members throughout the Association, centrally and locally, and to report the recommendations."

By accepting the proposal the Meeting would bring a fresh point of view into the deliberations of committees and other bodies of the Association. The dissatisfaction of the younger members of the profession and, indeed, much of the apathy generally and lack of interest within the Divisions was due to the feeling—however ill-informed—by those on the periphery that the B.M.A. was in the hands of a self-perpetuating caucus. They saw the same names on the same committees year after year, both centrally and locally.

The amendment having been accepted by the Meeting as the main motion, Dr. NOBLE said he was prepared to accept it if it were made a reference to the Council. The Council, he said, would investigate the question of service on committees.

The motion was passed as a reference to the Council.

Agenda Committee

The following motion by Cumberland was withdrawn: "That under the new constitution the A.R.M. Agenda Committee should have six members directly elected by the Representative Body, exclusive of the Chairman and Deputy Chairman of the Representative Body."

Dr. G. E. CRAWFORD (Liverpool) moved: "That the Agenda Committee should consist of the Chairman and Deputy Chairman of the Representative Body, the Chairman of Council, and six representatives not members of standing committees."

He said that the Meeting had reaffirmed that the Representative Body was the policy-making body of the Association. The most important committee of the Representative Body was its Agenda Committee. He had no criticism of the present Agenda Committee, but he believed that in the coming years it was going to have to take more and more unpopular decisions. It would be to the advantage of the Representative Body that the Agenda Committee should be completely independent of any other committee and responsible only to the Representative Body.

Dr. A. M. RANKIN (Council) supported the motion.

Dr. NOBLE said that the composition of the Agenda Committee was a matter for the Representative Body to decide.

Dr. CRAWFORD, in reply, said that Liverpool wanted the Agenda Committee to be completely independent and subject only to the Representative Body.

The motion was lost.

Approval of Revised Report on Constitution

Dr. NOBLE formally moved: "That, subject to any amendments arising out of the decisions of the Meeting, the revised Report on the Constitution of the B.M.A. be approved."

Dr. Noble thanked Dr. David Gullick for the tremendous work he had done on the Constitution Report.

Dr. B. TAYLOR (Tower Hamlets) moved an amendment: "That in the event of the amalgamation of Redbridge and Stratford Divisions, Council has power to make the necessary constituency adjustments without delay."

Dr. NOBLE accepted the amendment, but thought that in view of earlier decisions already taken it had no significance.

The amendment was carried.

Request for Delay

Dr. R. L. LUFFINGHAM (East Yorkshire) moved an amendment: "That, with reference to paragraph 213, recommendation 3, of the Annual Report of Council, no implementation of alterations to the present constitution provided for in the Annual Report of Council and the Report on the Constitution (*B.M.J.*, 26 November 1966) shall take place before the Memorandum on the Reform of the Constitution submitted by the East Yorkshire Branch shall have been considered by Council, and reported on at the A.R.M. 1968. Provided that nothing in this resolution shall prohibit the coming into force of the following:

> "By-laws 1, 9, 10, 16, 43, 59, 60A, 68, and sections (*d*), (*e*), (*f*), (*g*), (*h*), and (*i*) of 56. Or the alterations to the proposed Second Schedule, or the Amendment of Standing Orders of the Representative Body 9, 11, and 29."

Dr. Luffingham said that earlier he had prepared a speech to the effect that "We should fight on the beaches of Eastbourne, the fields of Leicester and of Aberdeen, and in the streets of Tavistock Square and should not give in"—a speech which was no longer necessary because the Representative Body had produced the delay that East Yorkshire had thought desirable. Substantial changes had been made in the revised report on the constitution. Some of the decisions could not be carried out: it would be impossible to get 14 additional chairmen of standing committees into the Council Chamber in 1967.

One very important constitutional change had been allowed to disappear altogether. The Chairman of the General Medical Services Committee had said, without a murmur of dissent from anyone, that the G.M.S. constitutional proposals had been withdrawn. The profession was moving much nearer a cohesive situation. The points of difference were much nearer to being ironed out than they had been previously. He sincerely believed that if the amendment was passed there would be no more delay than was already inevitable as a result of decisions already taken on the very same day.

Dr. Ronald Gibson said that if the amendment was passed it would put the clock back another year. He hoped the Representative Body would show its sovereignty and instruct the Council to get on without further delay.

Dr. D. C. Roberts (Hendon) opposed the amendment. He said that the Meeting had given its instructions as to what it wanted for the new constitution. It was now a matter that must be left to those who had been elected to work it out. Dr. G. R. Outwin (Council) said that the mistakes that had been about to be made had been pointed out, but the changes made could not be written into the constitution just like that. How it looked in full must be examined again next year. It might be that the clock was being put back, but that had already been done.

Dr. Noble said that on the third day of the Meeting there had been a recommendation from East Yorkshire that the report on the constitution should be referred back. The motion had been defeated. Did the Meeting wish to return to the matter again next year? Dr. Noble said he believed the majority of representatives had made up their minds.

Dr. Luffingham, in reply, said that the constitution had lasted for 60 years, and yet in the last 60 months it had suddenly become so unsatisfactory that another 12 months to look at it could not be afforded. That he could not accept. He sincerely believed that there would be delay year after year as the effects of the small print in the constitution became apparent. He urged the Meeting to accept the amendment.

The amendment was lost.

The motion by the Chairman of the Organization Committee was carried, together with the Tower Hamlets amendment.

That concluded the debate on the constitution of the B.M.A.

•

Autonomous Bodies

Dr. Noble formally moved: "That the autonomous powers of the General Medical Services Committee and the Central Consultants and Specialists Committee be renewed in respect of the year 1967–8 on the understanding that no action be taken by either of these Committees which may prejudice the interests of another part of the profession without full prior consultation with the interests concerned and that their autonomous powers will be used so as to expedite the work of the Association."

The motion was carried without debate.

Amendments to Articles, By-laws, and Standing Orders

Dr. Noble formally moved: "That the Schedule to the By-laws relating to the Organization Committee be amended so as to make it clear that the member of Council elected by the Junior Members Forum is an *ex officio* member of the Organization Committee."

The motion was carried.

Card Vote at Representative Meetings

Dr. Noble formally moved: "That By-law 52 (4) be amended by the addition of the words 'and of the Hospital Junior Staffs Group Council and of the Assistants and Young Practitioners Subcommittee of the General Medical Services Committee' immediately following the words 'Central Consultants and Specialists Committee.'"

The motion was carried.

Dr. Noble formally moved: "That, subject to any amendment arising out of the decisions of the Meeting, the Articles, By-laws, Schedule to the By-laws of the Association, and the Standing Orders of the Representative Body be altered in the manner shown in Appendix XIII, and that Council be instructed to submit the amendments of Articles concerned to an Extraordinary General Meeting of the Association."

The motion was carried.

Dr. Noble moved: "That the remainder of the Annual Report of Council under 'Organization' be approved."

The motion was carried.

Change of Address Cards

Dr. F. O. Wells (East Suffolk) moved: "That this Meeting notes with regret that many junior and newly qualified members of the Association are frequently not notified of the activities of the Division or Branch in the area in which they are working, and suggests that it would be in the interests of the Association to encourage better contact with these members by issuing them with pre-paid notification cards for them to notify the Association of their changes of address, which notification should be passed with a minimum of delay to the appropriate Division or Branch Secretary."

The motion was carried as a reference to the Council.

•

Annual Report of Council

Dr. J. M. Wallace (City of Aberdeen) moved: "That a shortened and summarized version of the Annual Report of Council be published and circularized to all members in addition to the publication of the full report in the *British Medical Journal.*"

He said that the Annual Report was one of the most important documents produced by the Association, but it got lengthier every year. This year it ran to 52 pages, plus 20 pages of appendices, and it was difficult to find time to read it. Dr. Wallace said surely it was in the interests of the B.M.A. that a shortened version should be published, which would more readily come to the attention of all doctors. It was a document that needed to be read by all doctors. He would be prepared to take the motion as a reference to the Council, if that would help.

Dr. Ronald Gibson said he preferred not to take the motion as a reference to the Council, or indeed to take it at all, because it was an impossible exercise, even if it were a desirable one. Who would do the summarizing of the report? The summary might suit him, but it might not suit various standing committees. He hoped the Meeting would not refer the motion to Council.

Dr. S. Wand supported Dr. Gibson and added that summarizing the report would be "a very expensive exercise."

Dr. Wallace, in reply, submitted that the suggestion should at least be considered.

The motion was lost.

(The A.R.M. thereupon adjourned for the Annual General Meeting of the Association and an Extraordinary General Meeting.)

Mr. A. Lawrence Abel (left) receives the honorary degree of Doctor of Medicine conferred on him by the Duke of Beaufort, Chancellor of Bristol University, in the Great Hall of the University.

Medical Science, Education, and Research

Mr. A. LAWRENCE ABEL (Chairman) moved: "That the Annual Report of Council under 'Medical Science, Education, and Research' (Doc. A.R.M. 2, paragraphs 181–194) be received."

He said that the B.M.A. had organized successful one-day meetings on the subject of computers in medicine. It was hoped to arrange follow-on courses, probably of four days' duration. Mr. Lawrence Abel said that there had also been a joint symposium during the winter with the Institute of Mathematics on the application of mathematical and computer methods to problems in medicine. The Annual Report of Council had already stressed the successful one-day conference on first aid held at B.M.A. House, and a similar conference in Glasgow was to be held at the beginning of the new session.

Work in the Nuffield Library had increased. B.M.A. lectures were available to postgraduate medical centres under the sponsorship of B.M.A. Divisions, to Branches, and to medical students' societies.

Mr. Lawrence Abel called attention to the B.M.A. Research Fellowship, which it was hoped would attract candidates in the registrar grade. The Fellowship was to the value of £1,500 a year plus superannuation contributions and expenses.

The year before the Representative Body had approved the recommendations of the Interdepartmental Committee on Drug Addiction (Brain Committee). One of the recommendations had been that a number of special treatment centres should be set up, particularly in the London area. It had also been agreed that the prescribing of heroin and cocaine to addicts should be limited to doctors on the staff of those treatment centres. It had been made clear that the centres might be either governmental or privately run. Mr. Lawrence Abel said that there had been discussions in his committee about those patients who might have to remain indefinitely under the care of treatment centres, and it was thought that there should be proper facilities for long-term rehabilitation, both psychological and physical. These were essential if a relapse was to be avoided.

The motion was carried.

B.M.A. Lectures

Dr. R. W. BIAGI (West Denbigh and Flint) moved: "That the Association should consider the relationship between postgraduate centres, where these exist, and B.M.A. activities, particularly the function of the annual lecture in the Division. The scope of the lecture should be enlarged so that the visiting lecturer can participate in the activities of these centres at the time of the visit, by prior consultation where possible."

Dr. Biagi said that East Yorkshire had suggested that the political functions of the Association should be separated from the clinical and scientific functions. The separation was taking place, said Dr. Biagi. It was difficult to arrange a medico-political meeting in some parts of the country in B.M.A. offices, as so often these offices were now used by the postgraduate teaching units of medical institutions. The B.M.A. should increase its influence in the field of postgraduate education, and as a first move B.M.A. lecturers should lecture to postgraduate medical institutions.

The motion was carried.

First Aid

A motion standing in the name of Derby, "That this Meeting considers that the present manual of instruction issued to first aiders (paragraph 186) needs drastic alteration, and that Council be requested to make representations to the appropriate authorities," was carried.

Accident Prevention

A motion standing in the name of St. Marylebone, "That this Meeting recommends that much more effort be expended in ensuring that crash helmets are worn by motor cyclists, and in publicizing the advice of the Medical Commission on Accident Prevention of the Royal College of Physicians and Surgeons to this effect," was carried.

Commonwealth Corresponding Members

The following motion by the Chairman of the Committee on Medical Science, Education, and Research, "That the provisions of the by-laws relating to Honorary Members be extended to include 'Commonwealth Corresponding Members' elected by the Council on the nomination of the Committee on Medical Science, Education, and Research," was carried.

Drug Addiction

Mr. LAWRENCE ABEL (speaking as representative of the St. Marylebone Division) moved: "That this Meeting recommends that when a patient has completed treatment for drug addiction there should be adequate provision for his rehabilitation and follow-up on a long-term basis."

He said that information was available to show that many people who had been taken off drugs by doctors working in the various drug centres were thrown back into their old surroundings, and little rehabilitation work was being carried out. It took a minimum of six months and often twelve months or longer for the successful rehabilitation of a patient. The Brain Committee had strongly advised the Government in July 1965 that rehabilitation centres should be set up. This had not been done in the National Health Service or anywhere else, except two places, so far as he knew.

Dr. R. C. GREENBERG (Finchley) moved as an amendment: "To add the words 'such rehabilitation should be directed by persons with proper skills and experience in this field.'"

He pointed out that a great many people were jumping into this field who had no real practical knowledge of drug addiction There was a real danger that more harm than good would be done unless the work was directed and co-ordinated by experienced people.

The amendment was carried.

A further amendment was also accepted: "To add the words 'and that the Government be urged to implement all the other recommendations of the Brain Committee's report of 31 July 1965.'"

The motion as amended was carried.

Dr. R. MAGGS (Eastbourne) moved on behalf of North Devon: "That the prescribing, manufacturing, and import of amphetamine drugs be prohibited."

He said that the motion was the result of more than 30 years' experience of the drug by the profession and the public. Both medical and social problems originated from this drug. It could be said that as a result of medical practice the social problem was being unnecessarily complicated. Moreover, there was clear evidence that continued medical prescribing had been associated through the years with an ever-increasing incidence of side-effects which doctors now had to treat. "The position regarding amphetamines," Dr. Maggs asserted, "is, in my view, quite out of control both medically and socially."

"Soft" to "Hard"

Dr. P. H. CONNELL, of the Maudsley Hospital, said there was evidence that patients moved from taking "soft" drugs to taking "hard" drugs. That brought further medical problems. He stressed that the Dangerous Drugs Act was purposely not aimed at the amphetamine group of drugs. Dr. Connell also said that there was no possibility whatever of the treatment centres being adequately staffed in the near future. The profession had its time cut out dealing with the current problems, and clearly there was an urgent need for research. What could be done about the situation, asked Dr. Connell. The only approach the profession could take was to tell the country that doctors could no longer hold responsibility for these drugs until a treatment had been found for addiction.

Dr. W. A. H. STEVENSON (St. Marylebone) opposed the motion because it called for the abolition of the manufacture of the drug. He pointed out that it had a limited but definite use in psychiatry and also anaesthesia, which no other drug had been able to replace. He considered it a pity if doctors should refuse to take responsibility for a drug. If something was prohibited a black market trade usually sprang up and he therefore felt strongly that these drugs should be controlled.

Dr. C. P. WALLACE (Council) opposed the motion on the grounds that it represented a negative approach.

Asserting that the recommendation went too far, Dr. F. STEEL (Finchley) asked why not ban other products like alcohol, tobacco, and barbiturates. Suddenly something that had been prescribed for years had become a deadly dangerous drug. There was also the more evil aspect of the problem. If the motion was passed doctors would force the sale of amphetamine drugs underground into the hands of the drug pedlars, who would carry on a vicious black market.

Dr. MAGGS, in reply, said that during the discussion the value of amphetamine in anaesthetics had been mentioned. The fact was that there was no justification for the continuation of amphetamine as a drug. It produced ever-increasing side-effects for which there was no ready treatment.

Dr. RONALD GIBSON said he was a member of the Home Office Advisory Committee on drug addiction and it was aware of these motions. The committee had met last week, and, particularly in respect of amphetamine, it was awaiting the result of the Representative Body's deliberations.

The motion was lost.

Dr. A. M. MAIDEN thereupon took the chair.

The motion in the name of Tunbridge Wells, "That the Representative Body wishes to draw to the attention of all medical practitioners the dangers inherent in the use of the amphetamine group of drugs," was, by leave, withdrawn.

Amphetamines

Dr. W. A. H. STEVENSON (St. Marylebone) moved: "That this Meeting recommends that the manufacture, storage, and supply of the amphetamine group of drugs should be under much more adequate control —subject always, of course, to the right of a medically qualified practitioner to prescribe what he considers necessary for his patients."

Dr. DORIS M. ODLUM (Bournemouth) moved as an amendment: "To remove the words 'much more adequate control' and substitute 'under schedule 1.'"

Dr. Odlum said that as a psychiatrist she thought there was a place for amphetamine in limited circumstances, but that if it was placed under Schedule 1 it would prevent use of the drug being abused and at the same time retain its use for the occasions when there was no alternative.

The amendment was carried.

Later in the Meeting standing orders were suspended to allow further debate on the St. Marylebone motion as amended by Bournemouth.

Dr. R. C. GREENBERG (Finchley) moved as a further amendment: "To add the words 'and other drugs widely prescribed for slimming and barbiturates.'"

He said he did not think it was widely enough recognized by doctors and patients that addiction to drugs prescribed for slimming was very common.

This amendment was lost, and the motion, as amended by the first amendment, was passed without dissent.

Penalties for Peddling

Dr. P. J. BURROWS (South Bedfordshire) moved: "That this Meeting views with concern the increase in drug addiction, and recommends that the laws against drug peddling and the penalties for this crime be far more rigorously enforced."

He said that nearly every day the national press had a colourful story on the subject of drug addiction. All were concerned with the increasing use of drugs by young people. Whereas the Home Office knew the approximate number of people taking "hard" drugs the numbers taking amphetamines or "soft" drugs was not known. One of the dangers of taking "soft" drugs was that it brought the teenager into contact with the less savoury characters who peddled cocaine and heroin. Pedlars made fantastic profits and caused untold human suffering. They were also difficult to catch.

Mr. LAWRENCE ABEL said that he had been told that in the State of Ohio a drug pedlar got a minimum of 20 years and a maximum of 40 years in prison, and as a result drug addiction had virtually been stamped out in that State. If English law allowed such sentences to be passed on drug pedlars only two or three convictions would do a great deal to stop the menace.

The motion was carried without dissent.

Mr. LAWRENCE ABEL moved: "That the remainder of the Annual Report of Council under 'Medical Science, Education, and Research' be approved."

The motion was carried.

Other Motions on Medical Science

The motion in the name of Croydon, "That this Meeting urges Council to take whatever steps it considers necessary to publicize the 1965 British Standard Specification on thermometers agreed by representatives of the profession distinguishing the average 'normal' temperature at 98.6° F. (37° C.)," was carried as a reference to Council.

The following motion in the name of St. Marylebone, "That this Meeting wishes to reaffirm the decision of the A.R.M., 1961, which was finally stressed by the World Health Organization to ensure that patients are not used as experimental guinea-pigs without their full knowledge and consent. This consent should be given only in circumstances of complete freedom," was, by leave, withdrawn.

A motion in the name of Exeter, "That this Meeting feels it desirable when writing prescriptions for scheduled poisons to put the quantity prescribed in words to prevent subsequent unauthorized alteration," was carried as a reference to the Council.

A motion in the name of Medway and Gravesend, "That this A.R.M. instructs Council to press for the inclusion of postgraduate studies as part of the official field of medical education and that postgraduate centres, particularly those specializing in obstetrics, should be given official status and the finance needed to recruit the necessary staff and to maintain research and teaching facilities," was accepted without discussion.

"Family Doctor"

Dr. CATHERINE M. GRAY (Chairman of the Family Doctor Committee) moved: "That the Annual Report of Council under 'Family Doctor' (Doc. A.R.M. 2, paragraph 165) be received."

Dr. Gray paid tribute to the work of the late Dr. Harvey Flack, to whose skill as an editor and determination the Association owed its present position in the field of health education.

Family Doctor had run for almost 16 years, said Dr. Gray. For seven years, until 1966, Dr. Annis Gillie had been the very able chairman of the Family Doctor Committee. When *Family Doctor* had ceased publication in February 1967 the Council had decided that a full Committee was no longer necessary, but that it was essential that the "Family Doctor" project should continue. The Association must press forward in health education and "Family Doctor" publications must go on and expand. The Council had decided that it could best be carried out by a small managerial board of three members—the Chairman of Council, the Treasurer, and Dr. Gray herself. It had been considered adequate to appoint a part-time rather than a full-time editor. Dr. Gray was pleased to tell the Meeting that Dr. Trevor Weston had been appointed. Dr. Weston had received his medical education at St. Bartholomew's Hospital and was a Butterworth Gold Medallist in 1959. He had had considerable experience in both medical practice and medical journalism. Dr. Gray wished Dr. Weston every success in the future.

On the booklet "Health on Holiday," Dr. Gray said that unfortunately restrictions on holiday travel had delayed the decision to print, and subsequently technical difficulties had prevented publication in time for the holiday season.

The motion was carried.

"British Medical Journal"

Dr. J. G. M. HAMILTON (Chairman of the Journal Committee) moved: "That the Annual Report of Council under 'British Medical Journal' (Doc. A.R.M. 2, paragraph 164) be received."

Dr. Hamilton reminded the Meeting that in 1966 he had reported that arrangements were being made for the *B.M.J.* to be printed and distributed in Australia. This had started in January 1967. The enterprise was progressing, and it had enabled subscribers in Australia and New Zealand to see the *British Medical Journal* within a few days of its publication in London.

The *B.M.J.* and its associated specialist journals had shown without exception in the past 12 months an increase in circulation. They covered the whole world, and had a reputation that stood higher than ever.

Dr. Hamilton congratulated the Editor and his staff.

Selective Reporting

Dr. F. O. WELLS (East Suffolk) moved: "That this Meeting regrets that the reporting of the proceedings of Council and of the General Medical Services Committee in the *British Medical Journal* appears to be selective, and suggests that complete reporting of these proceedings should be undertaken either by the *British Medical Journal* or by an independent medical publication."

Dr. Wells said the motion was not in any way intended to censure the *British Medical Journal*. There had been occasions when the reporting of the proceedings of the Council and of the G.M.S. Committee had been misleading, as parts of the debates had been left unreported. He thought there should be available some complete record of the proceedings so that members who wished to read it could do so. How such reporting could be done was best left to the *Journal* department to decide. It should be done as cheaply as possible, or for a fee if necessary.

Dr. HAMILTON observed that by definition reporting was selective. The suggestion from East Suffolk that the *Journal* should publish verbatim reports could not be accepted. Such reporting would be "astronomically expensive" and would leave no editorial responsibility.

Dr. S. WAND said that in connexion with a later motion he would give figures of the cost of such an exercise which would surprise the Meeting. That had to be measured against the need of the Association to use its money to the best advantage.

Dr. WELLS, in reply, said that the motion by North Glamorgan and Brecknock under "Information Services" suggested a medical "Hansard." He reiterated what he had said in moving the motion: it should be done as cheaply as possible and for a fee if necessary. He proposed a reference to the Council so that it could report next year.

Dr. HAMILTON thought a reference to the Council would be a waste of time and money.

The motion was lost.

Information Services

The CHAIRMAN formally moved a motion by North Glamorgan and Brecknock: "That the B.M.A. should print, for sale to members of the profession if necessary, a 'Medical Hansard,' reporting verbatim the proceedings of Council, the G.M.S.C., and the C.C. and S.C."

Dr. Wand explained that this proposal had been costed. The figures showed that if a separate "Hansard" was produced it would cost at least £18,000 to £19,000 a year. The cost of reporting, transcribing, proof-reading, and so on for this type of production was fantastic. The cost of producing it in the *Journal,* because of the increased cost of paper, postage, and so on, would bring the figure up to about £46,000 a year.

Dr. E. V. Kuenssberg (City of Edinburgh) asked, "What do we want all this money spent for? For unproductive words, for paper? I thought the B.M.A. had a purpose, the purpose being the advancement of science and learning."

Dr. Outwin (Council) emphasized that the motion merely asked for a verbatim report of proceedings of the Council and various committees. That should not be difficult and he thought the publication expense need not be great.

Dr. Hamilton explained that the parliamentary *Hansard* had been taken as the standard when this proposal had been considered. There were approximately 18 G.M.S. Committee meetings, 11 Council meetings, and 7 C.C. and S. Committee meetings during the year. That meant 37,500 words per day to be recorded. That was a costly job. Dr. Outwin was misleading the Representative Body if he thought it could be done on the cheap.

The motion was lost by a large majority.

Dr. Hamilton moved: "That the remainder of the Annual Report of Council under 'British Medical Journal' be approved."

The motion was carried.

Tribute to Dr. Hamilton

The Chairman announced that Dr. Hamilton was not putting himself up for election again as chairman of the Journal Committee. He had held the position for many years.

Dr. Hamilton was accorded a standing ovation.

Medical Teachers and Research Workers

Professor I. Rannie (Newcastle upon Tyne), speaking in the absence of the Chairman of the Committee, Dr. K. S. Zinnemann) moved: "That the Annual Report of Council under 'Full-time Medical Teachers and Research Workers' (Doc. A.R.M. 2, paragraphs 123–127) be received."

He said that the Meeting had already heard from the Chairman of Council that the clinical teachers had received their increased remuneration in full at the end of the "freeze." The increase had not been phased. He emphasized that that was largely due to the energetic intervention of the B.M.A. deputation led by the Chairman of Council.

Professor Rannie said that in future, all university teachers were to have their remuneration referred to the Prices and Incomes Board. There would be a special panel of the board to consider the remuneration of medical teachers which would consult with the Review Body, but which might report at an entirely different time. That could lead to one section of the profession being out of step with other doctors as had happened recently.

There had still been no agreement with the University Grants Committee about special responsibility payments. There was a certain amount of semantic difficulty here. University medical teachers considered that the posts they held in themselves merited special responsibility payments. The U.G.C. said they were payments given for people who had posts of special responsibility. It really meant that university medical teachers did not get this payment until they had reached the top of their salary scale, and then it was given in increments.

Remuneration of Clinical Teachers

A motion by Newcastle upon Tyne, "That this Meeting wishes to thank Council for its continuing support given to the standing committee for Full-time Medical Teachers and Research Workers in this Committee's efforts to obtain appropriate and just levels of remuneration for medical clinical teachers who were caught in the prices and incomes freeze," was carried.

A motion by Newcastle upon Tyne, "That this Meeting requests Council to continue to press for the inclusion of medical clinical teachers in the remit of the Kindersley Review Body," was carried.

Professor Rannie (Newcastle upon Tyne) formally moved: "That the remainder of the Annual Report of Council under 'Full-time Medical Teachers and Research Workers' be approved."

The motion was carried.

Armed Forces

Major-General J. C. Barnetson (Chairman of the Armed Forces Committee) moved: "That the Annual Report of Council under 'Armed Forces' (Doc. A.R.M. 2, paras. 203–205) be received." This was agreed to.

Referring to the remuneration difficulties he said that by applying sanctions and blackballing recruitment into the medical Services the Council had done all that it could do.

His second point was that, subsequent to the Annual Report of Council going to press, a working party had been set up, comprising Air Marshal Sir Richard Nelson, D.G.M.S., Royal Air Force, Surgeon Commander B. C. Morson, Royal Naval Volunteer Reserve, Mr. R. Myles Gibson, and himself, to look into pay and terms of doctors in the armed Forces so that they could have recommendations ready when negotiations were reopened. He thanked the Secretary of the Armed Forces Committee, Dr. Gordon Macpherson, for all the hard work he had put in.

Pay Review

A motion by Portsmouth, "That this Meeting deplores the failure to secure proportionate salary increases for Service medical officers and strongly supports Council's action in dissuading doctors from entering this service," was carried.

A motion by Buckinghamshire, "That this Meeting endorses Council's actions concerning Service doctors, but suggests a full review of their terms of service, including remuneration, in readiness for resumption of negotiations," was, by leave, withdrawn.

Constitution of Committee

Major-General Barnetson moved: "That the constitution of the Armed Forces Committee be amended so that the co-option of six members as at present be replaced by the co-option of nine members on the following basis: the Deputy Director General of the Medical Branch of each of the three Services; two representatives of the rank of major/lieutenant commander/squadron leader or below, one of whom should preferably be of specialist status, from the medical branch of each of the Services."

The motion was carried.

Dr. A. N. Mathias resumed the chair.

A motion by the Chairman of the Armed Forces Committee: "That the remainder of the Annual Report of Council under 'Armed Forces' be approved," was carried.

Hospital and Consultant Services

Mr. H. H. Langston (Chairman) moved: "That the Annual Report of Council under 'Hospital and Consultant Services' (Doc. A.R.M. 2, paras. 70–97), Memorandum on Current Problems of Hospital Medical Staff (Appendix III), and Report on Postgraduate Training (Appendix IV) be received."

He said that the Central Consultants and Specialists Committee had never experienced a busier, more momentous, or more stormy year. It was particularly unfortunate that the circumstances and the enormous Agenda of the Meeting had prevented discussion on so many matters. Mr. Langston expressed his thanks to those who had agreed to motions being treated as references to the Council. Those motions would receive the fullest consideration.

He believed that during the year the Committee had reached its full stature, and that its change of name was particularly appropriate. Not only had the Committee's constitution been substantially modified but its responsibility had been fully recognized. The Royal Colleges had accorded it full responsibility for negotiating on terms and conditions of service and for preparing and submitting evidence to the Review Body on remuneration. The Joint Consultants Committee would concern itself primarily with academic standards, teaching, research, and matters such as private practice, but both the C.C. and S. Committee and the Joint Consultants Committee were represented on the new negotiating committee, because terms and conditions of service had inevitably to be related to standards and matters of academic teaching.

The negotiating committee would be directly responsible to the new Central Committee for Hospital Medical Services. Their dental colleagues were also represented on the negotiating committee. Mr. Langston thought it could be said that not only was unity fully preserved but that the new Committee would be fully representative and had full authority to speak for all those who worked in the hospital service. He referred to the Committee's publication known as the "Hospital Charter." It had formed the basis of negotiations with the Ministry during the last six months.

The items discussed and brought to a conclusion with the Ministry, and about which circulars had been issued, were time off duty for hospital junior staff; study leave; sick leave; grants for removal expenses; telephone expenses; rents for married accommodation; locum services. New concessions had been obtained in all these items. The first two were the most important, and for the first time it had been recognized that a hospital junior doctor was entitled to a minimum amount of time off duty and that a doctor in the junior grades was in training, and therefore entitled to a minimum amount of time off for study during the year.

Mr. Langston said that discussions still continued on a number of items. One of those items concerned excessive work load and its identification. He believed that ultimately a satisfactory conclusion would be reached, though in part it was a matter for the Review Body, because it involved extra remuneration.

The most important discussion going on was one that would take a little time, and that was on career structure. It had to be ensured that a young man at the end of his senior house-officer training who wished to make a career in hospital medicine or wanted to have extra training for general practice should be able to get advice. Even more important, he should with the aid of a postgraduate course be able to plan a career, stage by stage, from the time he decided to take up medicine. This had never been possible before. The lack of a career structure was one of the major causes of dissatisfaction with which they had had to deal during the last year.

Negotiating Committee

Dr. T. D. CULBERT (Manchester) moved: "That this Annual Representative Meeting does not approve of the action already taken by the Central Consultants and Specialists Committee in reducing from four to three the numbers of the hospital junior staff representatives who sit on the negotiating committee for all hospital medical staff, which has 15 seats, and asks the C.C. and S. Committee to reconsider this matter in the light of the recommendations initially made by the Joint Consultants Committee."

It was very important that the Representative Body should support the motion, Dr. Culbert said. On the "committee of nine" which had been negotiating for hospital staffs with the Ministry there had been four junior representatives. The Joint Consultants Committee had recommended that on the permanent negotiating committee of 15 there should still be four hospital junior staff representatives. The C.C. and S. Committee, however, after discussion, had decided that junior staff representation should be "not less than three," which seemed to open the door to four. The negotiating committee would be up for re-election in October, and Dr. Culbert said that he wanted the Representative Body to see that the original recommendation of the Joint Consultants Committee should be accepted by the Central Committee for Hospital Medical Services (as the C.C. and S. Committee was now named) in the interests of the whole profession.

Dr. B. LIVESLEY (Manchester) wholeheartedly supported the motion as being one vital to the future interests of all hospital staff. He asked the Representative Body to give unanimous support to the motion, not only because of its importance but also to demonstrate unequivocally to all hospital junior staff that action could be taken on their behalf without recourse to a non-B.M.A. association.

Dr. E. A. HARVEY-SMITH (Chairman, Hospital Junior Staffs Group) supported the motion. Dr. J. S. ROSS (Council) said the impression that had been created by reducing the figure from four to three was not a good one among the young doctors. It had to be put right.

Mr. LANGSTON reminded the Meeting that the constitution of the new negotiating committee provided for "not less than three" junior members, which still allowed for another junior being elected into one of the other seats. The present constitution of the committee was provisional and would be reviewed in October.

The motion was carried.

Review Body

The CHAIRMAN moved formally the following motion by Morpeth and Blyth, which was accepted: "That this Meeting instructs Council (*a*) to strive for the abolition of meal charges for hospital medical staff necessarily eating in hospital; (*b*) that hospital medical staff should have their own dining-room."

Mr. H. H. LANGSTON said that this was the Committee's policy. The first part of the motion was a Review Body matter, and it would be pressed very strongly. He understood that the Ministry had advised regional boards to partition off sections of dining-rooms in new hospitals. It was not what had been asked for, but it was something.

The motion was carried.

Current Problems

A motion standing in the name of Southampton, "That with reference to Appendix II of the Annual Report of Council this Representative Meeting congratulates the Central Consultants and Specialists Committee on the clarity and vigour of the memorandum, and urges Council to press for the proposals made with unexampled vigour. Special attention should be given to realistic allowances," was accepted.

Dr. J. C. BROCKLEHURST (Bromley) moved: "That this Meeting welcomes the first joint report of the negotiations with N.H.S. doctors and dentists, which contains many important points. Even, however, on those points where agreement has been reached with the Ministry of Health they regard it as doubtful whether these can be implemented in some areas as certainly they cannot be unless additional finance is provided for the hospitals."

Dr. Brocklehurst said his Division welcomed the "Hospital Charter" and the terms in which it set out important developments, but there seemed no possibility of implementing the changes already agreed with the Minister unless considerably more money became available.

An amendment "to insert the words 'and personnel are' after the word 'finance'" was agreed.

Dr. CULBERT supported the motion because it drew attention to the fact that the whole of the National Health Service was starved of money. Dr. J. R. BENNETT (Council) asked the Representative Body to vote against the motion, not because more staff and money were not needed but because it was saying that the profession might as well not have gone to the Ministry of Health to try to improve the lot of hospital junior staff by obtaining agreements for study leave and so on.

Mr. LANGSTON said it was recognized on both sides that the immediate requirements would be difficult to achieve. It was something the profession had to give thought to.

Dr. BROCKLEHURST, in reply, said hospital medical staff committees had for many years been looking into the matter. It was a vicious circle: both money and manpower were needed.

The motion was carried.

Dr. K. W. BEETHAM (East Yorkshire) moved: "That, with reference to paragraph 75 of the Annual Report of Council, this Representative Body regrets that no opportunity was given to Divisions to discuss the contents of the Hospital Charter before this was submitted to the Minister, and resolves that in future no exercises of this type for any branch of the profession shall be conducted without formal opportunity for discussions in Divisions."

It had been said many times that hospital staffs were inadequately represented. "It seems fantastic when the Hospital Charter was drawn up that it was not sent to Divisions for adequate discussion," said Dr. Beetham. When any negotiations were contemplated involving any section of the profession, those matters should first be discussed at Divisional level.

Mr. LANGSTON said he hoped the Representative Body would reject the motion. The C.C. and S. Committee had had to produce the "charter" as a matter of great urgency. It had involved a great deal of work. The document had been published and acted upon on the express wish of the Council. It had been unanimously supported by all the members of Council, including the representative of East Yorkshire.

Dr. BEETHAM, in reply, said that the motion asked that in future matters that involved a large body of the profession should be discussed at Divisional level. If terms and conditions of service were to be negotiated with the Minister it was surely obvious that those concerned should have a chance to discuss them and to put forward their views.

The motion was carried.

Hospital Junior Staff

Dr. E. A. HARVEY-SMITH (Chairman of the Hospital Junior Staffs Group Council) moved: "That this Meeting earnestly desires a considerable improvement in the terms, conditions, and prospects of all hospital junior staffs, and pledges the full resources of the

Association to that end. In view of the obviously common aim of achieving such improvement it regrets, however, the wasteful division of the efforts of junior staff produced by the duplication of bodies representing this single group of the profession."

He said that there was no doubt that hospital junior staff must have one body that not only represented them but was seen by the periphery to represent them. That body, in his view, must be within the Association and the sooner all junior staff supported it the better, for their own sake. He did not wish to prejudge discussion on the suggestion of a third autonomous stream for hospital junior staff, but that could be seen only in terms of an autonomous standing committee, equivalent in stature and status to the General Medical Services Committee and the Central Consultants and Specialists Committee.

If it was decided that this was the right course, Dr. HARVEY-SMITH asked what would happen to the hospital junior staffs' representation. At present the whole executive committee, 12 members, were on the C.C. and S. Committee. Could junior staff expect any special privileged position on other standing committees if they became a standing committee? It could be that they would lose their 12 seats, as of right, and be reduced to one seat for an observer seat. That would effectively rule them out of a lot of discussion on the C.C. and S. Committee, said Dr. Harvey-Smith. The two important points were, he said, the status of the Hospital Junior Staffs Group in the eyes of the periphery and co-operation and agreement with the consultants in the matter of negotiations. They must go forward together.

The CHAIRMAN formally moved as an amendment: "To delete all words in the motion after the word 'end' in line 4."

Dr. J. R. BENNETT (Council) opposed the amendment. The whole purpose of the motion was served by the second sentence. Already two hours of the Representative Body's time had been wasted because of the duplication of these bodies.

The amendment was lost.

Association's Support

Dr. D. GUTTMAN (Council) said that he wanted to draw the attention of the Representative Body to that part of the motion which pledged the full support of the Association in obtaining improvements in the terms, conditions, and prospects of hospital junior staffs. "In pledging the full resources of the Association for the hospital junior staff, I would ask members of the Representative Body what they themselves can do when they get back to their Divisions to interest the hospital junior staff in their local hospitals and in the affairs of the Association, and in particular to become politically conscious in order to participate in their regional hospital junior staff groups. I would ask the co-operation of the Representative Body in this," said Dr. Guttman.

Mr. LANGSTON said he warmly supported the motion, and he hoped the Meeting would pass it.

Dr. HARVEY-SMITH said he would pledge himself, his executive, and, he was sure, the whole hospital junior staffs group, to see that during the coming year every member of the hospital junior doctors was satisfied.

The motion was carried.

The following motion by Brighton and Mid-Sussex was approved as a reference to Council: "That in view of the unsatisfactory career structure of hospital junior staff, it is proposed that in future 75% of the appointments to the ranks of registrar and senior registrar should be linked to major centres."

The following motion from Mid-Essex was also referred to Council: "That the consultant selection committees should be balanced in order to ensure that the application of the registrar with regional experience is always considered equitably."

Needs of Regional Hospitals

Mr. D. B. BROWN (Mid-Essex) moved: "That there should be proportional representation of regional and teaching hospital consultants on each joint advisory committee for senior registrars."

He said that recently 968 junior doctors had answered a questionary concerning their career intentions. Not only because of pay and terms of service but because of dissatisfaction with postgraduate and vocational training facilities 50% had said they intended to emigrate. Mr. Brown said that of the junior staff who stayed in hospital and wished to become specialists virtually all found that they must work in designated teaching hospitals as senior registrars if they wished to succeed. "May I remind you that, this being the case, most of these young people therefore gravitate to these hospitals as house-surgeons and registrars so as to be known when the senior registrar posts become vacant." So it is we have a situation where these designated teaching hospitals are overstaffed and yet the regional board hospitals serving 80 to 90% of the National Health Service needs of this country are understaffed. Mr. Brown said there were reasons why the present position should not be perpetuated. (1) Many of the large regional hospitals were the postgraduate teaching hospitals of today. (2) They provided enormous clinical and operative experience and so gave better practical training to junior doctors. (3) More consultants were needed and therefore more senior registrars in training were urgently required. (4) As each regional hospital was so poorly staffed compared with the undergraduate teaching hospitals this looked like a Ministry acceptance of two standards of doctor–nurse care of National Health Service patients.

If there were opportunities for a career in regional board hospitals as well as in the large teaching hospitals it would immediately attract many more graduates to them as house-surgeons, senior registrars, and consultants, which would result in those hospitals being more adequately staffed, helping the Exchequer and taxpayer by reducing emigration, and giving the patients a better service.

Mr. LANGSTON said this problem needed examining, and, though he was not entirely happy with the wording of the motion, he was prepared to accept it as a reference to the Council.

The motion was passed as a reference to the Council.

Dr. I. McD. G. STEWART (Blackpool and Fylde) moved: "That Council should concern itself less with the sectional interests of junior hospital staff, but more with the career prospects of the consultant staff."

He said that only about 10% of hospital junior staff intended staying on in the hospital service. But that had not prevented hospital junior doctors from giving a lot of advice. Much of it was inappropriate for patients and for staff, as everyone who worked in a hospital knew. What was the reason for playing to the public ear to such an extent? Was it scarcity value, and because the Government had shown itself willing to offer short-term bribes to this group of workers in the hospital service? The B.M.A. should be wary of ignoring the large body of B.M.A. opinion, which was hardly ever represented, and should refer to the thousands of relatively silent, middle-aged consultants.

Dr. K. W. BEETHAM (East Yorkshire) moved as an amendment, "That Council should concern itself not only with the sectional interests of the junior hospital staff but also with the career prospects of the consultant staff."

He said that the point of the amendment was that it would be undesirable to instruct the Council to become less concerned with the interests of any section of the profession. The Council could, however, show some evidence that it was also interested and concerned about established consultants. That might be the reason why consultants had done relatively badly in recent awards. The consultant was a docile animal, partly because he was established and middle-aged, and maybe he suffered under the secret merit award system. But the fact was that differentials within the consultant body were quite fantastic, the remuneration varied between £3,000 and £10,000, and in addition there was private practice. There were a number of consultants who were becoming concerned about the position, but until, like the hospital junior staff, they made a noise on T.V. and in the newspapers, little notice would be taken of their legitimate grievances.

Mr. LANGSTON accepted the amendment proposed by East Yorkshire.

The amendment was carried as the substantive motion.

Review of Medical Staffing

A motion by Cleveland and Middlesbrough, "That this Representative Body demands that the figures arising from the review of hospital medical staffing is modified, and brought up to date following the Platt Committee Report, should be published," was referred to Council.

Staffing of Accident and Emergency Departments

Dr. A. K. THOULD (Cornwall) said that it was proposed to take a block of motions under this section of the Agenda and refer them to the Council. That was just the sort of thing that many doctors would like to bring to the attention of the Representative Body. These motions were to be passed to the Council without anyone having the opportunity to discuss them. It was for this reason that he begged to dissent.

A motion concerning the staffing of accident and emergency departments from Southampton was accepted as a reference to Council.

Hospital Building Programme

Motions from St. Marylebone and Huddersfield Divisions concerning hospital building were passed as references to the Council.

Postgraduate Training

Mr. D. N. **Menzies** (Liverpool) moved: "That the authorities responsible for setting up committees to control postgraduate training at national and regional levels should be pressed to include a nominee of the Association on each committee."

He said that the B.M.A. was not represented on the central committee for medical education. There was ample reason for the Association to concern itself with postgraduate education. As the Association represented the whole profession it could look upon itself as co-ordinator for the whole profession.

Dr. J. R. **Bennett** (Council) said the Chairman of Council had endeavoured to have the Association represented on this body, but so far unsuccessfully.

Dr. I. Mc. D. G. **Stewart** (Blackpool and Fylde), supported the motion, and Mr. **Langston** hoped the Meeting would strongly support it. His only reservation was that he would have preferred the word in the last sentence to be "nominees" instead of "nominee."

The motion was carried.

Motions Referred

A number of motions dealing with postgraduate training; allocation of distinction awards; medical assistants; care of the young chronic sick; hospital inpatient facilities for juvenile psychiatric patients; hospital medical staff conferences; increased medical student intake; open access to hospital diagnostic departments; physiotherapy; and geriatric hospital beds were accepted as references to the Council.

Disturbed Geriatric Patients

Dr. R. C. **Greenberg** (Finchley) moved: "That this Meeting deplores the lack of facilities for the care of disturbed geriatric patients, and urges the appointment, on an area basis, of a senior doctor from either the hospital or the local authority service who has responsibilitiy for the co-ordination of services for these patients. It requests that representations be made to the Government to provide urgent financial assistance for adequate hospital and local authority care and accommodation, both day and residential."

He said that in his borough of 318,000 people there were 40,000 people over the age of 65. He would expect roughly 2,500 seriously mentally deteriorated, 2,500 mildly mentally deteriorated, and 3,600 severely neurotic old people among them, quite apart from those old people suffering from affective disorders amenable to treatment. Such a problem could never be solved in terms of institutional beds alone. Well over half the mental illness of old age could now be efficiently treated and the patients returned to their homes fit and well. Of the remainder, much could be done by kind, sympathetic, and informed management. This problem required a comprehensive programme involving a wide range of services including day centres, hostels, and supporting services. Dr. Greenberg concluded: "This is a problem that must be taken seriously and must have adequate financial provision and humane and imaginative planning."

The **Chairman** said there was an amendment to add the words "and in the light of recent publicity about alleged cruelty to patients, this Meeting affirms its admiration for and confidence in the nursing profession of this country, who often have to provide nursing care in adverse working conditions."

Mr. **Langston** said he was sure the Representative Body would accept the motion and the amendment.

A motion that the question be now put was carried by the necessary majority.

Dr. **Greenberg** said, in reply, that he had the greatest sympathy with the amendment.

The motion as amended was carried.

Other Motions

A motion standing in the name of Havering, "That this Meeting recommends the use of a standard discharge summary form giving details of the diagnosis, treatment, and follow-up recommendations," was carried as a reference to Council.

The following motion, standing in the name of Waltham Forest, was, by leave, withdrawn: "That, with reference to paragraph 96 of the Annual Report of Council, this Meeting would be grateful to be informed of the Minister of Health's reply to Council representation on this matter."

The following motion by Worcester and Bromsgrove was formally moved and carried without dissent:

"That this Representative Body urges the Ministry of Health and its regional hospital boards to take note of proposals in certain areas to increase population densities, by redistribution, redevelopment, or formation of new towns, and to provide in good time appropriate hospital services for these areas."

Remainder of Report

Mr. **Langston** moved: "That the remainder of the Annual Report of Council under Hospital and Consultant Services be approved."

He thanked the Secretary of the C.C. & S. Committee, Dr. E. Grey-Turner, and others of the staff who had done "a monumental amount of work for the Committee, often working at weekends."

Regret at Short Discussion

Dr. B. **Livesley** (Manchester) formally moved as an amendment: "The addition of the words 'and noting that it is the aim of the Representative Body to represent all sections of the profession, this Meeting regrets the short time available for discussion of hospital affairs.'"

Dr. G. E. **Crawford** (Liverpool) supported the amendment. He told colleagues: "Go to the B.M.A. and let your voices be heard." If such a short time were allotted to the hospital services in debates in the Representative Body more support than ever would be lost.

Dr. A. K. **Thould** (Cornwall) said: "We have seen this afternoon the farcical situation of the rubber-stamping of an entire and important section of motions." There were many matters that representatives would have liked to have discussed in full and to have obtained the views of the Representative Body. But this had not been possible, which was a matter of considerable regret.

Dr. J. S. **Ross** (Council) believed that as a result of the acceptance of the Constitution Committee's proposals such a situation would never arise again. For a whole day matters that had been discussed a fortnight before in the Conference of Representatives of Local Medical Committees had been rediscussed.

Dr. J. C. **Cameron** (Chairman of the G.M.S. Committee) added his regrets. In defence of his Committee he said that he had hurried its business as much as possible.

The amendment was carried.

The motion as amended was carried.

Fee for Cremation Certificates

A motion standing in the name of Liverpool, "That completion of cremation certificates parts B and C attract a fee for all doctors," was carried as a reference to Council.

Domiciliary Consultations

Dr. E. C. G. **Rhind** (Sheffield) moved: "That in the case of whole-time consultants and S.H.M.O.s full fees be paid for the first 42 domiciliary consultations in a quarter."

He pointed out that after 19 years of the National Health Service, despite support from the A.R.M. and the C.C. and S. Committee for the abolition of the eight free domiciliary consultations imposed on whole-time consultants and S.H.M.O.s, the rule still remained in force. This meant that many consultants who performed only a small number of consultations received no extra fees or only a small sum for extra services provided. The ruling applied to the first eight domiciliary consultations carried out in a quarter. A review conducted in 1964 showed that the average number of consultations was 14 and that one-third of all visits did not qualify for payment. "This is one of the best bargains the Ministry has in the Health Service and the highest level of slavery in the hospital service," Dr. Rhind maintained. The Review Body had repeatedly rejected the proposal for the abolition of the eight free consultations and therefore, said Dr. Rhind, Sheffield's motion seemed the best alternative.

Dr. R. A. A. R. **Lawrence** (Derby) moved as an amendment: "That, in the case of whole-time consultants and S.H.M.O.s, all domiciliary consultations should be paid for."

He said that the motion was merely an ingenious attempt to make an injustice tolerable. It did not remove the injustice. By making a ceiling of 200 per annum, which was the policy of the Association, the implication was that some consultants might do too many, which was a distasteful implication.

Mr. W. DRUMMOND (Fife), speaking as a whole-time consultant, opposed the amendment. If implemented it would in theory give whole-timers access to unlimited consultations and unlimited fees, but in point of fact it had been the policy of the C.C. and S. Committee and of the Association to limit the fees to 200 consultations in a year. The amendment cut right across this.

Mr. LANGSTON said he could not accept the amendment. To exceed the ceiling would mean that a consultant would have difficulty in doing his hospital work, as he would be out all the time.

Dr. LAWRENCE repeated that the implication that some full-timers would deliberately go out to do an excessive number of domiciliary visits was distasteful.

The amendment was lost.

Dr. I. McD. G. STEWART (Blackpool and Fylde) opposed the motion, which was a plain invitation to a whole-time service. A man should decide whether he wanted to do whole-time or part-time service and not try to get the best of both worlds.

Mr. LANGSTON said he would accept the motion as a reference to the Council.

The motion was carried as a reference to the Council.

Mileage Allowances

A motion standing in the name of Sheffield, "That this Meeting supports Council in its current negotiations on car mileage allowances in the hospital service," was carried.

Telephone Expenses

A motion standing in the name of Sheffield, "That this Meeting instructs Council to re-examine the question of telephone expenses for all grades of hospital medical staff," was carried.

Consultants and G.P. Units

A motion standing in the name of Dunbartonshire, "That there should be an investigation into a proper method of recognition for the services of a consultant who undertakes work in a general-practitioner unit," was carried as a reference to the Council.

Nursing Staff

Dr. E. H. J. COTTER (East Herts) moved: "That this Meeting deplores the 10% cut in nursing staff imposed by many regional hospital boards. This is disastrous to the morale of the nurses and to the efficiency of the hospital service."

He pointed out that this was not the first cut in the last five years. Taking five years ago as 100%, there had been a 12% cut previously, so this was now a 10% cut on 88%. Regional hospital board hospitals survived with staffs down to 60%, owing to the heroic efforts of the remaining staff. The Representative Body must show its appreciation of the nursing staff's efforts.

Dr. J. C. BROCKLEHURST (Bromley) said that as a result of the recent further arbitrary reduction in a number of hospitals nurses would be lost. In peripheral hospitals nurses were doing far too much work. Wards were sometimes left during the night in the care of nursing auxiliaries.

Mr. LANGSTON pointed out that every new hospital which opened meant more nurses were wanted. The increase in the number of nurses was not keeping pace with the increase in the number of hospitals, or with techniques which required a specially trained nursing staff. An intensive care unit immediately meant more nurses were required. Many regional boards had had to peg their establishments at a figure they regarded as below that desired, said Mr. Langston.

The motion was carried.

Pre-registration Posts

A motion standing in the name of Birmingham, "That this Meeting is of the opinion that any provisionally registered practitioner shall be allowed to take his pre-registration posts in any hospital approved for the purpose, regardless of its geographical location," was carried as a reference to Council.

Drug Addiction

Dr. DORIS M. ODLUM (Bournemouth) referred to the amended resolution, standing in the name of St. Marylebone, which had been passed earlier with regard to the manufacture, storage, and supply of amphetamines. Since then, she and Mr. Abel, the Chairman of the Medical Science, Education, and Research Committee, had talked with the Association of the British Pharmaceutical Industry. They had been advised that the form in which the resolution was passed, that the amphetamines should be put under Schedule 1, would not be helpful, and might even weaken the present position. She asked that the original motion be substituted which would leave the matter open for discussion by the Science Committee, which could report back.

A motion to suspend Standing Orders was carried by the necessary majority.

Dr. DORIS M. ODLUM moved, "That this Meeting recommends that the manufacture, storage, and supply of the amphetamine group of drugs should be under much more adequate control—subject always, of course, to the right of a medically qualified practitioner to prescribe what he considered necessary for his patients."

The motion was carried.

Standing Orders were restored.

Medical Ethics

Dr. S. NOY SCOTT (Chairman of the Central Ethical Committee) moved: "That the Annual Report of Council under 'Medical Ethics' (Doc. A.R.M. 2, paras. 128–136) be received."

He said that it was an understatement to say that the year had not been exactly without incident. In most of what the Committee had done it had tried to be "with it" without upsetting the traditional standards of the profession.

The report was received.

Sharing of Premises

A motion standing in the name of Liverpool, "That this Meeting rejects Advice 1 of paragraph 128 of the Annual Report of Council with regard to the above, and recommends that waiting-rooms should not be shared," was carried as a reference to the Council.

Professional Secrecy

The following motion standing in the name of Rugby was carried as a reference to the Council: "That policy re professional secrecy be rephrased thus: 'It is every practitioner's duty to observe the rule of professional secrecy by refraining from disclosing voluntarily, without the specific written consent of the patient (or his legal guardian), to any third party information which he has learnt in his professional relationship with the patient; and this duty remains even after the death of the patient.' The only exceptions to this rule shall be (*a*) on statutory compulsion, (*b*) for cancer registration (or other research project specifically approved for this purpose by the Association), (*c*) if maintaining secrecy would be gravely detrimental to the interests of the patient."

Disclosure of Specialists' Reports to Life Offices

Dr. D. S. PIPER (Enfield and Potters Bar) moved: "That paragraph 130 of the Annual Report of Council be referred back to the Council."

He said that paragraph 130 dealt with disclosure of specialists' and hospital reports to life offices. It stated that the Council took the view that if a life office wished to see a specialist's report it should make a direct approach to the specialist concerned. The Council considered it undesirable for the complete case notes held either by a hospital or by a general practitioner to be given to a life assurance company even with the consent of the patient. Such notes might be out of date by the time the company received them and, furthermore, case notes often included letters which had passed between general practitioners, specialists, and other specialists. The patient could not effectively consent to the disclosure of such correspondence without the additional consent of the doctors concerned.

His Division had agreed that it was undesirable for life offices to be sent notes and letters about the case concerned. A lot of this information could safely be left to the discretion of the general practitioner to disclose if it was to the patient's advantage for him to do so. This was not unethical, and might lead to the patient obtaining advantageous terms. If paragraph 130 was agreed no pathological or *x*-ray reports could be sent in full to the life offices without the specialist concerned first being consulted and, incidentally, rewarded. If the Council was trying to obtain a fee for the consultants it should say so.

Dr. W. WOOLLEY (Bristol) said that the insurance companies could get all the information they needed in other ways. Old records might be quoted from, but there was no need at all to show the original documents, which had been sent to doctors for an entirely different purpose. Dr. Woolley urged the Meeting to reject the motion.

Dr. J. G. M. HAMILTON (City of Edinburgh) supported the motion. It was the only practical proposition to overturn the recommendation of the Ethical Committee. The proposer's consent to the disclosure of his medical history was always obtained. Dr. Hamilton said that he was very much against hospital case records being sent to anyone but the patient's family doctor. The opinion of a consultant was necessary for the decision of a life office and it might be necessary urgently in order for the patient to obtain insurance for himself. Urgency was often of paramount importance, since the insurance might be required for the cover of a house purchase loan.

Mr. LANGSTON urged the Meeting to reject the motion. Letters sent to a general practitioner by a consultant giving him clinical information about his patient would contain opinions that he was sure the consultant would not wish to be used for other purposes. Mr. Langston had no objection to a general practitioner extracting whatever information he thought appropriate, and making a report.

Dr. NOY SCOTT appealed to the Meeting to reject the motion.

Dr. PIPER, in reply, thought the matter could be left to the discretion of the general practitioners. It might well be to the patient's advantage as well as to his disadvantage, and in his view it had nothing to do with medical ethics.

The motion was lost.

Reference of Patients to Specialists

Dr. NOY SCOTT moved:

"That the amendment approved in 1963 to the 1957 statement on the acceptance of patients be reworded as follows:

"'A practitioner, in whatever form of practice, should take positive steps to satisfy himself that a patient who applies for treatment or advice is not already under the active* care of another practitioner before he accepts him.

"'If he is so satisfied he may accept him as his patient, but his acceptance should be subject to the considerations set out below.

"'A practitioner in any form of specialist practice should not, except in circumstances stated below, accept a patient for examination and advice except on a reference from a general practitioner. If a specialist decides that it would be more appropriate for a patient to be examined not by himself but by a specialist in a different field of practice, the patient should be referred back to the general practitioner.

"'The specialist should ensure that the true position is ascertained at the time an appointment is booked and should ask that an introductory letter be brought.

Exceptions

(a) Emergencies.

(b) Where previous inquiry indicates that the consultation is for refraction examination only.

(c) Where the specialist to whom a patient is referred wishes, as part of his management of the case, to obtain either a confirmatory opinion from another specialist or specialist opinion on a different aspect of the case—e.g., the advice of a radiologist or cardiologist.

(d) Consultations in venereology, either at clinics or in private.

(e) Overseas visitors having no family doctor in the United Kingdom.

(f) Where the delay in reference back to the general practitioner would seriously inconvenience the patient and provided that in such a case the specialist informs the general practitioner at the earliest opportunity of the action he has taken and the reason for it.

"'After the consultation, where further medical care is indicated, and especially where such care is within the province of the general practitioner, the specialist should do all he can to persuade the patient to be referred to a general practitioner to whom a report and advice should be sent in the same way as if the consultation had arisen from a normal reference.

"'A general practitioner receiving such a report should be prepared to accept that the specialist is making a genuine attempt to establish a correct relationship between the patient and his doctor.'"

Dr. F. O. WELLS (East Suffolk) moved an amendment, "That in paragraph (f) there be substituted for the words 'would seriously inconvenience' the words 'would be seriously detrimental to.'"

Dr. Wells wondered if a consultant who discovered a hernia, and this did not concern his specialty, would be able to refer the patient to another consultant without reference back to the general practitioner, just because it would be convenient for the patient. Surely the patient should be referred back to his general practitioner unless the hernia was seriously detrimental to the patient's health?

Dr. NOY SCOTT said that if the condition was detrimental to the patient's health that would come under the "urgent" rule and would be dealt with accordingly. The consultant might be 40, 50, or even 70 miles away, and it would be very inconvenient to go 70 miles and back. That was the only reason that provision had been made under the urgency rule.

Dr. WELLS said he represented a rural area. He felt that a patient would be prepared to go 30 miles there and back if his general practitioner wanted him to see a particular consultant.

The amendment was carried.

The motion as amended was carried.

Dr. A. M. MAIDEN took the chair.

A motion by Birmingham, "That this Meeting agrees that when a gynaecologist considers that a patient, as part of her treatment, requires contraceptive advice, and he has not been asked by her general practitioner to carry this out, he should, except in special circumstances, refer the patient back to her own doctor and not to a family planning clinic, and should, in any case, inform the general practitioner of his action in this matter," was accepted.

Family Planning

The following motion by Liverpool was accepted as a reference to the Council: "That, while endorsing the seven subsections of para. 135 of the Annual Report of Council, this Meeting proposes the following addition: 'When practitioners acting as individuals, or collectively, prescribe an oral or an intrauterine contraceptive they shall remain, in that respect, responsible for the future management of the patient. This shall in no way alter the normal relationship between a general practitioner and a consultant.'"

Dr. NOY SCOTT moved: "That the remainder of the Annual Report of Council under 'Medical Ethics' be approved."

In doing so, he paid tribute to the services of Dr. J. D. J. Havard as secretary of the Central Ethical Committee.

The motion was carried.

Duties and Powers of Central Ethical Committee

A motion by Enfield and Potters Bar, "That this Meeting instructs Council to re-examine the articles, by-laws, and standing orders relating to the duties and powers of the Central Ethical Committee, and to report to the next Annual Meeting of the Representative Body," was carried as a reference to the Council.

Also referred to the Council was a motion by Dartford: "That the resolution of the Central Ethical Committee of the B.M.A., as adopted by the Association in 1959, which reads as follows: 'That there is no ethical objection to the current practice of stating the address, name, and qualifications on letter headings, provided that the qualifications are not displayed for the purpose of calling attention to the imposing collection of degrees,' should have added the words, 'and providing they are genuine professional achievements.'"

This concluded the business of the Central Ethical Committee, and the Meeting accorded Dr. Noy Scott a standing ovation.

Dr. A. N. MATHIAS resumed the chair.

Charities

Dr. R. COVE-SMITH (Chairman of the Charities Committee) moved: "That the Annual Report of Council under 'Charities' (Doc. A.R.M. 2, paras. 260–261) be received."

Dr. Cove-Smith spoke of the need to maintain a regular inflow of funds, particularly by means of seven-year covenants. He said that last year there had been only 42 new covenants, bringing in £2,482. He felt the number ought to be much higher. He asked representatives to give strong support to the Charities Trust Fund.

The motion was carried.

Dr. A. E. LODEN (Tunbridge Wells) moved: "That in view of the poor response to last year's appeal, every medical practitioner in active practice should again be asked to covenant a minimum of £1 to the B.M.A. Charities Trust Fund or to an individual medical charity."

He said that of the 42 new covenants he was glad to say that 25 of them came from Tunbridge Wells. An appeal letter had been sent to every member of the Division, and if there was no reply a follow-up letter had been sent and then a third letter. The Charities Fund had only gained £131 extra from the appeal last year. If every member of the Association covenanted £1 it would bring in £60,000.

Dr. COVE-SMITH said that if every Division could do the same as Tunbridge

---

* The word "active" refers to the patient being at that time under the clinical care of the doctor.

Wells, what an influence it would have on the Association's charitable funds.

The motion was carried.

Dr. COVE-SMITH moved: "That the remainder of the Annual Report of Council under 'Charities' be approved."

He said that he had hoped to make a report to the Meeting about a proposed Medical Charities Year. However, this had not been possible. But progress was being made towards organizing such a year, and in due course the profession would be circularized on the subject.

The motion was approved.

Private Practice

Dr. I. M. JONES (Chairman, Private Practice Committee) moved: "That the Annual Reports of Council under 'Private Practice' (Docs. A.R.M. 2, paras. 137–163, and A.R.M. 2A, para. 290), Report on the Procedure for Selecting Candidates for Election to G.M.C. (Appendix IX), Terms and Conditions of Service of Police Surgeons (Appendix X), and Fees for Certificates and Reports (Appendix XI) be received."

Dr. Jones said that in introducing the report of the Private Practice Committee at this late hour he would be brief, but he would direct the Meeting's attention to two particular items which had been included in the Supplementary Annual Report of Council. The first of those was the discount trading scheme which had been referred to by the Chairman of the Organization Committee. The arrangements for that scheme were well advanced though not yet crystallized. Dr. Jones said that he wanted to make something clear in reply to some letters which he had received expressing anxiety lest money that had been donated for an entirely different purpose should be deviated to this other activity. Independent Medical Services Ltd. had carefully considered that matter, and it had been precisely to allay such anxieties that the decision, which had been supported by the Council of the Association, to finance the discount trading scheme by special subscriptions which would be exclusively devoted to meeting the administrative expenses of the scheme, had been taken.

The second matter to which Dr. Jones wished to draw the Meeting's attention was that during the last few days of June negotiations with the Treasury had been completed on all major items covered by the Treasury agreement relating to part-time medical services. As a result all fees covered by that agreement would be raised by 10%, and the increase would be retrospective to 1 October 1966. That upward revision was in full accord with the arrangements for periodic review made between the Treasury and the Association following the report of the Royal Commission in 1960, and meant that with the sole exception of the six months' standstill imposed upon the nation by the Government, the full betterment factor adjudicated by an independent authority had been applied to those fees. Doctors would be paid at the new rates as from 1 July, and would receive the retrospective pay during the next few weeks.

Private Medical Services

Dr. Jones said it had surprised him and his committee that the dramatic announcement contained in the last paragraph of Section 140 of the Annual Report of Council had produced no motion of either assent or dissent upon the agenda. Dr. Jones thought perhaps its import had not been fully understood by the profession, and he quoted it for the benefit of representatives: "The Council, having reviewed the overall situation, considers that, in view of the totally inadequate finance and medical manpower available to the National Health Service as a result of short-sighted policies by successive Governments, a considerable expansion of private medical services is now imperative in the best interests of the community, and furthermore would encourage doctors to remain in this country. The Council will therefore take all action within its power to encourage participation by the profession in private practice in Britain."

Dr. Jones said he would try to explain why the Council had emphasized the importance of private practice. It was not because doctors wished to be richer, not because patients wished to get a wider choice, not because it sought to create a privileged class of patient, nor because it wanted to damage the National Health Service. "We want to promote private practice," he said, "because we must create new resources. It is not just more money that we require. We need more hospitals, more beds, more kidney machines, more clinics with better facilities. We must have better conditions for the profession so that fewer doctors emigrate. And we will get these things only by tapping unexplored and willing new sources of finance. That is why encouragement must be given to private practice, and that is why, in its obsessional concern with distributing existing resources equally, the Government is following a blind path."

Dr. Jones continued that the imperative necessity was to create new resources. The private, provident product had more to offer than the hard-pressed public purse. Let the Government have the bigness to encourage private practice, he said, and it would see then perhaps a real step being taken to prevent the threatening crumble and crash of the National Health Service.

Was it not lunacy that private clinics, in which patients exercised their choice and paid fees for their medical care, should be flourishing in Russia, in Yugoslavia, and in Socialist Sweden, while in Britain, which had done so much to preserve the essential freedoms for mankind, and established standards by which so much elsewhere was judged, little had been done by the profession to maintain a private sector of medical care, and much had been done to discourage it?

"I am well aware that I am not asking for efforts which will be free from pain, difficulty, and anxiety," declared Dr. Jones. "But . . . it is your duty to ensure that you hand on to those who will follow you . . . something better than that which you yourselves inherited. The public would respond if given a lead. There was a wide variety of choice available through the medium of Independent Medical Services Ltd. and the provident institutions. Each of them had been launched in the face of considerable difficulties and their defects were few. There could not be a town of any size in Britain which could not support a few family doctors providing a first-class service with the support of one of the available schemes.

The motion was approved.

Alternative Medical Services

The following motion by Lambeth was formally moved: "That this Meeting requests Council to introduce an item-of-service insurance scheme for private practice. Such a scheme of insurance for private practice must include medical care within hospitals and nursing-homes and should not be restricted to specialists."

Dr. JONES said there was no reluctance on the part of his committee to fulfil what Lambeth asked, but he must point out that, having taken all the expert advice it had been possible to obtain, the Committee had been advised that a project of that kind could not be set up without a fund of at least £200,000. In the next few months such a scheme would be investigated and the outcome made known to the profession.

The motion was passed as a reference to the Council.

A series of motions under the headings of "Drugs for Private Patients," "Fees for Services Outside the National Health Service," "Car-parking," and "Departmental Committee on Death Certification and Coroners" were approved as references to the Council.

Death Certification and Coroners

Mr. H. A. KIDD (Sutton) moved: "That Council be instructed to set up a new committee which shall include adequate representation of hospital and administrative staff for a review and clarification of the powers invested in coroners, with especial regard to post-mortems on hospital patients."

Mr. Kidd said that this was an important matter for everyone. The Government had been worried about the problem and had set up a committee. The preparation of evidence had been referred to the Forensic Medicine Subcommittee of the B.M.A. The subcommittee consisted of three general practitioners, three pathologists, three police surgeons, and a member of the Coroners' Association, but there was no consultant representative for the specialties of general medicine, general surgery, gynaecology, etc. His Division was concerned about this. The report of the subcommittee submitted to the Government's committee had not been published, and the subcommittee did not represent the consultants or general practitioners in the country, said Mr. Kidd.

Dr. A. SKENE (Council) agreed with almost everything the proposer had said, but asked the Representative Body to reject the motion. It was an instruction to the Council. Clarification and review were undoubtedly necessary on the powers invested in coroners, but the time was not opportune.

Dr. I. M. JONES also asked the Representative Body to reject the motion. He said the setting up of the Brodrick Committee by the Government had been the direct result of a report submitted to and unanimously approved by the Representative Body in 1964. That report had been the result of long discussions in which not only had a special committee of the Association been concerned but every major committee of the Association had been consulted before final approval of the report had been given by the Council and before it had been published in the Annual Report of Council for 1964.

That report had formed the basis of the evidence which had been given to the Brodrick Committee. The Forensic Medicine Subcommittee had been at great pains to give Mr. Kidd an opportunity to put his case to them. Every section of the profession that could be affected was represented in the deputation that gave evidence to the Brodrick Committee. Every point Mr. Kidd had made was fully dealt with in the report.

Mr. KIDD, in reply, said that the report had not been accepted by the Central Consultants and Specialists Committee, which considered it had not been properly consulted.

The motion was lost.

General Medical Council Election

Dr. I. M. JONES moved: "That the revised procedure for the support of candidates at General Medical Council elections, as set out in Appendix IX, be approved."

The motion was carried.

An amendment in the name of Rugby, "That Appendix IX be amended thus: (*a*) delete paras. (8) and (9) and add to para. (11): . . . (4) contain an election address by the selected candidates," was accepted.

Police Surgeons

Dr. I. M. JONES moved: "That the proposals of the Association of Police Surgeons of Great Britain as set out in Appendix X be approved."

Dr. H. FIDLER (Council) moved the following rider: "To add on page 66 of A.R.M. 2, item 5, in the scale of fees, new section (*h*) which would read: 'for services rendered to the police on Saturday afternoons, Sundays, and Bank Holidays the night rate will apply.'"

Dr. Fidler said that this was the policy of the Association and appeared to have been overlooked when the new proposals were being drafted.

The motion and rider were carried.

A motion by Mid-Glamorgan, "That this Meeting supports the principle that in each police division police surgeons be appointed on a contractual basis with adequate retaining fee plus item-of-service payment," was accepted.

A motion by Mid-Glamorgan, "That (with reference to Appendix X (Scale of Fees)) no certificate of fitness to be detained should be expected without medical examination," was accepted.

Certificates and Reports Paid for by Patients

Dr. I. M. JONES moved: "That, while reaffirming the policy that the fee to be charged is a matter for mutual arrangement between a patient and doctor, the list of recommended fees approved by the Representative Body in 1963 be increased as set out in Appendix XI to this report, and the additional recommended fees approved."

The motion was carried.

Emergency Sign on Doctors' Cars

The following motion by St. Marylebone was accepted: "That this Meeting recommends that as a vital necessity for the proper working of medical practice, doctors are allowed to have a distinguishing light on their cars when going to an emergency, and at all relevant times they should be allowed to show on their B.M.A. parking-badge their names and location."

Application for Postal Vote

The following motion by Rugby was accepted as a reference to the Council: "'That this Meeting considers that paragraph 10 of the Home Office's reply is absurd: accordingly it instructs Council to press for the wording of the medical certificate for postal voting to be amended to read: To ....I recommend that you be granted a postal vote on medical grounds for.........months* indefinitely* (*Delete as appropriate.) Signed .... Dated........................."

Medical Examination of Elderly Drivers

Dr. H. G. DOWLER (Gloucestershire) moved: "That this Meeting is dissatisfied with the outcome of discussions with the Motor Conference regarding the medical examination of elderly drivers, that it reiterates resolutions 191 and 192 of the Annual Representative Meeting 1966, and that it directs Council to reopen negotiations to this end."

Dr. Dowler said the resolutions referred to in the motion suggested, firstly, that the examination of elderly drivers should be undertaken by someone preferably other than the family doctor; and, secondly, that the procedure for such examinations should be similar to the procedure for ordinary life assurance examinations. The argument against the latter was that it would involve special administrative procedure and would raise the premium for elderly drivers' insurance policies. The wording of the certificate given by the Council in its report was very suitable when it was known the person could be passed to drive. The difficulty arose when the doctor was uncertain. Whoever stopped a man from driving his car would naturally be the subject of his resentment, which could be unpleasant. Insurance companies made cost the main reason for not falling in with the profession's wishes that the procedure should be carried out in roughly the same way as life assurance examinations. Dr. Dowler submitted the matter was serious enough to justify that cost. Though it was said a doctor could refuse to carry out such an examination, that was an awkward thing to do. "Regardless of what the life offices' feel about it, we ought to stick to our belief and say so," said Dr. Dowler.

Dr. B. L. ALEXANDER (Manchester) supported the motion, saying that doctors should not be put in the embarrassing position of having to examine their own patients and turning them down. It was of no account who paid for it. The B.M.A.'s policy was that such people should not be examined by their own doctors. "Let us say that fairly and squarely," said Dr. Alexander.

Dr. J. E. MILLER (Council) opposed the motion. He said that over many years the Private Practice Committee had pursued the subject relentlessly, and every possible avenue had been explored in an attempt to find a solution. A doctor placed in such a position could refer the patient to a colleague to examine, which was the simplest solution of all.

Dr. H. C. W. BAKER (Council) was certain that the insurance companies' first consideration was not cost. What they did care about was the certificate. The companies knew it was not the elderly drivers who caused all the accidents. Some of them were the most careful drivers one could see on the roads, and their mileage was not great.

Dr. R. S. B. ROGERS (Gloucestershire) said this was already established Association policy. It had been agreed already that doctors did not want to carry out these examinations and wanted them done in the same way as life assurance. Dr. Rogers urged the Meeting to accept the motion and give support to a later amendment in the name of Gloucestershire.

Dr. B. D. MORGAN WILLIAMS (South Warwickshire) said it was upsetting to have to turn a man down for life assurance purposes. It was much more upsetting, possibly because it hurt his pride, to turn a man down and say he was unfit to drive.

Dr. I. M. JONES said that no further concessions from motor insurance companies were possible. Indeed, they had refused to discuss the matter, regarding the previous discussions as having been exhaustive. There were only two courses to follow. It could be said that what had been achieved already must be accepted, and agreement reached with the accident offices. Or, in the sense of a later motion by Gloucestershire, doctors could be directed not to do these examinations. Before the latter course was taken the Meeting should ask itself how many doctors would heed that advice for long, and how foolish the B.M.A. would look if its advice was widely disregarded. "Prudence demands you accept what has been achieved," said Dr. Jones.

Dr. DOWLER, in reply, said that the principle was to make sure that the right people were insured for driving on the roads. What was required to ensure that was a proper history, examination, and an independent assessment.

The motion was lost.

A motion by Worcester and Bromsgrove, "That the opinion of this Representative Body is that the best person to decide whether an elderly patient is fit to drive is his own family doctor. The extent of the examination should be left to the doctor and the fee to be charged should be a matter between the doctor and his patient," was, by leave, withdrawn.

A motion by Cleveland and Middlesbrough, "That (with reference to para. 160 of the Annual Report of Council) this Meeting accepts the proposed form but recommends that the said form be sent by the insurance offices to applicants and not to family doctors," was passed as a reference to the Council.

A motion by Mid-Essex, "That a second paragraph be added to the suggested certificate concerning the fitness of an elderly person to drive reading 'I recommend that he/she be referred for a second opinion,'" was, by leave, withdrawn.

A motion by Newcastle upon Tyne, "That this Body considers that the present method of issuing driving licences to private drivers is grossly inadequate in that no real effort is made to confirm that the minimum medical standards, as stated on the application form, exist," was accepted as a reference to the Council.

A motion by Aberdeen and Kincardine, "That this Meeting considers that the fee for emergency treatment under the Road Traffic Act, 1960, is grossly inadequate," and an amendment to add the words, "and that steps be taken to see that the fee is paid to the doctor first attending the patient whether this be at the scene of the accident or at hospital," was carried as a reference to the Council.

Emergency Treatment Service

Dr. R. Peters (Redbridge) moved: "That the A.R.M. views with great concern the activities of the B.M.A. Emergency Treatment Service in the Greater London area and regrets the lack of liaison and co-operation of the central advisory committee with local Divisions. It urges that the central advisory committee exercises its proper authority by restricting the activities of the B.M.A. Emergency Treatment Service to those areas and those Divisions which request its assistance and have established local advisory committees."

He drew the Meeting's attention to the opening sentence of the Association's Emergency Treatment Service booklet, which stated that the service began in 1963, extending a year later to incorporate a telephone answering service. In one borough of his Division a comprehensive scheme of that nature planned, organized, and financed by the local practitioners had been continuously and successfully operating since 1948. This, he thought, was some justification for proposing the motion.

The service appeared to be pressing to establish itself in the Division's area without the formation of a properly constituted local committee to include representation from local medical committees, hospital staff committees, and public health departments. This was completely at variance with the introductory statement of the Chairman of the Central Advisory Committee in the booklet.

Dr. J. E. Miller (Council) said the inference might be drawn from the motion that the Emergency Treatment Service was being introduced without local doctors asking for it. The E.T.S. had been requested by doctors in various areas throughout the country. It was reasonable that the service should explore the possibility of introducing itself into particular areas. It was not true to say the service had not taken cognizance of local committees. Discussions had been going on with them and with the Metropolitan Counties Branch of the B.M.A. He asked the Representative Body to reject the motion.

Dr. W. P. Lambie (Sheffield) said it had ben agreed that the service should be made available to members. An assurance had been given that it would not be introduced where there was no demand. The service had become a part of life in the Sheffield area. The B.M.A. was now offering it to everybody and its acceptance should not be prevented.

Dr. G. Cormack (Newcastle upon Tyne) said it was implicit in the wording of the motion that some sort of monopoly should be created in the Greater London area. The service could do nothing but good, and it had proved its worth. He asked the Representative Body to reject the motion.

Dr. W. G. A. Riddle (Gateshead) disliked the implications in the motion rather than the exact wording. He had been a member of the local advisory committee on Tyneside since the inception of the E.T.S. in that area, and it had always had the greatest co-operation from the central advisory committee in London. It was difficult to see how the service could operate in any area until a local advisory committee had been established. It would be improper for it to do so.

Dr. I. M. Jones asked the Representative Body to reject the motion. It was false from beginning to end. The first part accused the service of lack of liaison and consultation. There had been informal discussions between himself, some colleagues on the central advisory committee, and the chairman of the Metropolitan Counties Branch Council. Subsequently the introduction of the service had been welcomed. There had been no word of dissent. The service had been a boon in every area and had attained a higher standard than anything else in existence of its kind.

Dr. Peters, in reply, said the motion was not anti-B.M.A., and his local area was not trying to obstruct the establishment of the E.T.S.

The motion was lost.

A motion by the Chairman of the Private Practice Committee, "That the remainder of the Annual Reports of Council under 'Private Practice' be approved," was carried.

A motion standing in the name of North Middlesex, "That this Meeting feels that the statutory fee for notification of diseases to local health authorities should be double," was accepted as a reference to the Council.

Annual Meetings

Professor F. E. Stock moved: "That the Annual Report of Council under 'Annual Meetings' (Doc. A.R.M. 2, paras 174–180) and the Report on Annual Meetings of the Association (Appendix VIII) be received."

He said the matter had been reported in considerable detail, and there was nothing further he could add.

The motion by the Chairman of the Annual Meetings Committee, "That the report 'The Annual Meetings of the Association' as amended (Appendix VIII) be approved and its recommendations adopted," was carried.

A motion standing in the name of Southampton, "That the Annual Representative Meeting should take place in London at the earliest opportunity, and certainly much before 1971," was, by leave, withdrawn.

Scotland

Dr. J. Riddell (Chairman of the Scottish Council) moved: "That the Annual Report of Council under 'Scotland' (Doc. A.R.M. 2, paras. 225–247) be received." He reported that during the year the Scottish Council had given evidence to no fewer than nine commissions or special committees, including those on medical education, senior nursing staff structure, local government in Scotland, and social work services. It had also considered the best way of applying the new constitution in Scotland.

The G.M.S. Committee (Scotland) and the C.C. and S. Committee (Scotland) reported to the Scottish Council, so the viewpoint was obtained of all sections of the profession.

Scottish House was now graced by a portrait of Dr. E. R. C. Walker, lately Scottish Secretary. Scotland had suffered severely in the loss of Dr. Kate Harrower. Dr. Riddell expressed the indebtedness of the Scottish Council to the present Scottish Secretary, Dr. S. J. Hadfield, and to Dr. C. D. Falconer, Assistant Scottish Secretary.

Constitution of Scottish Council

Dr. Riddell moved:

"That the Schedule to the By-laws be amended to include under members of Scottish Council otherwise appointed 'Three (two of whom must be departmental medical officers) appointed by public health service members in Scotland; five appointed by regional consultants and specialists committees in Scotland and two appointed by the Hospital Junior Staffs Group Council (Scotland)'; and to delete under Duties and Powers of Scottish Council the sentence 'The Scottish Council shall have power to add to its number not more than three members specially qualified to assist in the business of Scottish Council.'"

He said that the Scottish Council contained within its representation a member from every Division in Scotland, but this meant that there was a preponderance of general practitioners. In order to move with the times and to increase the representations of other sections of the profession it was proposed to alter the constitution as in the motion. This would enable junior doctors, public health members, hospital staffs, and university staffs to have an adequate say in Scottish business.

The motion was carried by the necessary majority.

Dr. Riddell moved: "That the remainder of the Annual Report of Council under 'Scotland' be approved."

The motion was carried.

Northern Ireland

Mr. H. I. McClure (Chairman, Northern Ireland Committee) moved: "That the Annual Report of Council under 'Northern Ireland' (Doc. A.R.M. 2, paras. 248–258) be received."

He drew attention to the question of the administrative practice of hospital management committees and to the anxiety felt by the Committee at any attempted reduction in the influence of medical staff. It was proposed to interpose another committee between the group medical advisory committee and the hospital management committee. It would contain lay people and it would have no effective advice from doctors. That would abolish the system of medical superintendents of hospitals.

Dr. I. McD. Brown (Eastbourne) moved: "That the Representative Body notes the concern expressed by Northern Ireland about the proposal made to base hospital administration on a system of possibly non-medical executive management with medical advisers, rather than on medical executive authority."

Mr. McClure said he was happy to have support from Eastbourne.

The motion was carried unanimously.

Mr. McClure moved, and it was carried, "That the remainder of the Annual Report of Council under 'Northern Ireland' be approved."

Wales

Mr. R. J. Williams (Chairman of the Welsh Committee) moved: "That the Annual Report of Council under 'Wales' (Doc. A.R.M. 2, para. 259) be received."

He said that a major part of the activity of the Welsh Committee this year had been taken up in preparing the final draft of its report on Wales as a pilot area for area health boards, according to a resolution of the Council of 2 December 1964. A progress report was approved by the Committee in May 1966 and subsequently circulated for comment to B.M.A. Welsh Divisions, the Welsh Association of Local Medical Committees, the Welsh Regional Public Health Committee, the General Medical Services Committee, the Central Consultants and Specialists Committee, the Public Health Committee, the Society of Occupational Medicine, the local medical committees in Wales, the Full-time Medical Teachers and Research Workers' Committee, and the Occupational Health Committee. Thus a broad spectrum of opinion and criticism had been obtained and formulated in the final draft drawn up by the subcommittee and approved by the Welsh Committee on 27 June for submission to Council.

The Welsh Committee had been deeply concerned at the proposal in the new Constitution to reduce the number of Welsh members of Council from three to two. Membership of the Association in Wales was giving rise to concern (it was in fact only 66.5% of the doctors in Wales), and the comparatively low percentage membership gave a false picture of the apparent satisfactory representation of one Council member to 1,150 members of the Association in Wales.

The Committee had proposed that the Chairman be *ex officio* a member of the Council, and it failed to comprehend any logic in the Council's proposal that the Chairman would be able to participate in Council proceedings but not have a vote. There was deep resentment in Wales at the decision, despite representations to the Organization Committee, and if a third Welsh member with full voting rights be not admitted to the Council the Welsh Committee considered that the future of the Association in Wales might well be bleak.

The motion was approved.

Dr. D. L. Williams (East Denbigh and Flint) moved: "That the Welsh Committee be renamed the Welsh Council and function on the same basis as the Scottish Council."

The Chairman asked the Representative Body to agree that the motion should be moved as a reference to the Council, and the Meeting agreed.

Dr. Ronald Gibson (Chairman of Council) said he was not happy about it, because the situations in Wales and Scotland were quite different. Scotland had its own Health Department, for example. He personally preferred that the motion should be put to the Meeting.

The Chairman: "The Meeting has already agreed to vote on it as a reference to the Council, and we must debate it on those lines." Mr. R. J. Williams (Chairman of Welsh Committee) said it had been approved by the Welsh Committee as a reference.

A speaker from the floor asked how many times had the Welsh Committee met in the past 12 months. Mr. Williams: "Twice."

Dr. D. L. Williams, in reply, said that Wales had a Board of Health. He was surprised that representatives had not heard of it. The Welsh Board of Health was the Ministry of Health's Department in Wales. It was quite separate from the Ministry. He hoped that that was understood.

The motion was carried as a reference to the Council.

Mr. R. J. Williams (Chairman of Welsh Committee) moved: "That the remainder of the Annual Report of Council under 'Wales' be approved."

The motion was carried.

Medical Films

Dr. Ronald Gibson moved, "That the Annual Report of Council under 'Medical Films' (Doc. A.R.M. 2, paras. 195–199) be received," and this was agreed to.

Dr. Gibson then moved, "That the Annual Report of Council under 'Medical Films' be approved," and that was also agreed.

Alcohol and Road Accidents

Dr. Ronald Gibson moved: "That the Annual Report of Council under 'Alcohol and Road Accidents' (Doc. A.R.M. 2, para. 201) be received."

The motion was carried.

Dr. Ronald Gibson (Chairman of Council) moved, "That the Annual Report of Council under 'Alcohol and Road Accidents' be approved."

The motion was carried.

Press and Information

Dr. Ronald Gibson moved: "That the Annual Report of Council under 'Press and Information' (Doc. A.R.M. 2, para. 202) be received."

The motion was carried.

Dr. Ronald Gibson moved: "That the Annual Report of Council under 'Press and Information' be approved."

The motion was carried.

Dr. G. Cormack (Newcastle upon Tyne) moved: "That the Representative Body requests Council to investigate the possibility of familiarizing certain key members of the Association in television and other public relations techniques."

He said that centrally and in the provinces public relations promotion could be done with great effect by a relatively small number of key men in the Association who were fully proved in Association affairs and who had some experience and knowledge of the techniques of television.

Dr. Ronald Gibson said it might not have escaped the notice of Dr. Cormack that in fact the B.M.A. had been concentrating as much as it could on its Secretary (Dr. Derek Stevenson), who had been appearing on television on every possible occasion on matters involving the Association. He did not want to publicize too much the question of training speakers, but he would be prepared to support others in trying to get seminars going.

Dr. Cormack said his motion was intended as a reference to the Council.

The motion was carried as a reference to the Council.

Other Association Activities

Dr. Ronald Gibson moved: "That the Annual Reports of Council under 'Other Association Activities' (Doc. A.R.M. 2, paras. 278–288, and A.R.M. 2A, paras. 292 and 293) and the Report on Identification of Tablets (Appendix XII) be received."

The motion was carried.

G.M.C.: Annual Retention Fee

Dr. A. M. Rankin (Council) moved on behalf of Cumberland: "That this Meeting rejects the principle of an annual retention fee by the General Medical Council."

He pointed out that only 11 out of 47 members of the General Medical Council were elected by the profession. If the principle of an annual retention fee was accepted, expenditure on the G.M.C. was being underwritten without effectively being able to control it. What would in fact happen when a doctor ceased to pay the annual subscription to the G.M.C. had by no means been settled. He saw no reason why doctors should have to meet the cost of what was described in the Annual Report as "heavy expenditure for additional accommodation which was urgently required." Obviously the accommodation of the G.M.C. should be provided by itself.

Dr. G. R. Smith (Birmingham) asked: When a practitioner had paid his registration fee in the belief that it was for his professional lifetime, what was the position if the General Medical Council asked for an annual retention fee? If the practitioner refused to pay an annual retention fee would he be removed from the *Register*?

Dr. Ronald Gibson said he thought that the motion went too far.

Expressing himself as against the motion, Dr. J. R. Bennett (Council) said that the burden could not be placed on the newly qualified and registered doctors. They could not bear the whole cost. Other organizations had an annual retention fee, and the Association could no longer resist it in the case of the G.M.C.

Dr. Outwin (Council) said it would be a mistake to let the General Medical Council become totally financed from Government funds. Saying it was right to oppose the motion, Dr. R. Maggs (Eastbourne) said the Meeting should support moves which had been proceeding for some time, "to get the G.M.C. out "of the red."

Dr. S. WAND said that the General Medical Council had failed to balance its annual budget. Its expenses had been high. It had to find more money. Comparable organizations had an annual retaining fee. He thought a retaining fee of £2 a small price to pay by doctors for the privilege of electing members of the G.M.C.

Dr. RONALD GIBSON said the profession would not want the G.M.C. to be "Government owned." Equally it was unfair that young doctors should have to carry the cost of the G.M.C. through an increase in the registration fee.

A motion, "That the question be now put," was carried by the necessary majority, and on the motion being put to the Meeting it was lost.

Dr. R. MAGGS (Eastbourne) moved: "That the amount of the annual fee (£2) which the General Medical Council propose should be levied for the retention of a doctor's name on the *Medical Register* is unjustifiably high."

He said that the Annual Report stated that £1 was inadequate but that £2 would be excessive. For these reasons Eastbourne was suggesting that the proposed fee was excessive and should not, therefore, be supported.

The motion was carried.

The following motion by Cleveland and Middlesbrough, "That this Meeting accepts in principle an annual retention fee but recommends that a life membership fee be payable in lieu," was accepted as a reference to Council. The Chairman ruled that the following motion by Blackpool and Fylde, "That Council should advise the General Medical Council that the initial registration fee should be increased as thought necessary, but that on no account should the registration fee be made repetitive," had been covered by the previous decision.

Motions under the headings of The European Economic Community, The Establishment of a Cervical Cytology Service, and Labelling of Containers were accepted by the Chairman as references to the Council.

A motion to approve the remainder of the Annual and Supplementary Reports of Council under "Other Association Activities" was approved.

Any Other Business

On the motion "Any other business," Dr. W. R. KING (North Glamorgan and Brecknock) moved: "That in future at Representative Meetings the Agenda be adhered to in strictly numerical order."

He said this was not intended as a vote of censure on anyone, but at times the proceedings had been confused and confusing. He thought it would be much easier if the Agenda were followed in numerical order, and he saw no reason why this should not be done in the future.

The motion was lost.

On the motion of Dr. F. G. TOMLINS (Waltham Forest), a vote of thanks to the Chairman and the Deputy Chairman was passed by a standing ovation.

Proceedings of Council

The first meeting of the Council of the Association for the session 1967–8 was held in Bristol on 10 July at the conclusion of the Annual Representative Meeting. Dr. RONALD GIBSON was in the chair.

After welcoming the new members of the Council, the Chairman formally moved that the Chairman of the Representative Body and the Chairman of Council be authorized to refer the resolutions of the Annual Representative Meeting to the appropriate committees.

The motion was carried.

Standing Committees

The Council then proceeded to the election of the standing committees, other committees, and representatives on outside bodies, for the session 1967–8.

Vice-President

It was reported that a letter had been received from Dr. J. O. Mercer (New Zealand) expressing his gratitude for the honour which the Association proposed to confer upon him by electing him a Vice-President of the Association.

Public Health Medical Officers

The Council received a letter from the Secretary of the County Councils Association and Association of Municipal Corporations expressing regret at the steps recently taken by the B.M.A. regarding public health appointments with local authorities. The County Councils Association and Association of Municipal Corporations said they were concerned at the possible effect of the actions of the B.M.A. on the public health service, and would welcome an opportunity of meeting representatives of the Council of the B.M.A. to discuss the position.

World Medical Association

The Council adopted a suggestion by Sir Clement Price Thomas, a Past-President of the W.M.A., which was supported by the Central Ethical Committee, that the Association should submit the following motions to the assembly of the World Medical Association in Madrid in September: "(1) That adequate instruction in medical ethics should be included in the medical curriculum. (2) That upon qualification each doctor be presented with a copy of the Declaration of Geneva and the Declaration of Helsinki and that at each graduation ceremony the Declaration of Geneva be read out by one of the graduates on behalf of the others."

Danish Medical Association

The Council received a report that Mr. N. G. C. Hendry (Aberdeen) had been appointed to represent the Association at the 85th Annual Meeting of the Danish Medical Association, to be held at Helsingør from 25 to 27 August.

Annual General Meeting

The 135th Annual General Meeting of the B.M.A. was held in the Anson Hall, University of Bristol Union, on Monday, 10 July. The President, Professor HAMID ALI M. KHAN, took the chair. At the conclusion of the formal business the meeting was adjourned until 8.30 p.m.

Extraordinary General Meeting

An Extraordinary General Metting of the B.M.A. was held in the Anson Hall, University of Bristol Union, at the adjournment of the Annual General Meeting. The President, Professor HAMID ALI M. KHAN, took the chair.

A special resolution to amend the Articles of Association, as published in the *British Medical Journal* (*Supplement*, 27 May, p. 138), was carried.

Adjourned Annual General Meeting

The Adjourned 135th Annual General Meeting of the Association was held at the University Great Hall, Bristol, on 10 July at 8.30 p.m.

Installation of President

The retiring President, Professor HAMID ALI M. KHAN, installed Mr. R. V. COOKE as President of the Association for 1967–8, and invested him with the President's badge of office. Mrs. HAMID ALI KHAN invested Mrs. R. G. COOKE with the President's Lady's badge.

Dr. RONALD GIBSON (Chairman of Council) proposed a vote of thanks to the retiring President for all he had done on behalf of the Association during his term of office, and particularly for representing the Association at the centenary celebrations in Canada.

The vote of thanks was carried with acclamation.

Delegates from Kindred Associations and Representatives of Overseas Branches

The CHAIRMAN OF COUNCIL then introduced to the President the following delegates from kindred associations and representatives of overseas Branches:

Dr. A. G. Boohene, Ghana; Dr. K. R. Borland, Canada; Dr. B. C. Cohen, West Australia; Dr. G. C. Dockeray, Kenya; Dr. J. A. Diaz, U.S.A.; Dr. K. A. Finck, West Germany; Dr. J. Fleischmann, U.S.A.; Dr. P. J. Fogarty, New Zealand; Dr. M. A. Kehoe, Ireland; Mr. R. Levy, Jamaica; Sir Leonard Mallen, Australia; Dr. R. M. H. Malone, Barbados; Dr. E. Moses, Trinidad; Professor M. G. Muazzam, Pakistan; Dr. J. St. L. O'Dea, Ireland; Dr. V. R. Patel, Kenya; Dr. H. H. Phillips, Ghana; Dr. A. Pederson, Denmark; Dr. Noel Reilly, Ireland; Dr. M. O. Rouse, U.S.A.; Dr. Lyon Playfair, Rhodesia; Dr. Marcel Poumailloux, France; Dr. F. T. A. Sevens, Belgium; Professor W. H. Struben, Netherlands; Dr. Zakia Shammeem, Karachi; Dr. E. Tan, Malaya; Dr. V. Thuraisingham, Malaya; Dr. P. Tienari, Finland; Professor Dr. J. Towpick, Poland; Dr. P. De S. Wijesekera, Ceylon; Dr. T. W. Wikramanayake, Ceylon; Dr. R. Winton, Australia.

Fellows of the Association

The CHAIRMAN OF COUNCIL next introduced to the President the following newly admitted Fellows of the Association:

Dr. R. Barrie, Taunton; Professor R. J. Brocklehurst, Plymouth; Dr. D. W. K. Buchanan, Dundee; Dr. A. G. Chamberlain, Charmouth, Dorset; Dr. H. M. Cohen, Birmingham; Dr. E. Colin-Russ, London; Dr. R. Cove-Smith, London; Dr. A. R. Fox, London; Dr. J. M. C. Gill, Inverurie, Aberdeenshire; Dr. R. E. Hadden, Portadown, Co. Armagh; Dr. J. S. Happel, Alresford; Dr. M. L. Hudson-Evans, London; Dr. F. R. B. H. Kennedy, Isle of Wight; Dr. H. B. Kilroe, Rochdale; Dr. Isaac Lipsedge, Birkenhead; Dr. H. B. Muir, Auchtermuchty; Dr. R. S. MacArthur, Stourport-on-Severn; Dr. R. G. Prosser-Evans, Langland, Swansea; Dr. Patrick Reel, Isle of Man; Mr. C. P. Robinson, Swansea; Dr. A. Robinson Thomas, Newton Abbot; Dr. L. J. Rosin, Darlington; Dr. H. P. Samson, Eccles, Manchester; Dr. Gerald M. J. Slot, Twickenham; Dr. Joan K. Sutherland, Edinburgh; Dr. L. J. Stoll, London; Dr. C. R. Nunan, Wallington; Mr. E. E. T. Taylor, Northampton; Dr. Ronald H. Vartan, Hucknall.

Association Prizes

The PRESIDENT presented the following Association Prizes:

Nathaniel Bishop Harman Prize, 1966, to John R. Bennett, M.D., M.R.C.P., of Liverpool, for his work on the differentiation of oesophageal pain from cardiac pain.

Sir Charles Hastings Prize, 1966, to W. D. Rees, M.B., B.S., of Llanidloes, for his dissertation on the mental and physical disabilities of 1,190 ordinary motorists.

Charles Oliver Hawthorne Prize, 1966, to Katherina D. Dalton, M.R.C.S., L.R.C.P., of London, for her work on the influences of menstruation.

Walter Jobson Horne Prize, 1966, to Ronald G. Macbeth, D.M., F.R.C.S., of Oxford, for his work in respect of laryngectomy, injection of oesophageal varices, frontal sinus surgery, and hypophysectomy.

The prize for 1967 has been awarded to Edwin G. Collins, M.B., F.R.C.S.Ed., of Aberdeen, for his work in connexion with the physiology and treatment of otitis externa.

Middlemore Prize, 1966, to Sohan Singh Hayreh, Ph.D., M.B., B.S., of London, for his work entitled "Pathogenesis of Oedema of the Optic Disc."

C. H. Milburn Prize, 1966, to J. Leahy Taylor, M.B., B.S., D.M.J., of Staines, for his dissertation entitled "The Adequacy of the Disciplinary Jurisdiction of the General Medical Council."

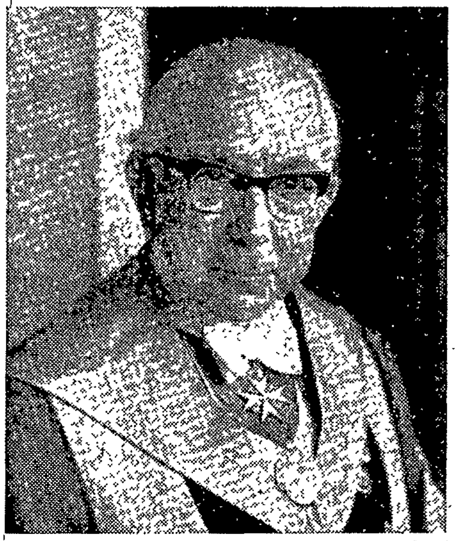
A second prize has been awarded to Werner K. E. Bernfeld, M.D., for his dissertation entitled "Medical Professional Secrecy, with special reference to Venereal Diseases."

Gold Medal

The CHAIRMAN OF COUNCIL announced that it had been resolved: "That the Gold Medal of the Association be awarded to the Right Honourable Lord Cohen of Birkenhead, M.D., D.Sc., Sc.D., LL.D., F.R.C.P., in recognition of his outstanding services to the Association and to the profession." He then read the following citation:

"Lord Cohen, in awarding you the Gold Medal of the Association, the Council is expressing its appreciation and gratitude for your tremendous services to medicine and to the medical profession.

"The pattern of your career was set, more than forty years ago, when you qualified at the University of Liverpool with first-class honours and distinction in every subject of the medical curriculum. Since then your career has been one of outstanding distinction.


Lord Cohen of Birkenhead wearing the Gold Medal of the Association.

"While still a relatively young man you were appointed Professor of Medicine at the University of Liverpool. You occupied this Chair with distinction for more than thirty years. As an outstanding clinician and as a medical statesman your unique gifts have been recognized by your presidencies of the Royal Society of Medicine, the Royal Society of Health, and other learned Societies. For six years you were chairman of the Central Health Services Council and many of its Committees. In 1961 you were appointed to the Presidency of the General Medical Council and the profession is happy to know that you continue in this office at this critical period of British medicine.

"Your wide reading and profound knowledge have led to many calls upon your time as a speaker. The numerous eponymous lectures and orations which you have delivered over the years, and your contribution to debates in the House of Lords, have been notable for their range of subject and lucidity of presentation. You have achieved a standard which few can emulate and have given immense pleasure to all who have heard you—whether members of the medical profession or not.

"Recognition of your many achievements has been widespread and you have received honorary degrees and fellowships from many universities and colleges both in the United Kingdom and overseas. In 1949 you received the honour of Knighthood, and in 1956 Her Majesty The Queen conferred on you a Barony, in recognition of your great services to medicine and to the community.

"Despite the demands of this very full life, the Association has always been able to call upon you for help and advice. The Association was honoured when you became its President in 1950 and after your distinguished year of office you continued to take a close interest in our affairs. Notable amongst the many services you have rendered the Association was the occasion of the celebration of the centenary of our Founder, when you delivered the memorial oration on 'Hastings and the General Medical Council.'

"We wish particularly to refer to the great influence you have had on medical education. You played a great part in the work of the first World Conference on Medical Education, though prevented by ill health from presiding over it. The reports of the two committees over which you presided, on the Training of the Doctor and of the General Practitioner, prepared at the beginning of the National Health Service, contained recommendations which were well ahead of their time. Any disappointment you may have felt at their initial reception some fifteen years ago must surely now be tempered by the current trends which follow so closely your original thoughts on training for general practice.

"The Association respects your pre-eminent place in Medicine. But its respect for you, Lord Cohen, goes deeper. It remembers with gratitude your kindliness, unfailing courtesy, and deep sense of humility. No call on your time has been refused. No task for the profession too small to undertake.

"We ask you to receive this Gold Medal as an earnest of the admiration and gratitude of all members of the Association for your magnificent leadership and achievement which will always be remembered in the history of British Medicine."

Presidential Address

The President, Mr. R. V. COOKE, then delivered his Address, "One Profession, One Purpose," which has been published in the *British Medical Journal* (15 July, p. 129).

Dr. A. N. MATHIAS, Chairman of the Representative Body, proposed a vote of thanks to the President for his address. This was carried by acclamation, and the 135th Annual General Meeting then terminated.

Representatives and their ladies then joined the President and Mrs. R. G. Cooke at a reception in the Bristol Museum and Art Gallery.

H.M. Forces

Appointments.—Group Captain D. O. Williams (surgical duties, Princess Mary's R.A.F. Hospital, Akrotiri, Cyprus); Wing Commander C. A. Bentley (to command, R.A.F. Hospital Khormaksar Beach, Air Forces Middle East); Wing Commander J. D. Crowlesmith (senior medical officer, R.A.F. Cottesmore, Rutland); Wing Commander W. J. L. Harries, O.B.E. (surgical duties, Princess Mary's R.A.F. Hospital Halton, Bucks); Wing Commander E. T. King (registrar, R.A.F. Hospital Nocton Hall, Lincs); Wing Commander J. D. MacAllister (senior medical officer, R.A.F. Henlow, Beds); Wing Commander B. Taylor (to command, R.A.F. Institute of Hygiene).

REGULAR ARMY RESERVE OF OFFICERS

ROYAL ARMY MEDICAL CORPS

Majors M. B. Macaulay, J. D. Macdonald, and J. E. Black have resigned their commissions.

Annual Meeting Religious Services

Official Service at Bristol Cathedral

The Service of Worship and Dedication at the B.M.A.'s Annual Meeting was held in Bristol Cathedral on Sunday, 9 July. At the Great West Doors the robed procession of the British Medical Association was met by the Dean, the Very Reverend D. E. W. Harrison, who also met the Lord Lieutenant of Bristol, His Grace the Duke of Beaufort, and conducted him to his stall. There followed the entry of the Civic Procession, led by the Lord Mayor of Bristol, Alderman the Reverend F. C. Vyvyan-Jones, also greeted by the Dean.

Trumpeters were provided by the 16th/5th the Queen's Royal Lancers, under the bandmaster, Mr. D. N. Taylor.

Dr. Ronald Gibson, Chairman of Council, read the first lesson, and Mr. Robert V. Cooke, President-elect, read the second lesson. Prayers were said by the Bishop of Malmesbury, the Right Reverend C. L. P. Bishop, and the Dean.

Concern for Persons and Truth

The sermon was preached by the LORD BISHOP OF BRISTOL, THE RIGHT REVEREND OLIVER TOMKINS, to a crowded congregation. He said: "We are all here with a common concern for persons and for truth. And in that common concern medical science and religious testimony are not as far apart as is sometimes suggested. We are all concerned for persons and we are all concerned for truth. And in that shared concern we are all aware of a shared polarity, or tension —a polarity between a given goal on the one hand, and on the other hand a considerable uncertainty about means."

Medicine, surely, accepted as given something which might be hard to define but which was concerned with health, with life as self-evidently valuable, with human beings as being so precious that endless patience, hard work, and devotion were rightly given to their care. The difficulties arose when they began to ask questions about the means by which the given goal was to be realized, for it was the very means themselves which posed the questions about the goal. They were all —whether doctors, clergy, teachers, or anyone else—living in an age when vast new resources of knowledge were calling into question the goals they sought, precisely because the means for reaching them seemed to challenge the goals themselves.

That had seemed to him to come out very clearly in some of the ethical questions in which medicine and religion had a common concern. He instanced the acute problems raised by the medical prolongation of life, abortion, birth control, and the survival of babies whose weakness or deformity would in earlier generations have meant their early death.

He continued, "It is easier to ask questions than to answer them. But a preacher is supposed to deal, in some sense, with answers." Taking as his text Colossians 1, verses 15–18, he said: "In Jesus Christ, the Christian faith affirms, the concern for persons and for truth meet in a Person who is the Truth. . . . Christ is the Logos of the Cosmos, the meaning of the world—He is the clue to what makes sense." He then dealt with four areas of Christian "answer" suggested by the passage from St. Paul reinterpreted in the thought of our own age.

On concern for persons, he said: "Whether a man would rate himself a churchgoer, or even a Christian, most of us would gladly admit that in Jesus we see supremely the right approach to people. He has been called 'the Man for others'—His whole life was one of deep concern and compassion; He cared for the whole man, body and soul alike, and He taught that to care about people was to care about God.

"In this aspect there can never be any separation between religion and medicine, and if over recent centuries the two have drifted away from each other it is partly because the Church has sometimes made a separation, which Jesus never allowed, between 'body' and 'soul'; it is partly due to the fact that the increasing complexity and effectiveness of medical science have appeared to owe nothing to Christian faith. But I am sure we can hope for more mutual sympathy at this point, as we all see ever more clearly that a person is an indivisible whole. His body, his mind, his unconscious motivations, his deepest beliefs, and his dependence upon others through heredity and environment are all so subtly related to each other that no aspect of a human being can be fruitfully considered without recognizing its connexions with all the other aspects."

Death in New Perspective

Death was put into a new perspective by Christ's perception that people had meaning only in relation to the God whom he called Father, and so life was grounded in a living God who had death itself under control. A doctor, both as a doctor and as a person, worked among those for whom death was not the last word, and who therefore need never in any final sense lose a patient—or, for that matter, a more deeply loved one.

St. Paul's conception of Christ's victory over "the invisible orders" must be reinterpreted in terms of our contemporary world picture. The phenomenon of man, as interpreted, for example, by Teilhard de Chardin, was to be understood as part of "the connexion between Christ and the known universe—no more intrinsically incredible than it was to St. Paul's contemporaries."

Finally, St. Paul's phrase, "He is the head of the body, the Church," implied that Christ did not stand alone, though He remained unique. He always fulfilled His universal work by calling men and women into a conscious co-operation with Himself in God's purposes.

Increasing complexity of problems demanded increased co-operation in answering them, said the Bishop in conclusion. "Life was meant to be a matter of relationship, of community, of co-operation. Society had no right to expect doctors to answer alone questions about abortion or euthanasia or contraception, in which parents, relatives, sociologists, teachers, theologians, and others all had their allotted part to play."

Roman Catholic Service

Mass was celebrated in the Pro-Cathedral, Park Place, Bristol, on Sunday, 9 July, at 5.15 p.m. The Bishop of Clifton, the Right Reverend J. E. Rudderham, officiated.

The BISHOP said that divine prophecies showed that there was a deep analogy between medicine and religion. Each involved a recognition that there was something amiss in human affairs. Doctors had to face physical and mental illness. The Church had to face sickness of the soul.

In the actual exercise of their respective ministries many doctors and many clergy would agree that the spiritual and physical or mental health of those to whom they ministered were often closely connected. The modern doctor could recognize there were times when the patient needed the divine more than the physician. The priest should recognize that of those who came to him with supposed spiritual problems some at least were more in need of medical help.

Doctors were doing the work of the Church when they carried out the work of their own profession. "We too easily suppose that the work of the Church is neither more nor less than the professional work of the clergy, but this is not so. The Church is the whole People of God, and she is in action wherever the believer, be he priest or layman, exercised the manifold charity of Christ."

The Church looked with lively interest and sympathy, and with a desire to help, on the efforts of her own sons and daughters in the medical profession. However, it might not be amiss to emphasize that not only would disease never be effectively conquered till man's spiritual ills had been healed but the bodily and mental ills of men were of a lower order of importance than his spiritual welfare and needs. "If bodily and mental health are good things they are so because they enable the human person to function normally and efficiently. But the ultimate good of the human person is something more than efficient functioning of his organism," concluded the Bishop.

Association Notices

Branch and Division Meetings to be Held

HUDDERSFIELD DIVISION.—At George Hotel, Monday, 24 July, 8.15 p.m., annual general meeting.

Correction.—Dr. D. S. HURWOOD moved the motion on the "Refund System" at the recent Conference of Representatives of Local Medical Committees (*Supplement*, 1 July, p. 3), not Dr. Whowell, as reported.

British Medical Journal Supplement

LONDON SATURDAY 29 JULY 1967

CONTENTS

Overseas Conference of B.M.A. - - - - - 101
Christian Medical Fellowship - - - - - 103
Golf at Bristol - - - - - - - - 103
General Medical Council - - - - - 104
Meeting of Doctors and Clergy - - - - - - 107
Ladies' Club - - - - - - - - - 107
Annual Dinner - - - - - - - - - 108
Association Notices - - - - - - - - 108

Overseas Conference of B.M.A.

The Overseas Conference of the B.M.A. was held in the University Union, Bristol, on 11 July. Dr. A. N. MATHIAS (Chairman of the Representative Body) took the chair in the unavoidable absence of Professor D. E. C. Mekie, Chairman of the Committee on Overseas Affairs.

After welcoming the overseas visitors the CHAIRMAN explained that the purpose of the conference was to have a frank exchange of views. The Association wished to be of every assistance to overseas branches, and was particularly anxious to know how it could best help overseas members when they came to the United Kingdom or Europe in organizing postgraduate study for them, or obtaining posts.

Before proceeding to a general discussion the Chairman invited Dr. D. L. Gullick, the Secretary of the Committee on Overseas Affairs, to report on the work of the Committee, and Dr. R. A. Pallister, the Medical Director of the Commonwealth and International Medical Advisory Bureaux, to talk about the Commonwealth Immigrants Act.

Commonwealth Foundation

Dr. D. L. GULLICK (Under Secretary) said that one of the most important events of the past 12 to 18 months had been the establishment by Commonwealth Governments of the Commonwealth Foundation in London, to which almost every Commonwealth country now belonged and subscribed. The Foundation had a fairly large sum of money which it could use to encourage intraprofessional contacts within the Commonwealth. Doctors did not have a prior call on the fund, and had to line up with architects, lawyers, engineers, dentists, and others. However, the Director of the Commonwealth Foundation had been very co-operative and a substantial grant had been made towards the cost of the Commonwealth Medical Association meeting in Karachi, and more recently to that of the Council of the Caribbean Branches.

The meeting of the C.M.A. Council in Karachi had been one of the highlights of the year, said Dr. Gullick. Most member associations had been represented, and a lot of hard work had been done in pleasant surroundings during one week. Several important decisions had been taken to strengthen the links between Commonwealth medical associations, and Dr. D. Stevenson, the Secretary of the B.M.A., had been working hard to implement those decisions. Regrettably, said Dr. Gullick, it had not yet been possible to implement one of the more important decisions, the resolution by the C.M.A. Council to appoint a travelling Fellow. The doctor appointed would be an eminent member of the profession who would travel round the world lecturing to member associations on clinical matters. He would also collect information about the C.M.A. and bring back first-hand reports of the problems of members, thus facilitating the exchange of information, which was so important.

In recent years constitutional changes within the Commonwealth had been followed by constitutional changes in the overseas branches of the Association, continued Dr. Gullick. During the past twelve months the Sierre Leone Branch had been dissolved and had been succeeded by the Sierre Leone Medical and Dental Association. The Medical Association in Rhodesia had established itself as an independent association, as had the Nigerian Medical Association, and very recently colleagues in New Zealand had taken a similar step.

Commonwealth Immigrants Act

Dr. R. A. PALLISTER explained that, as Medical Director of the Commonwealth and International Medical Advisory Bureaux, his work was concerned with assisting doctors visiting this country.

Referring to the Commonwealth Immigrants Act, passed in 1965 to control immigration to Britain, Dr. Pallister said that certain difficulties which affected doctors had arisen out of the Act. Under the Act there were three groups of people concerned: the first of these were the men who had jobs to come to in this country and who therefore obtained employment vouchers without difficulty. The second group comprised those who had some skill which was useful in this country. They could obtain an employment voucher without having jobs to come to, which was important from the doctors' point of view. The third group consisted of unskilled people without jobs to come to.

Dr. Pallister said that when the Act was first passed a Commonwealth doctor was able to obtain a voucher within weeks of making application, then the period became extended to six and eight months, and now it sometimes took more than a year to obtain a voucher. A person coming to this country without a voucher usually came with a tourist visa, and was allowed to stay for a certain period. He was expected to have sufficient funds to keep him during his visit. A doctor coming here in those circumstances normally had an extension of time granted if he was offered a hospital appointment. However, he could not stay indefinitely. A student could also be similarly admitted for a course of study. The problem was that there was no certainty that a doctor without an employment voucher would be allowed to stay for the length of time required for his purpose. That made it difficult if he had to spend a considerable sum of money travelling to Britain. Dr. Pallister said his experience had been that the Home Office used its discretion in favour of the doctor who wished to work for a time here, but the situation needed clarifying.

Australian Views

Mr. C. O. F. RIEGER (Australia) said that students coming to the United Kingdom for postgraduate study were grateful for the help they received from the Commonwealth and International Medical Advisory Bureaux. He said that the Australian Medical Association wished to maintain the closest possible ties with the B.M.A.

Referring to the Australian edition of the *British Medical Journal,* Mr. Rieger said that at first the Australian Medical Association had not welcomed it. It had been thought that it would detract from the A.M.A.'s own journal in terms of advertisements. So far, however, that did not appear to have happened. He personally found it very valuable to be able to keep in close touch with the B.M.A. through the Australian edition of the *B.M.J.*

Dr. G. C. DOCKERAY (Kenya) said that, on the whole, the relations of the medical profession with the Government and Ministry of Health in Kenya were good. House-officers in hospitals were overworked at the moment, and Dr. Dockeray suggested that it might help them if publicity was given to that fact.

Dr. V. R. PATEL (Kenya) said that certain Commonwealth countries feared that if Britain joined the Common Market connexions and relations with the Commonwealth would be severed, whereas relations between the B.M.A. and the overseas associations needed to be closer than ever.

"B.M.J." Overseas

Dr. M. WARE (Editor, *B.M.J.*) said that he had been interested to hear from Mr. Rieger of the reactions in Australia to the Australian edition of the *B.M.J.* In launching this edition it had been realized that one of the most important ways of maintaining contact was the speed with which the *B.M.J.* reached its readers, and doctors in Australia could now receive their copy within a few days of publication. A lot of thought had been given to the question of advertising. The *British Medical Journal* had been concerned that no damage should be done to the *Medical Journal of Australia,* and from experience of the pharmaceutical industry in Britain it had been thought that there was no serious threat. It had been gratifying to learn that this had proved to be correct. A number equivalent to half of those who had been receiving the *B.M.J.* by surface mail at the end of last year were now subscribing to the new edition.

The *British Medical Journal* thought of itself as an international journal, continued Dr. Ware. Some 26,000 copies went overseas, and members of the journal staff had been visiting medical schools in the Commonwealth and elsewhere overseas to find out at first hand how the service could be improved. When these visits were made one of the first requests usually received was for greater speed in delivery of the *B.M.J.* This was the main reason why the Australian venture had been undertaken.

Efforts were also being made to speed up the delivery of the *B.M.J.* to English-speaking medical schools in the Far and Near East and in Africa, and there was now more emphasis in the *B.M.J.* on the problems of tropical medicine.

Irish Medical Association

Dr. J. ST. L. O'DEA (Republic of Ireland) reported that relationships between the Irish Medical Association and the Department of Health in Ireland had remained good, and there was constant communication between the two bodies. The problems of the Irish Medical Association were shared by many other professional bodies in Ireland, and the Association had taken the initiative and had formed an organization known as the Federation of Professional Associations. The object was to obtain co-operation in the approach to certain problems which were common to the various professional bodies.

Membership of the I.M.A. had dropped a little for a couple of years, said Dr. O'Dea, but it was now restored to its former size. The Association had major committees working on infant mortality, poisons, and drugs, and their useful work had improved the image of the I.M.A.

Dr. C. VAUGHAN (Trans-Atlantic Territories) said that the new hospital of 600 beds in Barbados, which had been opened in 1964, had begun to take medical students for the first time. For the third year running there had been a seminar held in conjunction with McGill University and in his view this would become an annual feature.

Half of the senior doctors in these territories were in private practice, he said, and wished to maintain their ties with the B.M.A.

On the debit side, Dr. Vaughan said that specialists were expected to work for a salary of about £1,800 a year, which was supplemented by the Ministry of Overseas Development. There was also victimization in what he described as the "federal nonsense." Doctors born in the federal territories could not qualify for an inducement allowance. This meant that people from other countries could obtain a higher rate of pay than those born in the former federal territories. If all the salary scales were brought into line there would be no need to pay an overseas allowance.

Dr. Vaughan said that the central Government had taken over the district medical services in some places, but it was too early to say whether it would be of advantage or not. He suggested that the raising of the university fees in Britain from £75 to £250 required urgent consideration.

Dr. PAUL J. FOGARTY (New Zealand) brought greetings from the Medical Association of New Zealand, and he said that relations with the B.M.A. had altered very little as a result of the change in name and status of his Association. He thanked the B.M.A. for the honour done to the New Zealand Association by the election of Dr. J. O. Mercer as a Vice-President of the B.M.A. Dr. Mercer had been editor of the *New Zealand Medical Journal* for about 26 years.

Problems in Malaysia

Dr. V. THURAISINGHAM (Malaysia) said that a problem facing the Malayan Medical Association upon which guidance was required was that the Government had refused to negotiate with the association on terms and conditions of service of Government-employed doctors, the reason being that the Government would negotiate only with a registered trade union. Therefore, as a result of the association's inability to represent these doctors, they had formed a subdivision of the association called the Senior Government Officers Association.

An exchange scheme had been suggested some time ago, said Dr. Thuraisingham, between Malaysian and British doctors, and the idea had been mooted that senior registrars from the Liverpool Regional Hospital Board would be sent out to work in Malaysia, and Malaysian doctors would receive postgraduate training in Liverpool. It had been thought that such a scheme would be mutually beneficial, but the negotiations had fallen through. An effort had been made to revive the scheme two years ago, but the Malayan Medical Association had been informed by the Ministry of Health in Malaysia that in view of the formation of the Commonwealth Foundation the scheme would be best dealt with by that foundation.

Dr. Thuraisingham reported that "quack" doctors were appearing in large numbers throughout his country, and at the moment there was no effective legislation to curb them. The association was endeavouring to educate the public to recognize the properly trained doctors as opposed to the quacks. He said that on the question of ethics the Malayan Association had usually followed the B.M.A. code of ethics as a guide, but the code was not always workable in Malaysia, and it was in the course of being modified.

Dr. P. DE S. WIJESEKERA (Ceylon) told the Conference that owing to difficulties in Ceylon young doctors were unable to come to Britain for postgraduate experience unless they had a job to come to. Therefore he asked the Committee on Overseas Affairs to consider obtaining temporary appointments for these young doctors from Ceylon for possibly three or four months in the first instance.

Professor M. G. MUAZZAN (Pakistan) said it would also be of great help if doctors in Pakistan who wished to come to the United Kingdom for training could be found appointments before they left Pakistan. He urged reciprocity in respect of medical degrees and the setting up of a secondment scheme. He thought that the raising of students' fees in Britain would result in many students turning elsewhere for their training.

Dr. E. A. MOSES (Trinidad and Tobago) said it should be impressed upon the Home Office that if a doctor came from overseas for a postgraduate course he should be given sufficient time to complete the course, and not be subjected to the embarrassment of re-applying every six months, as had been his own experience.

In Trinidad the large increase in students' fees was considered a great burden, said Dr. Moses, particularly as the majority of students who came to Britain from Trinidad to study medicine usually came under their own steam.

As far as the *British Medical Journal* was concerned, it was important from the point of view of correspondence and notices of appointments that some copies should be sent by air to Trinidad. At present the *B.M.J.* was not received until at least four weeks after publication, which was far too long.

Referring to the question of Britain's entry into the Common Market and its effect on the standard of medicine, Dr. Moses reminded the Conference that Trinidad and Tobago had reciprocity with the General Medical Council, and he wondered how practitioners in his country would be affected if Britain entered the Common Market.

Finally, he said that salaries and conditions of service of Government-employed doctors in his area were generally far from satisfactory.

Higher Qualifications

Dr. H. H. PHILLIPS (Ghana) reported that the first graduates would be coming from the medical school in Ghana in June 1969. It was hoped that those graduates would be able to go all over the world for their post-graduate training, and that therefore the difficulties in connexion with the Commonwealth Immigrants Act would be overcome. Dr. Phillips said that an ever-increasing number of graduates and specialists from Ghana wanted to take higher examinations in the United Kingdom, but there were difficulties in that connexion, and Dr. Phillips asked whether consideration could be given to the possibility of establishing examination centres outside Britain.

He said that those concerned in Ghana were also alarmed at the big increase in fees for students in the United Kingdom.

Dr. W. HEDGCOCK (Principal Deputy Secretary), speaking about the Common Market, said that a legally recognized medical practitioner of any member State would be recognized by any other member State in which he practised. That meant that the registration methods in the countries concerned would be modified to enable that to happen. Once a doctor settled in the new country, he would have to obey the laws which obtained in that country.

Professor HAMID ALI M. KHAN (Immediate Past-President) pointed to an anomaly in the present situation which allowed a doctor to come to the United Kingdom, but which did not allow him to bring his wife if she happened to be a student.

The CHAIRMAN assured the Conference that the various points which had been raised would be considered by the Committee on Overseas Affairs at its first meeting of the session. He also gave an assurance that whether the United Kingdom went into the Common Market or not the associations which were affiliated to the B.M.A. and the Branches which were part of the B.M.A. would always be of prime consideration. The B.M.A. realized the immigration difficulties which were now being experienced by Commonwealth doctors coming to this country, and when sufficient material was to hand Dr. Mathias thought that the matter would be taken up with the Home Office.

Professor F. E. STOCK referred to the increase in overseas students' fees, and said that the Committee of Vice-Chancellors and the University Grants Committee had made the strongest possible protest in the matter. Every university in the country was anxious that the fees should be reduced. Referring to Dr. Thuraisingham's remarks about "quack" doctors, Professor Stock suggested that the Malayan Medical Association could possibly obtain help by studying the Hong Kong legislation, which prohibited practice by unregistered practitioners.

The conference then ended, and representatives attended a reception for overseas visitors at the Zoological Gardens, Clifton, by invitation of the Commonwealth and International Medical Advisory Bureaux.

The Chairman of the Representative Body, Dr. A. N. MATHIAS, proposed the health of the Overseas Representatives and Dr. V. R. PATEL (Kenya Medical Association) replied.

Dangerous Drugs Act: Restoration of Authority

The Home Office announces that the authorities granted by the Dangerous Drugs Regulations under the Dangerous Drugs Act, 1965, have been restored to Dr. J. Millar Matthew (Croydon, Surrey).

Christian Medical Fellowship

An address entitled "Science: its own Arbiter?" was delivered by Mr. ARNOLD S. ALDIS, Assistant Director of the Surgical Unit, the Welsh National School of Medicine, Cardiff, at the annual breakfast of the Christian Medical Fellowship held in Bristol on 11 July. Mr. ROBERT V. COOKE, President of the B.M.A., was in the chair.

Mr. Cooke introduced Mr. Aldis to the large gathering, which included Sir Clement Price-Thomas, a former President of the Association.

Codes of Conduct

Mr. ALDIS said that medicine had always been closely associated from early days with ethics. Doctors had never equated what was possible or feasible with what was right, but they had always accepted the guidance of principles in the practice of their profession. Those principles had been crystallized from time to time in codes of professional conduct such as the Hippocratic oath. The codes were not derived from medicine or science. They had been imposed upon and accepted by the profession from outside sources, and were derived from religion, moral philosophy, and from the general *mores* of the age in which they operated.

Today a new situation was facing the profession. Scientists were claiming the right to draw up rules for the application of scientific knowledge. They were claiming the right to build ethics on science alone, and it was this situation which he questioned.

Mr. Aldis stressed the vital need for ethical teaching in medical schools and universities. He challenged the right or competence of scientists alone to supply ethical teaching. The need for ethical teaching, he said, stemmed from two factors operating in opposite directions. The first factor was the enormous advance in medicine itself. It had expanded out of all recognition, and with each expansion in medicine there were new ethical and moral judgements to be made.

Mr. Aldis said that their forefathers had had very few drugs and medicines for treatment of disease. Today commercial firms produced a whole range of potent drugs. These drugs had brought in their train new ethical problems.

Science and Ethics

The argument of the present-day scientist and humanist, that science must provide its own ethics, was based on the view that in the past scientists had had to accept an empirical ethic because their knowledge was insubstantial and their powers limited. Today the scientist's powers opened up new fields for ethical consideration. It required ethical judgements to know when and how to use the new, powerful drugs which were coming on to the market. In the field of surgery, new problems had arisen with new techniques. "We are entering the era of transplantation surgery, and the ethical problems raised by this have been intense," said Mr. Aldis. There were also problems of human experimentation.

There was a lapse in the use of the Hippocratic oath. Most universities had dropped it, for something more appropriate to the age. Most students met the Hippocratic oath for the first time when they attended their graduation ceremony. In the past, even if students were not taught ethical principles during their training, it was assumed that they had a knowledge of the Christian faith and the principles it embodied. That situation no longer held. Young people were growing up in a world where the Christian faith was very largely discarded. There was a need in the rapidly growing scope of medicine for ethical judgement, and yet to meet that demand there was a relative vacuum.

The problem of ethical principles was not only experienced by students but by those high up in the medical profession. There had been conferences on the subject, and a directive issued by the Medical Research Council indicated a disquiet about some of the principles that were being allowed to operate in research work.

C. P. Snow had said he was surprised that medical education had turned out to be less humane than might have been expected. Canon G. B. Bentley had said that science established facts, but that that did not give a person knowledge of what he ought to do. To make the transition you need a third factor, teleology. Scientists were claiming that this missing factor of teleology had been discovered in the theory and principle of evolutionary development. It was stated that ethical principles must be judged on whether they possessed survival value or not. If they did then the ethical principles must be right. If they did not the principles must be wrong. Evolution seemed to be strangely linked to survival. They must accept survival as being good, because evolution did not seem to work towards it and was indeed working the other way, towards its elimination. Was this idea of survival value an adequate guide? He believed not. He believed it was fatally easy to use that argument to justify almost any line of action.

The second principle was progress and the advancement of the race. That was equally susceptible to error. What was meant by improvement? Who was to decide what was improvement? Improvement alone was no sure guide.

The solution, said Mr. Aldis, lay in the Christian faith. Here was an ethic which alone was capable of meeting the challenge of the hour. Christian ethics provided not only a rule but means for obeying a rule. That was what the Christian faith offered. Science alone could not confer wisdom. It was in the Scriptures that "the fear of the Lord is the beginning of wisdom"; that there is "a good understanding for all they that keep His commandments."

Golf at Bristol

The results of the golf competitions held during the course of the B.M.A. Annual Meeting at Bristol are as follows: Notts Ladies' Challenge Cup, Dr. Mary F. Roche (winner), Mrs. A. Macleod (runner-up). Treasurer's Cup, Dr. D. B. Kerr (winner), Dr. J. S. K. Stevenson (runner-up). Leinster Cup, Dr. R. A. Bradwell. Childe Cup, Dr. D. B. Kerr.

General Medical Council

Disciplinary Committee

An additional meeting of the Disciplinary Committee of the General Medical Council was held on 17 July in order to consider certain cases which could not be taken in May. LORD COHEN OF BIRKENHEAD, the President of the Council, was in the chair.

Four cases of conviction were considered, including two in which an inquiry had previously been adjourned. The Committee also considered one application for restoration and one case of conduct.

Indecent Exposure

In the case of WILLIAM IRVINE HARDY, registered as of 7 Bedford Street, Belfast, in which the inquiry had been adjourned from November 1965, Mr. A. P. P. HONIGMANN (of Waterhouse & Co., Solicitors) reminded the Committee that on the last occasion Dr. Hardy had been unable to appear before it on medical grounds, and that the Committee had asked Mr. N. Leigh Taylor (of Messrs. Hempsons, Solicitors to the Medical Defence Union), who represented Dr. Hardy, to provide regular medical reports from the medical officer in charge of the hospital in which Dr. Hardy was a patient.

Mr. LEIGH TAYLOR gave a certificate to the Committee from the consultant psychiatrist looking after Dr. Hardy regarding his condition, and he suggested that, as his client had been committed to hospital by the magistrates in March 1965 following a conviction for indecent exposure, the Committee might feel able to decide that the case need proceed no further.

After a consideration *in camera* the PRESIDENT announced that the Committee had determined to adjourn the proceedings until its next meeting in November 1967, before which time it would require a further report on Dr. Hardy's condition, including the diagnosis in detail and any medical treatment which may have been given.

Mr. LEIGH TAYLOR said that he would endeavour to get the consultant psychiatrist looking after Dr. Hardy to attend as a witness when the hearing was resumed in November.

Failure to Keep a Register

The Committee next dealt with the case of NOEL PATRICK BURNS, registered as of 19 Balfour Road, Acton, London, in which the inquiry had been adjourned from May 1967.

Mr. HONIGMANN reminded the Committee that Dr. Burns had been convicted (after pleading guilty) at the Acton Magistrates' Court in December 1966 of failing to keep a register of dangerous drugs and had been fined £50 and ordered to pay ten guineas for costs. Last May Dr. Burns had been present at the inquiry but had not been represented and had not produced any evidence in mitigation of the charge. The Committee had for that reason decided to adjourn the case in order to give him an opportunity to produce evidence in mitigation.

On this occasion, said Mr. Honigmann, Dr. Burns was represented by Mr. John Lee, Counsel, instructed by Messrs. J. A. Hostettler & Co.

The conviction had arisen, continued Mr. Honigmann, as a result of a routine inspection of chemists' registers in the West London area. The police, on investigation, discovered that Dr. Burns had been purchasing unusually large quantities of morphine and pethidine, and had failed to keep a proper register. Mr. Honigmann, referring to Dr. Burns's earlier history, said that while in Canada at the time of the "Medicare" crisis in Saskatchewan it had come to the notice of the narcotics authorities there that Dr. Burns had begun to purchase and prescribe quantities of barbiturates and amphetamines which were not thought to be in accordance with the size of his practice. In reply to an inquiry by the authorities Dr. Burns had said that he felt he was the best judge of how he should run his practice and that he proposed to carry on as he did before.

Mr. JOHN LEE put in a letter from a doctor who had been treating Dr. Burns since 6 May 1967 for pethidine addiction and was confident that the addiction would be overcome.

Dr. BURNS told the Committee in evidence that after qualifying he had spent two years, from 1952 to 1954, in New York State working in a hospital, after which he had spent five years in Malaya in what was then the Colonial Medical Service. On returning to Britain he had worked with an emergency call service in London for two years, from his present address. It was largely as a result of this that he had come to take drugs. "Anybody out and about in the early hours," said Dr. Burns, "is suspected by the police of being out on some nefarious purpose. One gets stopped, and my work was being impaired to such an extent that I complained to the authorities suggesting a change in the law." Dr. Burns said that he had been convicted of speeding offences and had been disqualified from driving for 12 months. The effect of all this worry, combined with long hours, had led to his succumbing to the temptation to take drugs.

Asked by Mr. LEE whether the addiction had in any way impaired his efficiency as a practitioner, Dr. Burns replied, "No, I think it has improved it, probably." He said that he was receiving regularly weekly treatment from his doctor for the addiction.

Cross-examined by Mr. HONIGMANN, the witness said that he believed his addiction had improved his communicability with other members of the human race. He had at present about 100 N.H.S. patients and was doing a good deal of work for another doctor in the neighbourhood.

In an answer to questions by the LEGAL ASSESSOR, Dr. BURNS said that following his disqualification from driving he had gone to Canada for a year. He had, as outlined earlier by Mr. Honigmann, experienced certain difficulties concerning the prescription of drugs while in Canada, but this had arisen because of his not being conversant with the regulations. He strongly denied having done anything improper. In reply to a question by Mr. LEE, in re-examination, Dr. Burns said that no disciplinary proceedings had been taken against him in any State in Canada.

Mr. LEE submitted to the Committee that there was evidence to show that his client was overcoming his addiction and desired to be cured, and that his practice had not been impaired by this personal misfortune.

After a consideration *in camera*, the PRESIDENT announced that the Committee regarded the conviction with grave concern, especially in the light of Dr. Burns's earlier difficulty with drugs and the late date at which he had resorted to treatment. In order, however, to give him an opportunity of rehabilitating himself and of implementing the assurances given as to his future conduct the Committee had determined to postpone judgement until May 1969. It would, however, expect Dr. Burns to make an interim appearance at its meeting in November 1967. Shortly before that time he would be asked to furnish the names of professional colleagues, including a consultant psychiatrist, and other persons of standing to whom the Council could apply for information, to be given confidentially, as to their knowledge of his habits and conduct in the interval, with especial reference to any addiction to drugs.

Accessory to Manslaughter

JOSEPH CHIMA ENWEZOR, provisionally registered as of 19A Bishop Onyeabo Street, Onitsha, Nigeria, appeared on the charge that he was on 19 May 1966 at the Liverpool Crown Court convicted on indictment of being an accessary before the fact to the manslaughter of Lynn Vickers Smith (date of offence on or about 11 February 1966), and was sentenced to four years' imprisonment.

Mr. G. J. K. WIDGERY (Solicitor to the Council) produced the certificate of conviction. The conviction was admitted by Mr. P. BAYLIS (of Messrs. Hempsons, Solicitors to the Medical Defence Union), appearing on Dr. Enwezor's behalf, and the PRESIDENT announced that the Committee found the conviction proved.

Mr. WIDGERY told the Committee that Dr. Enwezor, who was about 29 years of age, was a Nigerian subject and had a wife and two young children. He had held a post at Warrington General Hospital and while there had become friendly with a nurse, Miss Smith, aged 20. At the end of 1965 the girl had become pregnant and it was not disputed that Dr. Enwezor had been responsible for her condition. On 10 February 1966 Dr. Enwezor had arranged with a friend, Dr. Mohamed, an Egyptian, who was a registrar at Whiston Hospital, Lancashire, that Dr. Mohamed should perform an abortion operation on Miss Smith. This had been arranged without the knowledge of the hospital authorities. The next day Dr. Mohamed had performed the operation on the girl in his bedroom at the hospital. She had become unconscious, the medical staff had been summoned, and strenuous efforts had been made to save her life, but she had died the next day. A few days later Dr. Mohamed had been charged with killing Miss Smith, and Dr. Enwezor had been charged as an accessary and with procuring an abortion. Both had pleaded not guilty, and they had been committed for trial at the Liverpool Crown

Court and allowed bail. However, before the trial was due to take place Dr. Mohamed had committed suicide.

Mr. Widgery said that Dr. Enwezor had appeared at the Liverpool Crown Court in May last year charged with being an accessary to the manslaughter of Miss Smith, procuring an abortion, and supplying instruments for the purposes of the abortion. He had pleaded not guilty, the trial had lasted three days, and he had been convicted on the major charge of being an accessary; the other two charges had not been put to the jury. He had been sentenced to four years' imprisonment and had appealed against conviction and sentence, but the appeal had been dismissed by the Court of Appeal (Criminal Division) on 16 March 1967.

Dr. ENWEZOR told the Committee in evidence that his father was a civil servant in Nigeria and that he was one of a family of eight. Had it not been for these events he had intended to go back to Nigeria to practise. Apart from this offence he had never been in any sort of trouble before. Dr. Enwezor said that he had hoped to marry Nurse Smith. He had been separated from his wife, with very little hope of reconciliation, at the time he had met her. Despite his conviction, he maintained that he would have liked the girl to have had the baby, but she had been determined to end the pregnancy because she was afraid her nursing career would be terminated otherwise. Dr. Enwezor added that he was by religion a Roman Catholic. He had lost his job and his liberty and had disgraced his family. His father, who was responsible for his medical education, was almost heartbroken, and the other members of his family had been greatly upset.

Mr. BAYLIS submitted that this was a most tragic case in which a series of terrible disasters had followed a moment of irresponsibility on Dr. Enwezor's part. The sentence was a severe one and the Committee would not, he thought, have difficulty in imagining Dr. Enwezor's anguish. He urged the Committee to deal with the case as mercifully as it could.

After a consideration *in camera* the PRESIDENT announced that, by reason of the conviction proved against the doctor, the Committee had directed the Registrar to erase Dr. Enwezor's name from the *Register*.

Dr. Enwezor had 28 days within which to lodge an appeal.

Abortion Charges

RODERICK SUTHERLAND ROSS, registered as of 1 Lonsdale Terrace, Edinburgh 3, appeared on the charge that he was on 17 February 1967, at the Edinburgh High Court convicted (after pleading guilty) on charges of procuring the abortion of two women (dates of offences between 1 January and 20 February 1966) and sentenced to four years' imprisonment.

Mr. WIDGERY, Solicitor to the Council, produced the certificate of conviction, which was admitted by Mr. Archibald Bell, Q.C. (instructed by Donald M. McWilliam, Solicitor), appearing on Dr. Ross's behalf. The PRESIDENT announced that the Committee found the conviction proved.

Mr. Widgery told the Committee that some time ago Dr. Ross, who was about 46 years of age, had rented a room in Mayfield Gardens, Edinburgh, apparently for the purpose of playing the bagpipes. Observation had been kept on these premises by the police, and as a result of information thus obtained Dr. Ross had been arrested on 8 August 1966, and later four charges of illegal abortion had been brought against him, covering the period between January and May of 1966. He had been granted bail and the charges had been due to be heard at the Edinburgh High Court on 24 January 1967, but Dr. Ross had failed to appear, his bail had been forfeited, and a warrant had been issued for his arrest, but he had surrendered to the police two days later and had been committed to prison to await the preparation of a fresh indictment. He had then indicated his intention to plead guilty to two charges of illegal abortion and had duly appeared on these charges in February 1967 and had been convicted. The prosecution had not proceeded with the other two charges.

With regard to the charges on which Dr. Ross was convicted, Mr. Widgery stated that the first concerned a young single woman who had consulted her own family doctor, who had confirmed her pregnancy. The girl had not sought advice from him but later had obtained the name and address of Dr. Ross and had got in touch with him, asking him to terminate the pregnancy. He had agreed to do so for a fee of £100. Dr. Ross had given the girl the address of the bed-sitting-room in Mayfield Gardens and had arranged for her to attend there a few days later. She had done so and Dr. Ross had performed an abortion operation on her. This had not been successful and two further attempts had been made over the next week or so, and finally a miscarriage had occurred.

The second charge related to another young woman, a Glasgow student, who had been examined at the outpatients department of the Glasgow Royal Infirmary, where her pregnancy had been confirmed. She had been given certain advice and had also been advised to get in touch with her parents in England. She had been told about the arrangements which would be made for her care and treatment, but she had not taken advantage of this advice and instead had got in touch with Dr. Ross and had gone to see him at his surgery in Edinburgh. She had asked him if he would terminate the pregnancy, and he had agreed to do so for a fee of £100. He had given her the address of his room in Mayfield Gardens. She had gone there later by appointment, and he had performed an abortion operation. In due course the girl had aborted.

Mr. Widgery submitted that these were not therapeutic abortions but cash transactions.

Mr. Widgery added that on 1 March 1961 Dr. Ross had been convicted of driving a motor vehicle when under the influence of drink, for which he had been fined £50 and disqualified from driving for 18 months.

Mr. ARCHIBALD BELL submitted on behalf of Dr. Ross that in both cases another general practitioner of long standing had been consulted. He put in a letter to the Committee from the general practitioner concerned, who stated that he had seen Dr. Ross in January 1966 on two occasions. The letter went on to state why, in both cases, the general practitioner had considered the termination of pregnancy to be justified.

Mr. Bell also put in two references from medical practitioners, a reference from a university professor, and a further reference from a doctor of divinity in the Free Church of Scotland. Dr. Ross came from a professional family: his brother was a solicitor and his father a doctor of divinity. He was in fact not only a fine exponent of the bagpipes but a well-known composer in the piping world.

In reply to a question by the PRESIDENT, Mr. BELL said that the general practitioner consulted by Dr. Ross about the two cases had not given evidence, the reason being that Dr. Ross had pleaded guilty, and on a plea of guilty no evidence was led in a Scottish court in the normal way. Mr. Bell added that Dr. Ross had pleaded guilty on his advice, since he had thought that otherwise the Crown would have added a further charge of absconding, which would have prejudiced a jury.

After a consideration *in camera* the PRESI- announced that, by reason of the conviction proved against the doctor, the Committee had directed the Registrar to erase from the *Register* the name of Roderick Sutherland Ross.

Dr. Ross had 28 days within which to lodge an appeal.

Restoration to the Register

MARK STAINSBY BENTLEY, whose name had been erased from the *Register* in June 1965, made a successful application for restoration of his name to the *Register*.

Infamous Conduct

The last case before the Committee was that of WILLIAM ALBERT PAINE, registered as of Redwater, Alberta, Canada, who was charged that, being registered under the Medical Acts:

(1) On or about 1 December 1965, in connexion with his application for appointment to the medical staff of the Sacred Heart Hospital, McLennan, Alberta, he stated that he held the qualifications "M.Ch., F.R.C.S.(Eng.), F.R.C.S. (Edin.)," whereas he did not hold these qualifications; (2) he permitted the insertion of an advertisement in the *Peace River Record Gazette* of 8 December 1965, and subsequent issues, announcing his commencement in practice in Falher, Alberta, and falsely stating that he held the aforesaid qualifications; (3) having on 4 January 1966, at the Sacred Heart Hospital, McLennan, performed a gastrectomy on a patient, at the conclusion of which a pair of Spencer Wells forceps was left in the patient's abdomen, he subsequently concealed the accident from the authorities of the hospital, and failed to record the fact on the patient's record; and that in relation to the facts alleged he had been guilty of infamous conduct in a professional respect.

Dr. Paine did not appear before the Committee and was not represented.

Mr. HONIGMANN (of Waterhouse & Co., Solicitors) told the Committee that Dr. Paine was resident in Redwater, Alberta, Canada. A Notice of Inquiry had been sent to his registered address in Scotland and also by recorded delivery on 12 June to Dr. Paine in Redwater, which he had acknowledged by signing the notice of delivery slip. Dr. Paine had also written to the Council's solicitors on 22 June stating that he had nothing more to say than he had already said at the inquiry at Edmonton beyond reiterating the fact that he had been acting under the orders of his then employer. "As I have already said, my actions were against my better judgement, but I felt that it was my duty as an assistant to do as I was told. I had been in Canada only about six weeks when the incident occurred, and the advice that I had received up to then was that anything that occurred in the practice was the private business of that practice and was not to be communicated to anyone else, and that included the chief of staff of the hospital. I have not made any arrangements with any lawyer to represent me in London." Mr. Honigmann also read to the Committee the letter sent to Dr. Paine (to which the above was a reply) acquainting him of his position.

The Committee decided to proceed with the case in Dr. Paine's absence.

Facts of the Case

Mr. HONIGMANN told the Committee that Dr. Paine was about 47 years of age and his principal interest appeared to have been in surgical work in hospitals. For a period of about 22 years after qualifying he had worked in a number of different hospitals in Britain. Towards the end of 1965 he had applied for the post of assistant to a Dr. Campbell-Fowler, who had a practice in Falher, Alberta.

Dr. Paine had duly arrived in Edmonton, Alberta, on 23 November 1965, and later that day had gone with Dr. Campbell-Fowler to the College of Physicians and Surgeons in order to enter his name on the medical register for that province. Mr. Honigmann said that as far as he was aware Dr. Paine had given his proper degrees and qualifications to the Registrar.

A few days later he had applied to become a member of the surgical staff of a near-by hospital, the Sacred Heart Hospital, at McLennan. In reply to a question in the application form, "What experience have you in any special branch of medicine?" Dr. Paine had written, "Surgery (M.Ch., F.R.C.S. England, F.R.C.S. Edinburgh)." Dr. Paine, according to the transcript of evidence of the local medical inquiry, had not disputed filling out the form in his own hand. However, his evidence had been that he had filled out two application forms, one of which had contained his true qualifications and no others, and a second one as a joke for Dr. Campbell-Fowler's benefit, and which he thought Dr. Campbell-Fowler had subsequently destroyed. But, according to members of the Credentials Committee, the whole form had been read out in Dr. Paine's presence and Dr. Paine had raised no objection to the inclusion of qualifications he did not possess.

With regard to the advertisements in the *Peace River Record Gazette*, the charge had not been one of advertising as such, for this form of advertising was not a breach of medical etiquette in Canada; the charge had been that Dr. Paine had held himself out as having qualifications which he did not possess. There was some discrepancy in the transcript as to how the advertisement came to be placed, and, according to Dr. Paine's evidence, the first occasion on which he knew these particular qualifications had been inserted was when he had happened to see the advertisement in the newspaper dated 8 December 1965. His evidence had been that he had gone at once to Dr. Campbell-Fowler and and asked him to take steps to see that the qualifications were deleted from subsequent issues and that he had been assured that Dr. Campbell-Fowler would try to see that they were removed. Nevertheless, the advertisement appeared unaltered in two subsequent issues and the Committee might think that Dr. Paine had not done enough in this respect.

Mr. HONIGMANN then put in letters from the Royal College of Surgeons of England and the Royal College of Surgeons of Edinburgh confirming that Dr. Paine was not a Fellow of either College. The transcript showed that Dr. Paine also did not possess the degree of Master of Surgery.

With regard to head (3), Mr. Honigmann said that the operation on the patient concerned in the charge had been a hemigastrectomy. After the operation had been concluded the usual routine check of instruments had shown that a pair of Spencer Wells forceps was missing. The nurses had suspected that the forceps had been accidentally left inside the patient, and an immediate *x*-ray had revealed their suspicions to be correct. The Sister Superior and Administrator of the hospital had informed Dr. Paine by telephone of the accident, and Dr. Paine and Dr. Campbell-Fowler had gone over in order to decide what ought to be done. For a variety of reasons it had been decided not to open up the patient there and then, and one of the reasons had seemed to be that in view of the patient's physical condition it would be better to wait for 8 to 10 days. There was also evidence that Dr. Paine's colleague had been anxious not to bring the incident to the attention of other doctors connected with the hospital with whom there was apparently a certain rivalry.

The patient had seemed to make a normal postoperative recovery, and it had been decided to discharge him on the fourteenth day after the operation. But early in April 1966, after about three months, he had collapsed and Dr. Paine had had him brought back for an emergency operation, when it had been found that a large mass of gangrene had formed through one of the rings on the handle of the forceps. There was some evidence that Dr. Paine had taken care to remove the forceps in such a way that the anaesthetist present had not seen what was being done, as apparently he belonged to the rival group of doctors in the area. There had been complications following the operation, so that eventually the chief of staff of the hospital had had to be brought in for consultation. The patient had eventually made a recovery.

The charge had been concerned not with the accident itself but with the concealment of that accident from the persons in the hospital who ought to have known about it, and from the patient's official record chart. According to the by-laws of the hospital, the incident should have been reported at once to the chief of staff, but it had not been reported for nearly three months. Instead of the fact of the accident being mentioned in the patient's record chart, a wholly misleading report had been written up about the first operation in January, giving the impression that the patient had undergone a fairly simple routine operation with no untoward effects worth mentioning. Dr. Paine's own evidence had been that two reports were written, the false one which had been kept with the hospital records and a true record which he had kept at his own home. The third concealment was that the *x*-ray taken to show that the forceps were still inside the patient had been abstracted from the hospital and kept by Dr. Paine for several months. The fourth was that on the occasion of the second operation, for the removal of the forceps, the hospital records had again been made out falsely in such a way as to omit reference to the removal; and, fifthly, there had been the attempt to prevent the anaesthetist from seeing what was going on.

Mr. Honigmann said that the Committee had no doubt read the relevant parts of the transcript supplied to them of the proceedings of the Disciplinary Committee of the College of Physicians and Surgeons, Province of Alberta, held on 24 August 1966. The PRESIDENT confirmed that this was so. Mr. G. L. HARVEY, Q.C. (the Legal Assessor) said that as Dr. Paine was not present and had no one to defend him he thought it was his duty to draw the Committee's attention to a number of other passages in the transcript which indicated Dr. Paine's point of view. These passages were read out by the Legal Assessor, and after Mr. Honigmann had further addressed it the Committee considered the matter *in camera*.

The PRESIDENT then announced that the Committee had determined that the facts alleged against Dr. Paine in the charge (as amended by the deletion of the word "and" after the word "Alberta" in head (2)) had been proved to their satisfaction.

Mr. HONIGMANN informed the Committee that apart from the incidents mentioned in the charge Dr. Paine had had a perfectly respectable medical career.

After a further consideration *in camera* the PRESIDENT announced that the Committee had judged Dr. Paine to have been guilty of infamous conduct in a professional respect in relation to the facts proved against him in the charge. "These facts were deeply reprehensible," said the President. "The conduct revealed in head (3) of the charge may have had graver consequences for his patient, but, in view of all the circumstances and the fact that he has already been tried and suspended for a period from practice by the College of Physicians and Surgeons of Alberta, the Committee have not directed the Registrar to erase his name from the *Register*. That concludes the case."

B.M.A. Nuffield Library

The library service is available to all members of the Association resident in Great Britain and Northern Ireland (and by special arrangement to members of the Irish Medical Association). A copy of the library rules will be forwarded on application to the Librarian at B.M.A. House.

The following books have been added to the Library:

Kessel, I.: The Essentials of Paediatrics for Nurses, 3rd edition. 1967.

Lewis, G. M. and Wheeler, C. E.: Practical Dermatology, 3rd edition. 1967.

Liebman, S. D. and Gellis, S. S. (Editors): The Paediatrician's Ophthalmology. 1966.

Lim, T. P. K.: Cardiopulmonary Function Tests in Clinical Medicine. 1966.

Maccoby, E. E. (Editor): The Development of Sex Differences. 1967.

Misiak, H. and Sexton, V. S.: History of Psychology. 1966.

Meeting of Doctors and Clergy

The annual meeting of doctors and clergy, arranged by the Churches' Council of Healing, was held in the Winston Theatre, University Union, Bristol, on 8 July. The subject of discussion was "Religion and Health."

Mr. ROBERT V. COOKE, President-Elect of the British Medical Association, was in the chair. The panel of speakers were the Bishop of Exeter, Dr. Robert Mortimer; Bishop Basil C. Butler, Roman Catholic Bishop of Westminster; Dr. A. M. Maclachlan, former Sheriff of Bristol and a city councillor; and Dr. R. A. Lambourne, psychiatrist and theologian.

Major and Minor Prophets

Dr. MACLACHLAN referred to the days of his youth, when the major prophets of the new faith were H. G. Wells, Bernard Shaw, and Bertrand Russell. One of the minor prophets of the past had said that by the second half of the 20th century hunger and thirst would be unknown, population would greatly increase, war and conflict would be unthinkable, and the world would have become a garden. Dr. Maclachlan said it was something to be young in the early decades of the 20th century, but "now we are old and disillusioned. Hunger and thirst are as prevalent throughout the world as ever. Man is rapacious, deceiving, double-crossing, and as cruel as ever. It was my generation which coined the word 'double speak,' which invented the gas chambers, which devised the political concept of the police state. We have lost that grand vision of the perfectibility of man, but there has been no return to our faith in religion."

Interest in religion remained, said Dr. Maclachlan, but there had been no recapture of the old faith—only a seemingly hopeless searching for something to assuage a great human need. "In our dilemma," he said, "we no longer turn to the parson. He represents organized religion and we have long lost our faith in that." Not every wage earner had a solicitor, a bank manager, an accountant, or considered he had a parson, but everyone had a doctor. So why not go to the doctor with your troubles? He was the one professional man who was readily accessible.

Medicine was the one branch of science which had proved wholly beneficent. The doctor, and especially the family doctor, scientifically up-to-date, yet still the father-figure, the counsellor and friend, had become the priest of the modern world to whom people turned with most of their problems. They were the modern miracle workers.

Dr. Maclachlan said that our Lord spoke of those who had asked for bread and had been given a stone. He asked if that might not be true of many patients who came to see their doctor. With crowded waiting-rooms and more patients than they could adequately deal with, was it surprising that doctors accomplished so little? Was not much of their surgery time taken up with avoiding problems rather than facing them? This was the modern doctor's dilemma.

"Had religion anything to offer in this doctor's dilemma? He could only speak for himself, but one must be prepared to stand up and be counted. For himself, even at its lowest level, he had found religion "philosophically therapeutic." He had always found the arguments against religion formidable but not overwhelming. In the end, said Dr. Maclachlan, it was a matter of faith.

Religion and Purpose

BISHOP BUTLER said that religion's concern with purpose and with final causes was legitimate, if only because purpose was the mainspring of all human behaviour, including the behaviour of scientists. "If you could excise from the scientist his basic desire to know and understand, he would of course cease to practise as a scientist." It was one of the glories of Western medicine that it had become, was already becoming in the days of Galen, a scientific undertaking.

But could scientific medicine proceed without appeal to the notion of purpose or final causes? It might be said that, so far as medicine was scientific, it was concerned solely with the kinds of causality with which physics or chemistry concerned themselves. But, so far as scientific medicine was medical, it was controlled by an overriding purpose of maintaining or restoring health.

The Bishop said that health could hardly be defined in terms which avoided mentioning the well-being of the organism. But well-being was a form of the good, and once the notion of the good was brought into the argument the notion of purpose was admitted. Just as medicine "saved" people from disease, so religion had the notion of a saviour, said the Bishop. There was a deep sympathy of outlook between religion and medicine. The inspiration of both was the good of men. Religion should recognize its debt to medicine, inasmuch as when a person was ill or suffering he was less capable of attending to his spiritual predicament, but, on the other hand, many doctors would agree that very often the underlying cause of their patients' illness was an unresolved spiritual problem, or a "sickness of the soul."

Religion and Disease

The BISHOP OF EXETER asked if there was some specific contribution which Christian religion could make towards health and disease and, if so, what was it? There were two threads to be discerned from the New Testament stories of Christ's healing activities. One was that all disease was somehow or other due to the baneful power of the Evil One; that it was almost contrary to the will of God. The second thread was that of compassion. If God so loved us, then we should also love one another. It was the duty of the strong to help the weak; it was the duty of the healthy to relieve the pain of the sick.

The Bishop said that there was also another tradition in the Bible, which said that disease was not so much something wrought from the Evil One and contrary to the will of God as a visitation or a punishment for sin, or was a testing of a man's faith. That kind of tradition was apparent in the Old Testament. Many illnesses, he said, were a physical expression of a deeper mental or spiritual malaise. But the root of many diseases was excessive anxiety caused by a false scale of values, such as wealth, social status, etc.

To bring any man to the point where he could recognize himself and his condition took time and much preparation. It was especially difficult to accomplish that task when he was not so much demoralized or materialistic as completely unfamiliar with any religious ideas. That was the condition of the great majority of Western civilized communities of the 20th century, and to bring those people to a recognition of their need for mental and spiritual healing was particularly difficult in modern hospital conditions, which lacked quiet and privacy. But the Christian religion did have its specific contribution to make towards the healing of men and women in body and in mind.

Mediator of Social Change

Dr. LAMBOURNE said that those who had hoped to see psychiatry establish itself as a separate discipline, achieving great success after the style of conventional medicine or religion, had been disappointed—providentially disappointed, he believed, since it had made it possible for psychiatry to play its part in a greater success. This had been as a mediator between medicine and religion by revolutionizing both in their understanding of the religious concepts of sin, saving, and salvation. As a result, two disparate views of good and evil, which so often had made discussion and co-operation between the medical profession and the clergy impossible, had given way, over the last 50 years, to a third, shared view.

For now, said Dr. Lambourne, instead of an almost exclusive view of disease as local material badnesses in the flesh, both sin and disease had increasingly come to be seen as joint evidence of a relational disorder within and between man and his environment. That revolution had largely been mediated through psychiatry.

Ladies' Club

The Ladies' Committee, under its Chairman, Mrs. J. Angell James, and with Mrs. Allen Roberts as Secretary, found many very willing helpers among the women doctors and doctors' wives of the Bristol Division, and over 150 took part in the arrangements.

The Ladies' Club within the Union building was planned and organized by the local committee of the Ladies' Guild of the Royal Medical Benevolent Fund, under the chairmanship of Mrs. Herbert Bourns. During the Meeting 523 ladies registered, and those from overseas (38) were made particularly welcome. The spacious lounge afforded a peaceful and friendly atmosphere for tea and coffee. The beautiful flower arrangements throughout the university buildings and in the cathedral were widely admired.

Bristol's sunshine, though welcome, may have made the well-attended shows of autumn fashions somewhat unrealistic. Large parties visited Badminton House, where the Duchess of Beaufort received the guests; Athelhampton, the home of Mr. Robert G. Cooke, M.P.; Clevedon Court; and Longleat. Two well-supported visits were made to Berkeley Castle and to the Severn Wildfowl Trust at Slimbridge. Those who so obviously enjoyed the excursions to Bath, Wells, and Glastonbury greatly appreciated the generous hospitality given by local ladies, which was a feature of other shorter outings.

Annual Dinner

The Annual Dinner of the British Medical Association was held at the Grand Hotel, Bristol, on 11 July.

Among the many distinguished guests received by the President (Mr. ROBERT V. COOKE) were the Duke and Duchess of Beaufort; the Lord Mayor of Bristol, Alderman the Rev. F. C. Vyvyan-Jones, and Mrs. Vyvyan-Jones; the Sheriff of Bristol, Mr. K. Lalonde, and Mrs. Lalonde; the Bishop of Bristol, the Rt. Rev. O. S. Tomkins, and Mrs. Tomkins; the Rt. Rev. J. E. Rudderham, Bishop of Clifton; the Vice-Chancellor of the University of Bristol, Professor J. E. Harris, and Mrs. Harris; Mr. C. O. F. Rieger and Mrs. Rieger; the Dean of Bristol, the Very Rev. Douglas Harrison, and Mrs. Harrison; General Sir Robert Drew; the Chief Constable of Bristol, Mr. George Twist, and Mrs. Twist; Alderman Cyril Hebblethwaite; Colonel Sir Denys Hicks and Lady Hicks; Professor J. S. Heller and Mrs. Heller; Professor C. F. Powell and Mrs. Powell; and Professor T. F. Hewer and Mrs. Hewer.

"City and County of Bristol"

Proposing the toast "The City and County of Bristol," Lord COHEN OF BIRKENHEAD, President of the General Medical Council, said it was quite natural that a city, the nucleus of which was founded where the Frome and the Avon ran together, should be a great port of commerce and a port from which many explorers left to discover new lands. Among those were two who had a special interest for medicine—John and Sebastian Cabot. Lord Cohen said that members of his generation would remember Richard Cabot's differential diagnosis. He was a descendant of the Cabots who left Bristol and landed in America, where they instilled that spirit of ethical superiority which characterized Balliol, which characterized Bristol, and which now characterized Harvard.

Bristol was a city of "firsts," continued Lord Cohen. It was the first city to have a free library; it was the first city to publish a newspaper outside London; it was the first city to have a savings bank; and it was the first city from which a steamship, the *Great Western*, sailed. Many great names were associated with Bristol, and of those connected with medicine the first must be William Budd, the greatest epidemiologist of his age. Then there were James Pritchard and John Addington Simmonds, the great progenitor of the medical school and university.

The University of Bristol was one of the most vigorous schools of teaching and research in this country, and was the envy of many universities throughout the country. Coupled with the toast was the name of the Lord Mayor. He was the first ordained priest to occupy the mayoralty, concluded Lord Cohen.

The LORD MAYOR congratulated Lord Cohen on the honour which had been conferred upon him by his colleagues, and congratulated the British Medical Association on being able to assemble in person four holders of the Association's Gold Medal out of a total of nine.

The Lord Mayor applauded the wisdom of the Association for electing Mr. Robert Cooke to the high office of President. It was the fourth occasion on which the B.M.A. had visited Bristol, and Bristol hoped that it would not be another 73 years before it came again.

"British Medical Association"

The DUKE OF BEAUFORT proposed the toast "The British Medical Association." He said that the B.M.A. had frequently been described as the doctors' Parliament, and, if so, it was a very remarkable one. The Medical Act of 1858 was almost entirely the work of the Association, and if it was a doctors' charter it could reasonably have been said to be no less a patients' charter as well. Since 1858 the Associaton had fought long, hard, and successfully for an improvement in the conditions of the medical service in poor law hospitals, the armed Forces, schools, and hospitals.

When the meeting of the Association was held in Bristol in 1863, the dinner was held in the Victoria Rooms. The *British Medical Journal* rather crushingly remarked at the time that the gallery was occupied by a number of ladies. They were not to be permitted to become members of the Association until 1892, in spite of the fact that Dr. Elizabeth Blackwell of Bristol registered in 1858. The speeches at that dinner in summary form occupied some 7,000 words in the *B.M.J.* "You organize things a bit better today," concluded his Grace.

The PRESIDENT, in response, said that the contribution made by the Duke and the Duchess to the life of Bristol and the whole of the west country was well known.

On behalf of the Association the President thanked many people who had contributed to the success of the meeting in Bristol.

"The Guests"

The toast of "The Guests" was proposed by the Chairman of Council, Dr. RONALD GIBSON, who extended a particularly warm welcome to the ladies.

The Vice-Chancellor of the University of Bristol, Professor J. F. HARRIS, responded.

Association Notices

Sutton Coldfield Division: Change of Name

The Council hereby gives notice that the name of the Sutton Coldfield Division has been changed to the Sutton Coldfield, Lichfield, and Tamworth Division.

Election of Members of Scottish Council

Notice is hereby given that nominations for the election of three members of the Scottish Council by public health service members in Scotland must be forwarded in writing to reach the Scottish Secretary, 7 Drumsheugh Gardens, Edinburgh 3, not later than Saturday, 26 August, 1967. In accordance with the Schedule to the By-laws, as amended by the A.R.M., 1967, two of the three members elected by the public health service members in Scotland must be departmental medical officers. Candidates must be members of the Association.

Nominations must be on the prescribed form, copies of which can be obtained on application to the Scottish Secretary. Nominations may be by a regional public health committee in Scotland or by a public health service member.

If a contest occurs voting papers containing the names of duly nominated candidates will be issued by the Scottish Office, British Medical Association, to each public health service member in Scotland.

DEREK STEVENSON, *Secretary*.

Ballot on Special Distinction Awards for Consultants

The British Medical Association is conducting a postal ballot of all consultants and senior hospital staff and senior registrars to ascertain their views in respect of merit awards for consultants. Ballot papers were sent in June to consultants, S.H.M.O.s, and senior registrars in the United Kingdom, together with a covering letter, a memorandum of information, and a business-reply envelope. Any consultant, S.H.M.O., or senior registrar who has not received these papers and who wishes to participate in the ballot should inform the Secretary of the Association, B.M.A. House, Tavistock Square, London W.C.1.

Diary of Central Meetings

AUGUST

23 Wed. Hospital Junior Staffs Group Executive Committee, 2 p.m.

Branch and Division Meetings to be Held

Members proposing to attend meetings marked ● are asked to notify in advance the honorary secretary concerned.

FURNESS DIVISION.—At Duke of Edinburgh Hotel, Monday, 31 July, 8 p.m., annual general meeting.

Correction

In the report of the Annual Representative Meeting (*Supplement*, 22 July, p. 88) Air Marshal Sir Richard Nelson was wrongly described as D.G.M.S., Royal Air Force. Air Marshal Sir George Gunn succeeded Sir Richard Nelson as D.G.M.S. in January 1967.

British Medical Journal Supplement

LONDON SATURDAY 5 AUGUST 1967

CONTENTS

General Medical Services Committee (Scotland) - - 109
Telephones for Hospital Staff - - - - - - 110
H.M. Forces - - - - - - - - - - 110
Association Notices - - - - - - - - - 110

General Medical Services Committee (Scotland)

The General Medical Services Committee (Scotland) held its first meeting of the new session in Edinburgh on 29 June.

Dr. A. A. Clark was re-elected Chairman, and Dr. J. E. Miller Vice-Chairman.

The CHAIRMAN welcomed the following new members: Drs. A. D. Mitchell, W. M. Paterson, Elizabeth Rose, H. A. Stewart, and J. S. Scobbie.

Dr. J. CORMACK said he was somewhat unhappy about the procedure for appointing the young practitioner member to the Committee. He thought that it did not necessarily give him the full democratic backing of those he represented. He suggested that all young practitioners in Scotland should be circularized and asked for nominations. The Committee could still have the final say in the appointment. Dr. C. D. FALCONER, Assistant Scottish Secretary, explained that the list of young practitioners in Scotland was compiled yearly. The new list would be available at the next meeting of the Committee, and consideration could then be given to holding an election in the way suggested by Dr. Cormack.

General Practitioners in Hospital

Dr. C. J. SWANSON, chairman of the working party on general practitioners in the hospital service, reported on the outcome of a meeting with the Joint Consultants Committee (Scotland). The Committee resolved that representations should be made to the Scottish Home and Health Department in support of Dr. Swanson's proposals, which included more adequate security of tenure of appointments and additional pay for "specialist responsibility" in 10(*b*) appointments.

It was agreed to keep the working party in being to make the representations.

General Practice Finance Corporation

The Committee considered a letter from the Scottish Home and Health Department about the General Practice Finance Corporation. The Department stated that it would be prepared to confer powers on the Finance Corporation to provide loans to doctors for purchasing equipment only if it could be shown that doctors were having difficulty in borrowing money for this purpose.

Dr. E. V. KUENSSBERG was dissatisfied with what the Department said and wished it to reconsider its policy as a matter of urgency. The Finance Corporation should be able to make loans available for the equipment which was so essential for the practice of modern medicine. The Committee agreed to ask that this point should be taken up by the General Medical Services Committee in London and direct with the Finance Corporation.

Subcommittee Reports

The Committee was informed that the Chairman's Subcommittee had asked the Department on 31 May to circularize the *Report on Dental Anaesthesia* (S.O. Code No. 32-536) to all general practitioners, as had been done in England and Wales.

The report of the Ad Hoc Subcommittee on the Administration of Health Centres was received, and the Secretary was instructed by the Committee to forward copies to the Scottish Home and Health Department, the Central Consultants and Specialists Committee, and the Public Health Committee (Scotland) for further discussion.

Dr. G. WATT said that the administration of his own new health centre, which was about to be opened at Langholm, would have to be considered without delay.

The report of a subcommittee of the Standing Medical Advisory Committee on Hospital Medical Records in Scotland was also received. Dr. W. W. FULTON pointed out that the recommended size of the hospital outpatient referral forms did not conform to the "post-office preferred" dimensions, and the Committee instructed the Secretary to make urgent representations to the Department on this matter.

Maternity Medical Services

A memorandum was received from the Stirling and Clackmannan Local Medical Committee proposing a fixed fee for "combined care" services. The memorandum stated that under the scheme antenatal care was carried out by the general practitioner and the patient was booked into hospital for delivery. The patient entered hospital in labour and was discharged by the obstetrician to the care of the general practitioner, who attended to her in the normal way and carried out the postnatal examination at or about the sixth postpartum week. The suggested fees for this service were as follows: (1) for full antenatal services £8 15s.; (2) for two visits after confinement £1 5s., and for three visits after confinement £1 17s. 6d.; and (3) for a final pelvic examination at six weeks £1 5s. That would give an average fee for the service of £11 11s.

The memorandum stated that the fees for maternity services, as indeed for all other services, often bore little relationship to the time, thought, and care that might have been expended on the individual case, and could "average" out only over all the cases—the easy and the difficult.

Dr. FALCONER reported that the Scottish Home and Health Department had agreed this arrangement together with the fee of eleven guineas.

Health Centres

The CHAIRMAN reported on the outcome of discussions with the Secretary of State for Scotland about the allocation of funds for the building of health centres.

The Committee was greatly disappointed that the Secretary of State had been unable to give a more hopeful prognosis about the amount of money that would be allocated for this purpose. It was thought that no time should be lost in letting members of Parliament know that if health centres were to be built in their constituencies then much more money would be required.

Proposals for new health centres at Golspie, Thurso, and at Bonnyrigg were approved. In each case the Secretary of State had been asked to delegate powers to the local authority, and, in deference to the wishes of the local doctors, the Committee agreed. However, the Committee wished to point out to the Department that what it saw for the future were health centres as defined in Section 15 of the N.H.S. (Scotland) Act, 1947, rather than the renting of space within a local authority building.

Section 15 of the Act states that the Secretary of State should provide, equip, and maintain health centres.

Other Matters

A syllabus was received from Edinburgh College of Commerce which detailed a course for medical secretaries, starting in September and lasting for 18 months. The four-term course would lead to the diploma of the Association of Medical Secretaries. Correspondence courses were already under way in Glasgow.

The Committee was informed that Professor A. Mair, of the Department of Public Health and Social Medicine at Queen's College, Dundee, had succeeded Dr. H. Miller as Medical Adviser to the Ministry of Labour in Scotland. Members of the committee emphasized the special need for the holder of this appointment to be well versed in general practice.

Stirling and Clackmannan Local Medical Committee proposed that the Committee should ask the Department to introduce a computer for cervical cytology records and for notifying executive councils about the payment due to the doctor.

The Committee agreed to make representations to the Department.

It was reported that the Secretary of State for Scotland intended to establish a new health education unit within the Scottish Department which would be responsible for stimulating health education in Scotland. This unit would work in close association with the Scottish Council for Health Education.

The Committee thought that this development was closely connected with general practice, and asked for further information on the matter from the Department.

Telephones for Hospital Staff

The joint first report of the negotiations between the Ministry of Health and representatives of hospital medical and dental staff (*Supplement*, 27 May, p. 135) stated that telephone expenses of hospital staff had been one of the matters considered in the discussions.

A memorandum recently issued to hospital boards and management committees by the Health Departments (H.M. (67) 44: S.H.M. 42/1967) sets out the revised conditions for the payment of the cost of installation and the rental of telephones in the residences of hospital staff. In future boards and committees will pay the cost of installation and rental of a telephone for a hospital doctor, provided that (1) it is essential for the efficiency of the hospital service that he should be on call outside normal working hours; (2) the telephone is the only practicable way of communicating with him; and (3) his salary does not exceed £2,050 a year.

Boards and committees will pay the cost of installation and rental of an extension from the hospital to a doctor's residence, provided the telephone is the only practicable way of communicating with him and that his home is within or adjacent to the hospital curtilage.

All staff, including those using telephones provided at their own expense, will be able to claim the cost of outgoing calls made on official business.

Hospitality

A German doctor living in Karlstadt (Northern Bavaria) would like his 19-year-old son to stay with a British medical family for two to three weeks in August as a paying guest or on an exchange basis.

A Swedish girl who is the sister of a doctor and is at present living in London would like to stay *au pair* with a medical family until Christmas, starting as soon as possible.

Would anyone who is interested please get in touch with Dr. R. A. Pallister, Medical Director, International Medical Advisory Bureau, B.M.A. House, Tavistock Square, London W.C.1.

H.M. Forces

A *Supplement* to the *London Gazette* has announced the following awards:

Army Emergency Reserve Decoration.—Colonel H. S. Davis, Q.H.P., and Major T. B. Boulton, R.A.M.C.

First Clasp to the Territorial Efficiency Decoration.—Major H. Bloom, R.A.M.C., retired.

Territorial Efficiency Decoration.—Majors J. S. G. Blair, H. Bloom, retired, J. Humphreys, C. H. Jones, T. A. Piggot, I. C. Roddie, and P. J. W. Rowell, R.A.M.C.

Appointments.—Group Captain J. P. Sewell (ear, nose, and throat duties, R.A.F. Hospital Wegberg, Germany); Group Captain R. Mortimer (pathological duties, Institute of Pathology and Tropical Medicine, R.A.F. Hospital, Halton, Bucks); Group Captain F. D. Campbell (to command, R.A.F. Hospital, Uxbridge); Wing Commander F. C. Hurrell (to the Directorate-General of R.A.F. Medical Services, Ministry of Defence); Wing Commander D. M. Fanning, O.B.E. (acting principal medical officer, Headquarters, Coastal Command); Wing Commander F. R. Jones (pathological duties, R.A.F. Hospital Wegberg); Wing Commander R. A. Riseley-Prichard (senior medical officer, R.A.F. Khormaksar, Air Forces Middle East); Wing Commander J. L. Facer (senior medical officer, R.A.F. Tengah, Singapore).

ROYAL NAVY

Surgeon Commanders G. A. Binnes, R. S. McDonald, and J. M. Hanson to be Surgeon Captains.

Surgeon Lieutenant-Commanders T. P. Oliver, L. C. Banks, T. R. W. Hampton, D. C. Beckingham, T. L. Fallowfield, and D. M. Ackery to be Surgeon Commanders.

ROYAL NAVAL RESERVE

Surgeon Captain C. E. Shafto, V.R.D., has been placed on the Retired List.

Surgeon Commander D. B. Moffatt, V.R.D., to be Surgeon Captain.

Surgeon Commander H. D. Doyle has been placed on the Retired List.

Surgeon Lieutenant-Commanders J. J. McMullan, R.D., and R. J. Howd to be Surgeon Commanders.

Surgeon Lieutenant-Commander R. W. Bazeley has been removed from the Active List.

Surgeon Lieutenant-Commanders R. A. J. Baily and G. L. Bolt have been placed on the Retired List.

Surgeon Lieutenants J. R. Newstead and B. C. Wyatt to be Surgeon Lieutenant-Commanders.

ARMY

Brigadier E. H. P. Lassen, D.S.O., late R.A.M.C., has been appointed Honorary Physician to the Queen, in succession to Major-General W. B. F. Brennan, C.B., retired.

Colonel C. S. Nicol, T.D., R.A.M.C., T. and A.V.R., has been appointed Honorary Physician to the Queen, in succession to Colonel J. W. A. Crabtree, O.B.E., T.D., tenure expired.

Colonel S. Curwen, T.D., R.A.M.C., T. and A.V.R., has been appointed Honorary Surgeon to the Queen, in succession to Colonel B. B. Hickey, T.D., tenure expired.

Association Notices

Diary of Central Meetings

AUGUST

17	Thurs.	Public Health Committee, 3 p.m.
23	Wed.	Hospital Junior Staffs Group Executive Committee, 2 p.m.

SEPTEMBER

21	Thurs.	General Medical Services Committee (Scotland) (at 7 Drumsheugh Gardens, Edinburgh), 2.15 p.m.
22	Fri.	Planning Unit, 4.30 p.m.
29	Fri.	Joint Committee of B.M.A. and Magistrates' Association, 11 a.m.

Branch and Division Officers Elected

SALISBURY DIVISION.—Chairman, Dr. J. D. Baston. Chairman-elect, Dr. J. R. H. Pinkerton. Vice-chairman, Mr. G. T. Smedley. Honorary Secretary and Treasurer, Dr. O. S. Hart. Assistant Honorary Secretary, Dr. J. B. Illingworth.

WEST DERBYSHIRE DIVISION.—Chairman, Dr. A. W. Harcus. Honorary Secretary, Dr. A. Redford. Honorary Treasurer, Dr. J. L. S. Alexander.

WEST SUFFOLK DIVISION.—Chairman, Dr. A. J. Russell. Vice-chairman, Dr. S. Blaxland. Honorary Secretary and Treasurer, Dr. K. E. Doran.

WORCESTER AND BROMSGROVE DIVISION.—Chairman, Dr. A. M. Spencer. Chairman-elect, Dr. M. Knowles. Honorary Secretary, Dr. J. A. Rigby. Assistant Honorary Secretary, Dr. H. M. White. Honorary Treasurer, Dr. A. A. Vickers.

British Medical Journal Supplement

LONDON SATURDAY 12 AUGUST 1967

CONTENTS

General Medical Services Committee - - - - - 111
Negotiating Machinery for Hospital Doctors - - - 117
Appointment of Police Surgeons - - - - - 117
Fees for Life Assurance Examinations - - - - 117
Increase in Part-time Fees - - - - - - - - 117
H.M. Forces - - - - - - - - - - 118
Association Notices - - - - - - - - - 118
Diary of Central Meetings - - - - - - - 118

General Medical Services Committee

The General Medical Services Committee spent a long time examining the ills of general practice. Many thought that these were largely self-induced, and some feared they might be mortal. One older member declared that all his working life he had heard it said that general practice was going to the dogs. But, he said, it was done well and would continue to be done well. Other speakers, however, were less confident. The majority saw an urgent need for treatment and for the eradication of the basic causes of the disease. The Committee tried to define these and to prescribe the appropriate therapy. A small working party is to put together in a report the various opinions expressed, and it will present this in due course to the Committee for approval.

In a discussion on the "Asset" case, Dr. Speakman posed the question: Who is a general practitioner in contract with?

A meeting of the General Medical Services Committee was held on 27 July. Dr. J. C. CAMERON was in the chair.

Annual Conference

Dr. W. HEDGCOCK (Secretary of the Committee) reported that complaints had been received from some local medical committees that the Annual Conference of Representatives of Local Medical Committees (*Supplement*, 24 June, p. 177) had been unable to finish its business.

Dr. R. B. L. RIDGE (Chairman of the Conference) said that the responsibility for the Conference running out of time had lain with the speakers. For instance, they had been asked not to repeat remarks or to read written speeches when it was clear that the meeting was behind the motion. Dr. R. A. KEABLE-ELLIOTT said that many small points which had been brought up at the Conference could have been answered beforehand if there had been a preliminary inquiry, and a lot of the motions could have been referred direct to the G.M.S. Committee. Dr. B. L. ALEXANDER agreed that the problem had arisen because of the repetition of speeches. Late amendments had also contributed to the difficulties. He wondered whether the Agenda Committee should be given power to reject late amendments, unless they were urgent. Possibly there should be a limit to the number of motions that a local medical committee could put forward. Dr. Alexander thought that steps should be taken to bring some order to the Conference agenda, because the chairman was not now in a position to reject amendments on the day of the meeting.

Dr. A. J. ROWE said that both the Conference and the Annual Representative Meeting were in the same plight. Both bodies would have to be more firm in future in deciding what business should be debated. He believed that the Conference should direct itself to general policy and not to details, which could be referred to the G.M.S. Committee. Dr. A. SPEAKMAN said he hoped that if any local medical committee objected to its motions being referred to the G.M.S. Committee its objection would be upheld. The Conference was the local medical committees' chance to give their point of view and to hear that of others. It should not be assumed that any motions not dealt with should automatically be referred to the G.M.S. Committee.

Changes Delayed

Dr. A. ELLIOTT said that the Constitution Subcommittee had been aware of the situation, and had decided to introduce certain changes, including changes in the standing orders of the Conference. Unfortunately, those changes had not yet been made, and until they were the situation would not improve. The Agenda Committee should be asked to consider this early next year, because of its importance. He hoped that, in consultation with local medical committees, the Agenda Committee would think also of other ways to facilitate the business of the Conference.

Dr. F. E. GOULD thought that the hand of the Agenda Committee needed strengthening. Its job should be to make up an agenda, not to accept everything that local medical committees sent in. The Committee should be able to send motions back to local medical committees with comments and suggestions. Dr. JOAN CHAPPELL suggested that when the Chairman of the G.M.S. Committee was prepared to accept a motion he should say so immediately after it had been moved. That might save time.

The CHAIRMAN said that both the Conference and the Annual Representative Meeting had been important occasions, because they were the first opportunity general practitioners had had of discussing the results of the new system of remuneration. It was true that many of the Conference motions could have been accepted without debate, but he thought it was important that local medical committees should be allowed to put forward their points of view. He had looked at the record of the proceedings of the Conference, and he did not think that there had been superfluous debate on many points. Representatives had put their points succinctly. If there had been many A motions local medical committees might have complained that discussion was being stifled. Likewise it would have been entirely wrong to have given the A.R.M. the impression that its business was being rushed because the decisions had already been taken in the Conference.

Dr. T. K. COOKE agreed that discussion should not be stifled. Speeches at the Conference had been limited first to three, then to two, and finally to one minute, and it had become a farce. If agendas continued to be long both the A.R.M. and the Conference should be extended a day.

Dr. I. M. JONES insisted that criticism should not be directed at the Chairman of the Conference. He said he believed that conferences of this kind served two main functions. Firstly, they were a forum for determining views on major issues of principle, and, secondly, they served a public relations function. The Annual Representative Meeting was open to the lay press. The proceedings of the Conference of Representatives of Local Medical Committees were reported in the *British Medical Journal*, and it was a public relations exercise between the G.M.S. Committee and general practitioners. Dr. Jones said that the Committee now had to think in terms of next year's Conference. He thought the Committee might appeal to local medical committees to bear in mind what he had suggested were the functions of the Conference, and to accept that the Conference agenda was not the proper place for matters of detail.

Logical but Undemocratic

Dr. C. J. SWANSON agreed that what Dr. Jones had said was logical but it was not democratic. He believed in the right of every local medical committee to put forward a motion if it wanted to and expect it to be put on the agenda. What was a detail to the G.M.S. Committee might be most important to a local medical committee. If extra time was needed it would have to be given. There should be no attempt to stifle debate.

The CHAIRMAN, in reply to a question, said he intended to ask that rural practice matters should be taken earlier in the agenda of the next Conference.

Dr. RIDGE, replying to the debate, said that the Conference was a most important instrument of democracy. "Without the Conference and the answerability to it of this Committee the system becomes an autocracy and a dictatorship. . . . I am certain that there must be no restriction either on the submission of motions or on the amount of speech." However, Dr. Ridge continued, it should be remembered that there were different ways in which these freedoms could be used. There could be injudicious use of both agenda space and speaking time. It was in these respects that the solution to the problem lay in the hands of the local medical committees and their representatives.

At the end of the first day of this year's two-day Conference the mid-point of the agenda had been reached. Provided that everybody paid reasonable regard to economy in time the job could be done in the time. On the second day the Conference had got behind time, and Dr. Ridge attributed that to the fact that it had come to items which required longer examination. There was the public relations aspect, said Dr. Ridge. It was important that those who had the power to make decisions in the N.H.S. should know what the doctors thought.

Compensation for Rural Doctors

The Committee considered a recommendation of the Rural Practices Subcommittee that representations should be made to the Ministry of Health that doctors practising in scattered rural areas should receive some form of compensation for being unable to join a group practice and thus get the extra pay available to doctors in group practices.

Dr. SPEAKMAN suggested that urban doctors should be included. For various reasons it was not always possible for them to form group practices.

Dr. J. S. HAPPEL, Chairman of the Rural Practices Subcommittee, said that the point was that in some areas it was impossible to form groups. When urban doctors found themselves in the same position the subcommittee would support them, but it was quite a different position when general practitioners did not wish to form groups.

The Committee adopted the recommendation.

Recruitment to General Practice

The Committee proceeded to debate memoranda by Dr. Hedgcock and Dr. Alan Gilmour (Assistant Secretary) on the shortage of family doctors.

Dr. Hedgcock's memorandum stated that the reason for the shortage could not be pinpointed. There were many factors outside pay and workload, important as those were. The departure of established general practitioners was not balanced by the entry of young doctors.

Dr. Hedgcock thought that the main reason why young doctors did not enter general practice was that they were discouraged by what they heard and by what they saw and experienced. They might have also heard unhappy experiences of some of their contemporaries.

Dr. Hedgcock went on to state in his memorandum that it was wrong that young doctors should have been allowed to get into bad situations. It was a waste of their training. Yet the tragedy was that they did not know, and did not believe, that the great majority of practices in this country were now of the type that they would have liked and which they believed could be found only overseas. General practitioners must now be willing to show young doctors that family doctoring could be a fine career, if only there were enough of them. They must also actively try to ensure that young doctors were guided to the sort of practices that they wanted, and that these practices had in fact got what they wanted. Unless family doctors themselves did this—and quickly—they must soon expect to see general practice disappear, and a great deal of the blame for that would be theirs.

There should be, the memorandum stated, a carefully organized service guiding young doctors to sound practices as a sequel to sound vocational training. There should be a well-planned, long-term publicity campaign to show medical students and young doctors what good general practice was and how they would be helped to enter it. That could be done only by family doctors themselves through the G.M.S. Committee.

Profession's Responsibility

Dr. HEDGCOCK, speaking to his memorandum, said that the responsibility for the future of general practice lay with the profession. It might be argued that, since there were some 20,000 general practitioners and they were decreasing at the rate of 300 a year, there was not very much to worry about yet. But if the drop in numbers in certain areas went on the system would soon crack.

Dr. Hedgcock said he had analysed the reasons why young doctors did not enter general practice, and he had picked on two: they did not like the way they had to practise, and they did not like the way they were paid. The young men were also being discouraged by doctors themselves. Doctors told their sons and their son's friends that general practice was not the occupation for well-trained scientific doctors.

Dr. Hedgcock said that it was a very long-term problem. He suggested that the idea of going into general practice should be put into the minds of young doctors at an early stage in their training. Referring to internal publicity, he suggested that articles could be commissioned for medical school magazines on various aspects of family doctoring. The possibility of providing lectures and films could also be considered. Possibly one number of G.M.S. *Voice* in the near future should be sent to all hospital junior staff, because many of them would become general practitioners. Articles, lectures, and films could be followed up by appropriate career leaflets prepared by the B.M.A.'s "Career Service." To encourage some of the best young doctors to enter general practice, Dr. Hedgcock suggested that the Claire Wand Fund should offer a few general practice fellowships each year. These should be highly competitive awards to recently fully-registered doctors, providing funds over three years to assist in training for general practice.

"Placing" Service

Dr. GILMOUR, introducing his memorandum on a "placing service" in general practice, said that there was a tendency for young doctors to drift into a vacancy, and hope that it would suit them, instead of there being some organized system which would assist them to go into practices where their ability and temperament would be best expressed. Whatever the outcome of the deliberations of the Vocational Training Subcommittee and similar groups, there was likely to be a longer period of vocational training developed for general practice and even more need for the doctor to have a career pattern.

Dr. Gilmour suggested that the G.M.S. Committee should provide a placing service as a necessary and practical corollary to its campaign to encourage entry into practice. The service would have to be co-ordinated on a national basis. The service should look for applicants of above average aptitude before finding them "pullman-class" practice vacancies. The assessment of practices was likely to meet with some opposition, said Dr. Gilmour, but rather less so in a seller's market. The assessment should be done by medical men. Local medical committees might be too local to make, or to appear to make, an objective assessment. There was likely to be much resentment in some quarters at any assessment being made at all, and any committee which was formed should be widely representative and as nearly acceptable as possible to the profession as a whole. It might be a committee covering a hospital board region and consisting of nominees of local medical committees, of the faculty of the Royal College of General Practitioners, and of local postgraduate medical personnel.

General Debate

Dr. GOULD said he believed that the function of the G.M.S. Committee was to look after the interests of doctors in the N.H.S., to try to improve the Service, and to make it a suitable one for general practitioners. But they were being shot at in their own family. Dr. Gould referred to a heading in a daily newspaper, "Move to woo doctors

World Problem

Dr. A. ELLIOTT reminded the Committee that there was a shortage of general practitioners all over the world. Young men could not be expected to go into general practice when the established doctors were not sure of their position. Many of the best British doctors were trying desperately to get into the hospital service, and of the remainder those who did not emigrate found themselves in general practice. The standard of those applying for general practice vacancies was not high. He knew of a practice in an urban area on the outskirts of London where it was a question of either appointing a doctor with no experience or of appointing no one.

Dr. Elliott said he preferred the term " community doctor " to general practitioner. The family doctor of the past—the horse-and-buggy doctor who knew all there was to know about medicine—would go. Specialization was increasing, and to secure his status a general practitioner must have vocational training in the same way as his specialist hospital colleagues. General practitioners could not sustain their demands for better pay and a career structure if they did not take courses of specialist training equivalent to those taken by hospital doctors. The first step must be to educate the teachers. There should be departments of general practice in the universities so that students could see that general practice was a " dignified section of the profession."

Dr. A. J. ROWE agreed that recruitment of doctors to general practice was a world problem. " But," he said, " we want to look a little nearer our own shores—to Europe." Certain countries had been through the acute stage, and they had attempted remedies. Their experiences must be taken into consideration.

In one country in Europe which had a postgraduate diploma and a master's degree in general practice the relationship between general practitioners and their consulting colleagues was clear. There was no denigration of general practice. Attempts had been made to give some sort of definition to the specialty of general practice. Dr. Rowe agreed that there was need for a group to study the position of general practice in Britain, but it was not a matter which could be dealt with quickly.

Praise for General Practice

Dr. H. N. ROSE said that he had been in general practice for over 40 years, and if he had his time over again he would still be a general practitioner. But, having said that, he would consider why doctors preferred to go into the hospital service. Nowadays young men in hospital got enough to live on. There was not the economic necessity to go into general practice. All his working life it had been said that general practice was going to the dogs—more so since the Health Service. People were always studying what was wrong with general practice—there had been the Cohen report and the Gillie report—but there were never inquiries into consultant practice. General practice was a worth while job. It was done well in this country and would continue to be done well. Students must be told that the system of remuneration had been altered and that the work load was being eased gradually by appointment systems, by ancillary help, by rotas, and by emergency services. General practice was not as bad as some people made out, said Dr. Rose.

Dr. B. D. MORGAN WILLIAMS said that it was the teachers who had to be taught, otherwise they would give the wrong impression to young men at their most impressionable age. Teaching-hospital consultants saw only the worst side of general practice; they did not see the successes. They often did not see the work of the good general practitioners who did their best to keep patients out of hospital. Papers were written by hospital doctors. One had suggested that patients should be seen by a " general physician." Unfortunately, sociologists took notice of this and so did the Ministry, because they were not aware of what was going on in general practice, and, worse still, they did not seem to want to know.

Dr. Morgan Williams said that before the war and up to 1948 morale in general practice had been high. After the war, about 1948, morale began to go down. " I suggest that this is due to poor feed-back and poor administration. I maintain that this fall in morale has been almost entirely due to sheer blind ignorance on the part of the administrators of the Health Service. . . . It is time that not only the profession but the whole country was woken up to the fact that morale in general practice is at its lowest because the Ministry doesn't want to know."

Dr. J. L. MCCALLUM hoped that the Committee would make it known that it was taking the lead in reforming general practice. He said that the biggest evil had been the division of doctors into three groups since the start of the Health Service. Now was the time for general practitioners to say that that was wrong. Dr. McCallum said that he believed students went into medical school too early. " There is no doubt in my mind," he said, " that over the years the doctor has become a less educated person. He has tended to become too specialized too early. When he comes out into general practice . . . he is not interested enough in what the patient is doing and how to fit medicine round him. The consultant is in a worse position, because he never leaves the hospital confines." Like other speakers, Dr. McCallum wanted medical students to see what went on in general practice, because otherwise they had no idea of either the fun or the difficulties. Despite the prospective increase in the number of medical students general practice would find it difficult enough to compete for recruits.

Dr. G. W. HOUSTON commented on the extreme rapidity of the advances in medical and scientific knowledge in the past 20 years. " We have to decide the direction in which general practice is to go. There are two main lines of thought. One is the community care concept. I suggest that this is wrong, and that the manner in which general practitioners are trained for this concept is wrong. General practice is a specialized environment. I would like to see a far greater development of the concept of group practice. We have to chase after a certain amount of specialized knowledge, so doctors must group together, with each doctor having a particular interest and taking a detailed postgraduate course in his own subject. The practice as a group will then be in a far greater position to deal with the medical problems that arise within the community."

Dr. A. D. MITCHELL reminded the Committee that the teachers to whom much of the vocational training for general practice was entrusted had had little or no experience of general practice. General practice was a specialty, and it was as important for senior registrars and consultants to go out into general practice as it was for the reverse to happen.

Unattractive Areas

Dr. C. J. WELLS said that recriminations between the various branches of the profession would not serve to help. He paraphrased the titles of the memoranda which had been presented as " How to place not enough young family doctors in an attractive career in unattractive areas." That might sound amusing, he said, but that was what the Committee was talking about. It was discussing how to attract young doctors into the heavy industrial areas, where the standard of living and the morale of the population were low. For that reason the people tended more than in other areas to go to the person whom they thought could help them for the least financial outlay. The result was that the morale of the general practitioner was also low.

Dr. Wells suggested that the time for talk was over. The profession, perhaps the Committee, had got to finance general practice. If the profession did not do this nobody else would. The Government had failed to offer any inducement to doctors to go into the heavy industrial areas. The time had come, he said, when general practitioners should go to the aid of their colleagues in these areas, even to the extent of providing them with some financial assistance.

Dr. D. E. HEATH thought that the lack of doctors and poor doctoring arose from undue demand by patients. The Minister must face up to the problem of patient-demand and be asked to experiment with a five-year trial of item-of-service payments by the patients.

Dr. RIDGE recalled that many of the points that had been made by the Committee had been published in the Gillie Report, and he quoted from that report. There was only one aspect of the practice of medicine in general practice, continued Dr. Ridge, which demanded the concept of general practice, and that was the personal approach of the patients to the doctor. Anything else in general practice could be done equally well under some other arrangement. But only the general practitioner, with his own place for patients to come to and the facility to visit the patients in their own homes, could provide that personal contact. It was what the people wanted.

The Gillie Report had stated: " The real incentive to good general practice is and can only be the professional conscience and sense of vocation of the doctor himself. Without this, other incentives are vain." That, said Dr. Ridge, must underlie any approach made to the problem of not enough young family doctors. " I suggest that as well as talking about vocational training we should set up some machinery to provide vocational guidance. . . . With our knowledge of general practice and our belief of what the essence of general practice really is, surely we are in a position to help young men to decide whether they are the right type of person to go into general practice." Vocational guidance could be combined with a placing service.

Dr. Hedgcock, replying to the debate, said that the trustees of the Claire Wand Fund had underwritten, subject to what the G.M.S. Committee decided, the idea of awarding fellowships in general practice to try to encourage the right type of young doctor to enter general practice. That did not necessarily mean the best academic young doctor.

Dr. Ridge had put forward an excellent idea about vocational guidance. This had already started in the B.M.A.'s new " Careers Service." Referring to the placing service, Dr. Hedgcock said he preferred to use the word guidance. Guidance should be available on vocation and on placing, and if the Committee agreed with the Claire Wand Fund proposals that could be included in the remit.

The Committee agreed that the proposals that had emerged from the debate should be set out in detail by a small working party and presented in due course to the Committee for final approval.

Other Items on Agenda

Model Assistantship Agreement

A model assistantship agreement, which had been discussed by the Assistants and Young Practitioners Subcommittee, was considered by the Committee.

Dr. M. A. Wilson said that it had been recommended that paragraph 7, which entitled the assistant to only 14 days' sick pay, should be extended to entitle the assistant to two weeks' sick leave on half pay in addition to the two weeks at full pay.

The Committee agreed to the recommendation.

Paragraph 10 was to the effect that if the assistant committed any breach of the contract or absented himself from the practice without the consent of the principal or became bankrupt or was guilty of misconduct or neglect prejudicial to the interests of the principal, the principal might end the contract without notice or payment in lieu of notice but without prejudice to any other rights and remedies of the principal. The clause concluded with the following words: " should the contract be determined under this clause then the assistant shall not be entitled to any holiday period or payment in lieu of holiday that might have become due to him under clause 6 hereof."

Dr. Ridge pointed out that the clause was in line with contracts of service between employer and employee in many walks of life, and the Committee agreed that it should not be deleted.

Attachment Schemes

The Committee considered a letter from the Association's solicitor which stated that section 24 of the N.H.S. Act, 1946, imposed a duty on a local health authority to make provision for health visitors whose duty was to visit persons in their homes for the purpose of giving advice. The position about home nurses, under section 25 of the Act was precisely similar. That was an obligation imposed on the health authority but there was nothing in that obligation to prevent the health authority taking other additional measures.

A letter from the Ministry of Health said, however, that the Ministry's lawyers did not accept that, in addition to their *duty* to provide services in patients' homes, local health authorities also had *power* to provide services elsewhere. But this did not mean that the Ministry was any less anxious than general practitioners to encourage attachment schemes as much as possible, and the letter stated that if necessary the Ministry would always be prepared to see if it could assist.

The Committee agreed that it wished to see any impediment to the progress of attachment schemes removed as soon as possible, and that any specific instances of difficulties should be brought to the attention of the Ministry.

Cervical Cytology

A letter received from the Chief Medical Officer of the Ministry of Health about the progress towards establishing a nation-wide cervical cytology service stated that the present aim was to provide facilities for the examination of women over 35 once in five years, and the service was now more than half way to the target. It would involve screening 2,600,000 women each year. In due course the service would be extended, but in the meantime planning of the service must proceed towards its first objective.

The Chairman said that the age limit of 35 was an arbitrary figure and had been fixed by the Ministry so that the demand would be channelled into what, in its opinion, was the high-risk group. However, the Ministry had given an assurance that where possible smears should be done at an earlier age.

The Committee agreed that the Council should seek an opportunity for the Association's *ad hoc* cervical cytology committee to give oral and written evidence to the Ministry's committee on gynaecological cytology.

" Asset " Case

Dr. Speakman commented on the G.M.S. Committee's statement to local medical committees, which had been agreed by the Association's solicitor, about the Court of Appeal's decision in the case of Allen *v.* Thorn Electrical Industries Ltd. (the " Asset " case). The statement had pointed out that the essential feature of the Asset case was that an oral contract had been entered into between an employer and his employees prior to 20 July 1966 to pay an increase in wages. The question to be decided by the courts had been whether that contract was enforceable in view of the Government's incomes policy. However, in law, the statement pointed out, there was no similarity between the circumstances of the Asset case and that of doctors in the National Health Service.

The statement continued: " Prior to 20 July 1966 the Government had accepted the findings of the Review Body and had agreed that general practitioners and hospital staffs should receive increases in pay with effect from 1 April 1966. Nevertheless, by 20 July 1966 this had not been promulgated and neither hospital authorities nor executive councils had received instructions to pay out the additional monies. Neither had they entered into contracts with individual doctors to do so. No contractual relationship between hospital authorities or executive councils and individual doctors existed on which any legal action similar to that in the Asset case could be based. Although the ultimate responsibility for increasing doctors' pay in the N.H.S. rested with the Government, there was no contract between doctors and the Government, and the agreement reached between the profession's representatives and the Government has no legal status until the Regulations putting it into effect are made."

Important Issues

Dr. Speakman said that if that opinion was right it raised some important issues. It stated that there was no contract between doctors and the Government. If that were so with whom had doctors a contract? Presumably the answer was the executive council. If that was so, then why were negotiations not carried on with executive councils instead of with the Government? One possible answer to that question was that executive councils were only agents for the Government via the Ministry of Health. If that was not so nothing agreed with the Ministry was binding on executive councils.

Presuming the contract to be between the executive council and the doctor, then the doctor was not responsible to the Ministry of Health. If he was, then it could be only through the executive council acting as agent for the Ministry, or by the Ministry contracting with executive councils, and the executive councils subcontracting with the doctors. However, since the Minister of Health was responsible to Parliament for the Health Service, there must be somewhere a contract or implied contract between doctors and the Ministry of Health. Whether this was by subcontract with the executive council or by an agency of the executive council did not matter.

After posing further argument based on various suppositions, Dr. Speakman concluded: " Nothing short of a test case which went to the House of Lords will satisfy me as to the true position, and if it turned out that the Asset decision cannot apply to us, or that the Government cannot be shown to have a moral responsibility to apply it, then we must take immediate steps clearly to define, firstly, if we have an enforceable contract with anyone; secondly, with whom that contract is; thirdly, if it is not with the Minister of Health through the executive councils, the legal basis on which we negotiate with the Minister and not executive councils. Having done that, every general practitioner must be made fully aware of his true legal position vis-à-vis the executive council and the Minister of Health."

The Committee agreed that Dr. Speakman's comments should be referred to the solicitor.

Negotiating Machinery for Hospital Doctors.

In formally adopting its new terms of reference on 25 July the Joint Consultants Committee relinquished its position as the sole negotiating body for hospital medical staff. The new terms of reference are:

A. To formulate policy and to consider all matters of policy that may from time to time arise relating to consultant and hospital practice, including (1) the maintenance of standards of professional knowledge and skill; (2) the encouragement of education and research; (3) the utilization to the best advantage of skills and resources, but excluding the remuneration and terms of service of hospital medical and dental staff and so that the committee shall not engage in the pursuit of political purposes.

B. To discuss (either alone or jointly with other bodies) with the Ministry of Health, the Scottish Home and Health Department, and other appropriate bodies all matters falling within the terms of the foregoing paragraph.

C. To nominate members of such bodies as the committee may from time to time decide.

The interim Negotiating Subcommittee of the Central Committee for Hospital Medical Services has taken over from the Joint Consultants Committee the functions of negotiating the terms and conditions of service of hospital medical staff. Its terms of reference are:

(1) To negotiate with the health departments and other authorities on the remuneration and terms of service of hospital medical and dental staff.

(2) To prepare and present evidence to the Review Body on behalf of hospital medical staff, and to do all such things as may be necessary in connexion therewith, including consultation with expert advisers, maintenance of liaison with other branches of the medical profession, and the appointment of members to give oral evidence.

(3) To report regularly to, and receive the views of, the Central Committee for Hospital Medical Services and the Joint Consultants Committee.

(4) To undertake such of the work of the Staff Side of Committee B of the Medical Whitley Council as is not otherwise covered by these terms of reference for so long as that Committee remains in "suspended animation."

Negotiating Subcommittee

The membership of the Negotiating Subcommittee is to be reviewed at the first meeting of the parent committee in the new session. It now consists of Dr. C. W. Clayson; Sir John Richardson, Bt.; Dr. K. Robson; Sir Thomas Holmes Sellors; and Dr. Derek Stevenson (nominated by the Joint Consultants Committee); Mr. J. R. Blackburne; Mr. H. G. Hanley; Mr. N. G. C. Hendry; Mr. H. H. Langston; Mr. W. S. Lewin, and Dr. R. M. Mayon-White (appointed by the Central Committee for Hospital Medical Services); Mr. P. W. R. M. Alberti, Dr. D. Guttman, and Dr. E. A. Harvey-Smith (appointed by the H.J.S. Group Council); Mr. N. L. Rowe (appointed by the Central Dental Consultants and Specialists Committee).

At the Negotiating Subcommittee's first two meetings the main items considered were evidence for the Review Body and the question of what work was outside a doctor's contractual hospital duties and for which therefore a fee could be charged. Schedules of work which is within and which is without the scope of N.H.S. hospital and specialist services are set out in Categories I and II of the terms and conditions of service of hospital medical and dental staff in the section headed "Retention of Fees." A preliminary discussion has been held with Ministry officials on the principles involved, and the Subcommittee stressed the view, stated out in paragraph 50 of "An Appraisal of the Hospital Service" (*Supplement*, 17 July 1965, p. 70), that "any services which are not directly concerned with the prevention, diagnosis, and treatment of illness should be regarded as outside the scope of the National Health Service."

"Committee of Nine"

The nine negotiators appointed by the Joint Consultants Committee in December 1966 to negotiate with the Health Ministers on the basis of the B.M.A.'s memorandum "Current Problems of Hospital Medical Staff" (the hospital doctors' "charter": *Supplement*, 13 May, p. 93) are to continue their task until it is completed. The joint first report on the negotiations was printed in the *Supplement* of 27 May (p. 135), and a second report is expected shortly.

The nine negotiators ("Committee of Nine") are: Sir Thomas Holmes Sellors (Chairman of the Joint Consultants Committee); Sir John Richardson, Bt. (Vice-Chairman of the Joint Consultants Committee); Mr. H. H. Langston (Chairman of the Central Committee for Hospital Medical Services); Mr. N. G. C. Hendry (Chairman of the Scottish Committee for Hospital Medical Services); Drs. J. R. Bennett, E. A. Harvey-Smith, W. P. U. Kennedy, and T. H. Taylor (Hospital Junior Staffs Group); and Mr. D. S. Hayton-Williams (Central Dental Consultants and Specialists Committee).

Appointment of Police Surgeons

The Annual Representative Meeting at Bristol accepted a memorandum submitting a case for a review of the terms and conditions of service of police surgeons which had been prepared by the Association of Police Surgeons of Great Britain and approved by the Private Practice Committee and the Council of the B.M.A. (*Supplement*, 13 May, p. 104).

The B.M.A. is trying to get a national agreement with the police authorities on the terms and conditions of service of police surgeons. The Home Office has an interest but no mandatory authority in the matter. It has accepted in principle the objectives outlined by the B.M.A. for a forensic medicine service to the nation, but it cannot instruct local authorities.

The Private Practice Committee has heard that some local authorities are seeking, in advance of a general agreement, to make local agreements with doctors which could prejudice the long-term interests not only of the doctors concerned but of the community. The Committee hopes that doctors will make their services available to the police during any period before the terms and conditions of service for police surgeons are settled. Negotiations are continuing. But doctors are urged meanwhile not to accept any contract offered to them by a police authority which imposes an obligation to be on call which is contrary to the B.M.A. recommendations, or to accept a scale of fees which is contrary to the recommendations. The Committee states that no contract should be accepted unless it binds the police authority to retrospective adjustment based upon the outcome of the negotiations now in progress.

The Committee further suggests that for the time being no agreement which departs from the B.M.A.'s recommendations and which is not regarded by both sides as an *ad hoc*, interim arrangement should be made for more than three months.

Doctors in any doubt about the terms being offered to them by a police authority are requested to seek advice from the Secretary of the B.M.A. before concluding any arrangement.

Fees for Life Assurance Examinations

The Life Offices Association has agreed to increase the fee for a "short" form of medical report for life assurance purposes from £1 10s. to £2 2s., subject to the inclusion of blood-pressure readings in the medical report.

The following fees are also paid for medical reports for life assurance: full examination and report, £3 3s.; report without examination of the proposer, £1 11s. 6d.

Increase in Part-time Fees

The B.M.A. has agreed with the Treasury a 10% increase in the fees for part-time medical services for Government departments, back-dated to 1 October 1966. The existing fees are set out in Section XI ("Fees for Part-time Medical Services") of the *Members Handbook* (B.M.A., London, 1965).

Discussions are continuing with the Treasury on certain special fees.

H.M. Forces

Surgeon Lieutenant-Commanders D. G. L. Davies, W. M. Mackean, B. W. Petty, and E. J. Williams, R.N.R., have been awarded the Royal Naval and Royal Marine Forces Reserve Decoration.

Appointments.—Wing Commander J. E. Routh (senior medical officer, R.A.F. Headquarters Unit, High Holborn); Wing Commander W. E. J. Kirby (senior medical officer, R.A.F. Oakington); Wing Commander J. B. Parsons (anaesthetic duties, Princess Mary's R.A.F. Hospital, Halton); Wing Commander J. K. Oyston (orthopaedic duties, R.A.F. Hospital, Cosford); Wing Commander E. Ward (registrar, R.A.F. Hospital, Cosford); Wing Commander R. W. Povey (orthopaedic duties, R.A.F. Hospital, Wegberg, Germany); Wing Commander R. G. Covell (senior medical officer, R.A.F. Luga, Malta); Wing Commander S. C. Rexford-Welch (directing staff duties, Royal Naval Medical School, Alverstoke).

ROYAL NAVY

Surgeon Captain W. Wilson has been placed on the Retired List.

Surgeon Lieutenant-Commander G. D. Lister has been placed on the Emergency List.

Surgeon Lieutenants D. J. McKay and D. M. Davies to be Surgeon Lieutenant-Commanders.

ROYAL ARMY MEDICAL CORPS

Lieutenant-Colonels S. B. Telford, D. H. Provan, J. D. Hughes, and J. B. J. Mulvey have retired on retired pay.

Majors I. A. R. Watson, E. R. Briant, T. M. Goodall, A. H. Dimond, and H. Q. Hutchings to be Lieutenant-Colonels.

Captains H. MacD. Sanderson and D. K. M. Thomas to be Majors.

Short Service Commissions.—Major W. D. Smith has relinquished his commission. Captain J. D. Garry to be Major.

REGULAR ARMY RESERVE OF OFFICERS

Royal Army Medical Corps

Lieutenant-Colonel G. C. Dansey-Browning, having attained the age limit, has retired, retaining the rank of Lieutenant-Colonel.

Lieutenant-Colonel A. R. Horler, from T.A., to be Lieutenant-Colonel.

Lieutenant-Colonel K. W. N. Palmer, E.R.D., T.D., from A.E.R.O., to be Lieutenant-Colonel.

Major G. T. Curtis, from A.E.R.O., to be Major.

Major A. F. Dukes has resigned his commission, retaining the rank of Major.

Short Service Commission.—Major A. Bennett, from Active List, to be Major.

ROYAL AIR FORCE

Air Commodore P. J. O'Connor, O.B.E., has been appointed Honorary Physician to the Queen in succession to the late Air Vice-Marshal W. K. Stewart, C.B., C.B.E., A.F.C., Q.H.P.

Air Commodore L. M. Crooks, C.B.E., Q.H.S., to be Air Vice-Marshal.

Group Captains E. B. Bright, A.F.C., and M. W. L. White to be Air Commodores.

Group Captains P. A. Lee and J. L. Roche have retired at their own request.

Group Captain A. S. Amsden has retired.

Wing Commanders H. A. N. Hammersley and C. J. W. Soutar, M.B.E., to be Group Captains.

Wing Commander Elspeth M. McKechnie to be Group Captain (woman medical officer).

Wing Commander F. G. Cumming, M.B.E., has retired at his own request.

Squadron Leaders F. S. Black, B. A. J. Barrow, and D. L. Price to be Wing Commanders.

Squadron Leader R. T. A. Ross has been transferred to the Reserve.

Flight Lieutenants S. B. Lydon, B. C. Corke, D. F. V. Matthew, and D. M. Denison to be Squadron Leaders.

Royal Air Force Reserve of Officers

Flight Lieutenant W. C. Hetherington to be Squadron Leader.

Association Notices

Amalgamation of Redbridge and Stratford Divisions

Notice is hereby given by the Council to all concerned that as from 1 October 1967 the Redbridge Division and the Stratford Division will be amalgamated to form the Redbridge and Stratford Division.

DEREK STEVENSON,
Secretary.

Diary of Central Meetings

AUGUST

17 Thurs. Public Health Committee, 3 p.m.

23 Wed. Hospital Junior Staffs Group Executive Committee, 2 p.m.

SEPTEMBER

13 Wed. Joint Formulary Committee, 10.30 a.m.

21 Thurs. General Medical Services Committee (Scotland) (at 7 Drumsheugh Gardens, Edinburgh), 2.15 p.m.

22 Fri. Hospital Junior Staffs Group Council, 11 a.m.

22 Fri. Planning Unit, 4.30 p.m.

29 Fri. Joint Committee of B.M.A. and Magistrates' Association, 11 a.m.

Branch and Division Meetings to be Held

Members proposing to attend meetings marked ● *are asked to notify in advance the honorary secretary concerned.*

WEST SUFFOLK DIVISION.—At Walsham-le-Willows, near Bury St. Edmunds, Thursday, 17 August, 8 p.m., fête-champêtre and barbecue. Guests are invited.●

Branch and Division Officers Elected

AYRSHIRE DIVISION.—Chairman, Dr. T. Rutherford. Chairman-elect and Vice-chairman, Mr. R. H. Simpson. Honorary Secretary, Dr. A. G. Sked. Honorary Treasurer, Dr. B. R. Nisbet

CITY DIVISION.—Chairman, Dr. M. G. O'Donoghue. Vice-chairman, Dr. M. Ross. Honorary Secretary, Dr. A. C. M. Inwald. Honorary Treasurer, Dr. J. M. Alston.

DUMFRIES AND GALLOWAY DIVISION.—Chairman, Dr. A. H. L. Wilson. Chairman-elect, Mr. W. Seright. Honorary Secretary and Treasurer, Dr. J. B. Wilson. Assistant Honorary Secretary, Dr. P. Pearce.

EAST DENBIGH AND FLINT DIVISION.—Chairman, Dr. K. Gammon. Vice-chairman, Dr. H. W. James. Honorary Secretary and Treasurer, Dr. W. E. Lewis.

EAST HERTS DIVISION.—Chairman, Dr. J. M. W. Sedgwick. Vice-chairman, Dr. W. H. Allen. Honorary Secretary and Treasurer, Dr. J. A. Hersey.

GREENWICH AND DEPTFORD DIVISION.—Chairman, Mr. W. R. O'Flynn. Chairman-elect and Vice-chairman, Dr. Jeane B. Donaldson. Honorary Secretary, Dr. N. H. Smith. Honorary Treasurer, Dr. D. L. T. Parsons.

GUERNSEY AND ALDERNEY DIVISION.—Chairman, Dr. J. B. Tucker. Vice-chairman, Dr. T. A. Fox. Honorary Secretary, Dr. T. A. Fox. Assistant Honorary Secretary, Dr. A. B. Seth-Smith. Honorary Treasurer, Dr. J. C. Bulstrode.

HALIFAX DIVISION.—Chairman, Dr. D. L. S. Johnston. Chairman-elect, Dr. J. D. G. Turner. Vice-chairman, Mr. A. B. Hamer. Honorary Secretary and Treasurer, Dr. P. H. Holmes. Assistant Honorary Secretary, Dr. D. Lightley.

HOLLAND DIVISION.—Chairman, Dr. R. G. Flower. Chairman-elect, Mr. R. F. Lawrence. Honorary Secretary and Treasurer, Dr. J. D. Brackenridge.

KETTERING DIVISION.—Chairman, Dr. J. Notley. Vice-chairman, Dr. T. Partington. Honorary Secretary, Dr. N. Cash. Honorary Treasurer, Dr. P. Rowe.

KINGSTON-UPON-THAMES DIVISION.—Chairman, Dr. G. G. Pollock. Chairman-elect and Vice-chairman, Dr. L. D. de Launay. Honorary Secretary, Mr. J. V. O'Sullivan. Assistant Honorary Secretary, Dr. G. Cohen. Honorary Treasurer, Dr. R. B. Ottley.

LANARKSHIRE DIVISION.—Chairman, Dr. H. A. Gibb. Vice-chairman, Dr. C. C. Cuthbert. Honorary Secretary and Treasurer, Dr. A. G. Jamieson. Assistant Honorary Secretary, Dr. R. J. Lumsden.

LINCOLNSHIRE BRANCH.—Mr. F. Joselin Jauch. President-elect, Dr. A. C. Fraser. Vice-presidents, Dr. C. F. E. Stanford, Dr. J. E. Darlow. Honorary Secretary, Dr. H. G. H. Richards.

NORTH GLAMORGAN AND BRECKNOCK DIVISION.—Chairman, Mr. R. H. B. Mills. Vice-chairman, Dr. F. J. Doherty. Honorary Secretary, Dr. J. B. R. Lewis. Assistant Honorary Secretary and Treasurer, Dr. W. B. Davies.

SOUTH-EAST ESSEX DIVISION.—Chairman, Dr. D. Caldwell. Chairman-elect, Dr. G. Leyden. Vice-chairman, Dr. B. Quinn. Joint Honorary Secretaries, Dr. A. Clappen, Dr. D. Hayley. Honorary Treasurer, Dr. A. Clappen.

SOUTH EASTERN COUNTIES DIVISION.—Chairman, Dr. A. F. McCoubrey. Chairman-elect and Vice-chairman, Dr. R. M. McGregor. Honorary Secretary and Treasurer, Dr. T. B. Anthony.

SOUTH WARWICKSHIRE DIVISION.—Chairman, Mr. M. W. Smith. Chairman-elect, Dr. A. R. McWhinney. Honorary Secretary and Treasurer, Dr. J. R. Lamb.

SURREY BRANCH.—President, Mr. G. N. Golden. President-elect, Dr. W. S. Lund. Vice-president, Dr. J. H. Newmark. Honorary Secretary, Dr. G. Slot. Honorary Treasurer, Dr. J. H. Moir.

SUTHERLAND DIVISION.—Chairman, Dr. R. F. Antonio. Vice-chairman, Dr. K. J. Macdonald. Honorary Secretary and Treasurer, Dr. J. Macleod.

SUTTON DIVISION.—Chairman, Dr. P. Westcombe. Chairman-elect and Vice-chairman, Dr. W. Unger-Hamilton. Honorary Secretary, Dr. Rosemary Hill. Assistant Honorary Secretary, Dr. W. Unger-Hamilton.

In the *Supplement* of 15 July (p. 68) it was stated that at the meeting of the General Medical Services Committee (*Supplement,* 8 July) Dr. C. J. Wells had been wrongly reported (p. 20) as speaking on the subject of information to hospitals. It was Dr. D. B. Wallis who spoke on this matter.

British Medical Journal Supplement

LONDON SATURDAY 19 AUGUST 1967

CONTENTS

Negotiations with N.H.S. Hospital Doctors and Dentists:
Joint Second Report - 119
B.M.A. Nuffield Library - 122
H.M. Forces - 122
Diary of Central Meetings - 122
Branch and Division Meetings - 122

Negotiations with N.H.S. Hospital Doctors and Dentists: Joint Second Report

Printed below is the second report on the negotiations which have been continuing between the Health Ministers and their Departments and representatives of hospital medical and dental staff. The first report was published in May (Supplement, 27 May, p. 135). The negotiations, which began in December 1966, have been on the memorandum, "Current Problems of Hospital Medical Staff" (Supplement, 13 May, p. 93), prepared by the Central Consultants and Specialists Committee (now named the Central Committee for Hospital Medical Services) of the B.M.A. The professions' negotiators have been the "Committee of Nine" (Supplement, 12 August, p. 117) and the members of the special working groups or "panels." The three appendices to the second report are printed in summarized form. The report and appendices are to be sent to hospital authorities.

1. In the Joint First Report on the negotiations between the Health Departments and the representatives of hospital doctors and dentists it was stated that the intention was to issue a full report later this year. Agreements would, however, continue to be implemented as quickly as possible, without awaiting the final report. This Joint Second Report gives an account of agreements reached since the issue of the first report.

2. Two further plenary meetings have been held, with the Minister of Health in the Chair, and there have been a number of meetings of the working groups (panels) described in the first report. The special working party of the Compensation and Superannuation Committee of the B.M.A. set up to consider pension matters submitted a memorandum and met representatives of the Health Departments for a first discussion on 2 August.

3. Effect has now been given to the agreement, described in paragraph 5 of the first report, that boards should advertise additional consultant posts or re-advertise vacant posts in order to establish whether or not there are doctors well qualified by training and experience for consultant posts who have hitherto been deterred from applying for them because they have not spent sufficient time in the senior registrar grade. All requests from boards for additional posts will be considered by the Advisory Committee on Consultant Establishments, a joint committee of representatives of the profession and the Ministry of Health which considers for approval all requests for the establishment of new consultant posts. Doctors with satisfactory training will not be excluded from consideration merely on the ground that they have spent little or no time in the senior registrar grade.

Staffing Structure

4. Discussions continue in Panel 1 (manpower, career structure, career planning) on a revision of the staffing structure which will facilitate integrated training schemes, on special measures in respect of registrars who have spent a long time in the grade, and on improvements in the medical assistant grade. The work of this panel is of the greatest complexity and importance. It is being pressed forward as quickly as possible but cannot be hurried. Before it can be completed, wider consultation within the profession is likely to be desirable.

Workload and Study Leave

5. The work of Panel 2 (workload and study leave) has now been completed. In the first joint report it was stated that agreement had been reached in principle on possible ways of identifying and rewarding excessive duty but that a reference had been made to the Review Body on Doctors' and Dentists' Remuneration on a difference of opinion about the extent to which they took account of excessive duty in their Seventh Report. The Review Body have now replied that in recommending substantially increased salary levels for junior staff they took into account the excessive workload that could result for remaining staff when posts were vacant. Accordingly the professions and Health Departments will now submit their agreement on the principle of extra duty allowances to the Review Body for "pricing" at their next review. Meanwhile boards are being advised that the normal response to any unplanned or prolonged staff absence, where duties cannot be reorganized, should be the engagement of a locum. The memoranda on minimum off duty time and study leave issued at the time of publication of the first report are also relevant.

6. Panel 2 has also considered some of the problems that arise from those departments, usually described as casualty departments, which attempt to provide a twenty-four-hour service for accidents and emergencies even though the work does not justify full manning on this basis. It is agreed that the need for such provision should be exceptional and that, in general, accident and emergency services should be concentrated in departments fully manned by staff specifically appointed for the purpose, but where this has not been possible special problems arise. Agreement has been reached on a number of principles that should govern the staffing of such departments. It has also been agreed that there should be special arrangements for extra duty allowances in these departments. The nature of these arrangements has not yet been settled and the "pricing" of the allowance, as of extra duty allowances generally, is a matter for consideration by the Review Body at their next review. The conclusions of Panel 2 on these matters are described more fully in Appendix 1.

7. The conditions of locum service have been considered and agreement reached on the removal of various disadvantages of locum as compared to regular service; these will be given effect in a hospital memorandum to be published shortly. The improvements will enable locum service in a grade to count in part towards incremental credit on appointment to a regular post in that grade.

Improvements have also been agreed in the arrangements for travelling expenses and sick leave for locums. Consideration is being given to remuneration in lieu of annual leave which cannot be taken during the course of the locum appointment.

8. In discussion of the reference in the professions' memorandum to medical administration the Health Departments and the professions agreed on the importance of this work and are united in a desire to see an increase in the number of doctors qualified by training and experience to be medical administrators.

Medical Research

9. Consideration has been given to the part to be played by the hospital service in furtherance of medical research. Basic long-term medical and dental research and opportunities for medical research as a career are primarily the concern of the universities and Medical Research Council, but the National Health Service provides unique opportunities for research, and it is important to create conditions in which hospital doctors can carry it out. Indeed they should be encouraged to initiate projects which may be of value and should be able to make reasonable use of secretarial and other facilities (for example, to establish the value of a project). The Health Departments assured the representatives of the professions that the provision of time for research within contractual sessional time should be possible where this is necessary, and did not consider it appropriate for sessional time to be permanently allocated to research in the contract. They agreed that it was important that applications for approval of research projects should be dealt with expeditiously.

10. The scope of the research activities already being undertaken within the hospital service is far wider than is often appreciated. The Departments supplied information about the measures that have and continue to be taken to support research, to bring hospital libraries up to date, and on the use of computers and other technical equipment in the National Health Service, and this information is reproduced as Appendix 2 to this report.

General Conditions of Service

11. Panel 3 (conditions of service generally) have completed their examination of removal expenses, annual leave and sick leave, telephone expenses, ancillary help, quarters (including married quarters), and provision of meals. They still have to consider the problem of home-to-headquarters mileage allowances, on which the Health Departments await further evidence being prepared by the professions. Mileage allowances generally have been discussed for some considerable time in the General Whitley Council and elsewhere, and an account of the discussions is given in Appendix 3. An interim increase in rates has recently been made.

12. The following hospital memoranda giving effect to the agreements reached in the Panel have been published since the first report: (*a*) H.M. (67) 37, "Improvement in Sick Leave Entitlements" (15 June); (*b*) H.M. (67) 39, "Extension of Present Arrangements for Assistance with Removal Expenses" (22 June); (*c*) H.M. (67) 44, "Reimbursement of Telephone Expenses (18 July).*

13. A hospital memorandum on the need for the provision of residential accommodation for hospital staff is in preparation, and will deal with ways in which hospital authorities can help in this. The Panel has also considered the arangements in England and Wales for determining the rents of hospital-owned flats and houses. A hospital memorandum bringing together the existing circulars as a single document, and extending the present discretion of hospital authorities in rebating rents charged to medical staff who are compulsorily resident, is also in preparation.

14. It is agreed that there is a good case for an increase in annual leave for registrars from four weeks to five. An improvement in annual leave is, however, in the context of the Government's Prices and Incomes policy, equivalent to an increase in remuneration (see paragraph 20 of Cmnd. 3235), and the attention of the Review Body will be drawn to the matter.

15. The Health Departments cannot accept the professions' strongly argued contention that any non-resident doctor kept on duty, recalled for duty, or required to be resident overnight should not have to pay for meals taken in hospital on these occasions. In their view such a request is clearly contrary to one of the principles which the Review Body assumed would be followed in making the recommendations on remuneration in their seventh report—namely, that "all doctors, whether . . . they are on duty or off duty, should pay for meals they take in hospital." The Health Departments had agreed before the Review Body reported that a non-resident doctor recalled from his home while not on duty (or on call), in circumstances accepted as constituting an emergency, or detained on duty in such circumstances, need not be charged for refreshment provided. They do not propose to withdraw this concession but see no justification for extending it.

Scottish Panel

16. The Scottish Panel has met twice since the first joint report was issued. Memoranda on the extension of existing arrangements for assistance with removal expenses and the reimbursement of telephone expenses have been issued, and the various reports and papers referred to in the foregoing paragraphs have been considered from a Scottish aspect. The arrangements for fixing rents of hospital accommodation in Scotland differ from the arrangements applying in England and Wales, but the Panel is reviewing the Scottish position on the same lines as described in paragraph 13.

Final Report

17. It remains the intention that a full and final report on the negotiations should be issued later. Agreements will continue to be implemented as quickly as possible, without awaiting the final report.

---

* These circulars were summarized in the *Supplement* to the *British Medical Journal* on the following dates: 17 June, p. 175 (Sick Leave); 1 July, p. 12 (Removal Expenses); 5 August, p. 110 (Telephones).

Summarized Appendices

I. Relief of Excessive Work Load

The Review Body is to recommend how the agreement of the Departments and the professions on the principle of extra-duty allowances should be given effect. Meanwhile, excessive work load is not to be regarded as an unavoidable feature of medical life but as a problem requiring action. The first response to excessive work load (boards are advised) should be to try to reorganize duties, and when nevertheless unreasonable work load persists the appointment of a locum should be the normal remedy.

"Unreasonable" has been defined, in relation to the provisions on guaranteed minimum time off duty (*Supplement*, 27 May, p. 136) as follows:

(*a*) when failure to fill a post will significantly affect the service available to patients unless a substantial part of the work of the post is done by other staff; (*b*) when the medical staffing of a hospital is such that the maintenance of essential services during absences would result in excessive work for the staff remaining; (*c*) when other circumstances give rise to an exceptionally heavy workload, such as an excessive sickness rate among staff; (*d*) when a post is vacant or the holder is absent for any reason and the minimum off-duty periods would be available to staff only at the expense of unreasonable conditions for patients or for staff during working hours.

When a locum cannot be obtained boards should be authorized to pay an extra duty allowance to the staff carrying the duties for which a locum had been sought. The Review Body will be asked to "price" the allowance.

It has been agreed that hospital authorities should be asked to review the work of casualty departments to ensure (*a*) that preregistration house-officers should never work unsupervised in them; (*b*) that when regular duties in casualty departments are to be required of junior staff this should be mentioned in the advertisement and in the letter of appointment; (*c*) that duties in casualty departments should not be combined simultaneously with other liabilities unless there are overriding reasons stemming from either the isolation of the hospital or the sparsity of the population served.

Eligibility for extra duty allowances in casualty departments should extend to situations when liability for duty must be undertaken simultaneously with liability for duty in other departments and excessive work load results. The pricing of the allowances would be a matter for the Review Body.

The professions strongly contend that all doctors (including general practitioners) other than casualty officers doing sessions in casualty should be paid at the same appropriate sessional rate. The Health Departments argue that frequently some additional burden can be accepted without imposing an unreasonable work load, but they accept "that there should be a prima facie case for recognizing excessive work load in casualty departments not only when the agreed minimum time-off periods are not available but whenever hours of duty and on-call are increased through the incidence of casualty duty by more than one night on call in each week (subject to a qualifying period) whether or not the employment of a locum is justified. Both sides will give evidence independently on this subject to the Review Body."

II. Research

Medical research in its broadest sense is supported by public funds from three main sources: the University Grants Committee; the Medical Research Council; and the Ministry of Health. In 1966–7 expenditure on research by university departments of medicine and allied subjects was about £16m. The Medical Research Council spent £770,000 in 1948–9, £11½m. in 1966–7, and in 1967–8 it is estimated it will spend £14m. Roughly two-thirds of this sum goes to support the Council's own staff and units—mainly in universities and teaching hospitals. The remaining one-third goes on grants, usually short-term, to individual research workers—the majority in university, medical school, or teaching hospital departments. The Ministry of Health spent £1.5–£2m. on research and development in 1966–7 and will spend an estimated £2.5m. in 1967–8. The current expenditure by the Scottish Home and Health Department is estimated at £190,000.

Hospital authorities in England and Wales and Scotland may use non-exchequer funds for research subject to the terms of individual trusts. A proportion of the endowment funds of the Scottish hospitals taken over in 1948 was used for the establishment of a Scottish Hospitals Endowments Research Trust, which makes grants to research workers in hospitals and universities. The annual income of the Trust is about £120,000.

Roughly speaking the Health Departments' role is to initiate and support research and development as a direct aid to the discharge of their own policy and responsibilities, while the Medical Research Council is the government agency responsible for the support, advancement, and proper balance of research in the medical sciences.

Research Financed by Departments

About two-thirds of the Ministry's expenditure on research and the greater part of that of the Scottish Home and Health Department is on centrally promoted projects. The remainder is on decentralized research. Centrally promoted projects are undertaken by universities, other academic and research institutions, individuals, and hospitals acting on behalf of the Departments.

Hospital circulars H.M. (57) 36 (England and Wales) and S.H.M. (57) 60 (Scotland) described the arrangements for a scheme for locally organized research to be carried out at the expense of Exchequer funds. Further guidance to boards on conditions under which grants from decentralized funds should be distributed was issued in June 1964.

The scheme is complementary to the Medical Research Council's scheme of temporary research grants to individuals, and is intended to encourage local initiative in research and foster local talent. In England and Wales the scheme has become the mainstay of support for research in district hospitals and an increasingly important supplementary service in some teaching hospitals. Allocations under this heading in 1966–7 amounted to about £600,000. Boards are being encouraged to include local authority and general practitioner representatives on the local research committee and to make grants available to individuals in all three parts of the service. In Scotland current expenditure under the scheme is £10,000.

The Medical Research Council's advice is sought on major projects, and when possible collaboration is arranged. Links are also being established with the Social Sciences Research Council, and there is consultation and collaboration in special fields with a number of Government departments—for example, the Ministry of Technology over the use of computers in medicine.

Libraries

Advice on the organization of hospital libraries is being prepared. The staff library in each hospital group will be expected to have a basic stock of books covering the needs of doctors and dentists and all other hospital staff and to subscribe to the important journals in each field. There should be a good selection of "reference tools" (including the *Index Medicus*, the principal abstracting journals, and the main bibliographies), a subscription to one of the medical and scientific circulating libraries, and arrangements to borrow from national libraries. A qualified librarian will be able to give assistance to doctors and dentists in the most economical use of the newly developed mechanized bibliographical services.

All boards are advised that accommodation for research should be provided in new hospitals.

Research Equipment

The Health Departments are giving increasing attention to the development and evaluation of medical equipment. Particular interest attaches to items such as the use of ultrasonics and thermography in diagnosis, the laser, fibre optics, the automation of pathological laboratory work, pattern recognition systems for the detection of malignant cells, artificial kidneys, and patient monitoring devices. It is expected that about £400,000 will be spent in 1967–8.

Medium-sized computers are likely to be installed for research, experimental, and routine use in a few major hospitals before 1970. Their use on this comparatively small scale will pave the way for the more widespread provision of computing facilities in following years. Among the most important functions proposed for hospital computers is the storage, maintenance, and sorting of patient records. This, as well as aiding the efficiency of hospital activities, will enable more analysis of patient records to be undertaken for research purposes.

III. Mileage Allowances

Mileage allowances are a matter for all hospital employees, and therefore they are discussed in the General Whitley Council. General Council agreements, however, apply to hospital medical and dental staff only if the Staff Side of Medical and (Hospital) Dental Committee B agree. The last general revision of mileage rates was in 1965, but the Staff Side of Committee B refused to accept the increase (of ¼d. a mile) for medical and dental staff. The Management Side of Committee B did not accept that there was a case for special treatment for hospital medical and dental staff, and the matter was referred back to the General Council.

In Panel 3 of the current negotiations the professions successively proposed:

(1) That hospital staff (especially junior staff) should be assisted with car purchase—e.g., by the provision of loans at low rates of interest or even free of interest.

(2) That mileage allowances should (*a*) include an annual lump sum to cover depreciation and interest on capital; or (*b*) be on a steeply graduated scale of rates per mile, so as to cover a relatively high proportion of the standing charges in the early miles; or (*c*) cover (for every mile travelled on duty) the total cost of motoring as calculated by the A.A. or by the R.A.C. at 10,000 miles per annum.

The principal objection to these proposals, other than that for assistance with car purchase, was that they involved reimbursement on a scale which was, in the Health Departments' view, likely to be substantially in excess of expenditure properly attributable to motoring on official business. The proposal for assistance with car purchase was rejected on the grounds that there were many more pressing demands on National Health Service resources and that loan facilities for car purchase were readily available from banks and hire purchase finance companies.

The General Whitley Council has agreed that a survey should be undertaken to obtain information about the actual annual mileages travelled by N.H.S. officers on official business and, pending the results of the survey (on which a progress report is to be made by 15 September), that there should be an interim increase in mileage rates. For doctors and dentists these will be ¾d. a mile for the first 7,000 miles a year and ½d. a mile thereafter.

In accepting this interim settlement for hospital medical and dental staff the Staff Side of Committee B has stated:

> "(1) The medical and dental professions do not regard these interim increases as reflecting at all adequately the rise in motoring costs since 1952; and (2) having regard to the complete dependence of the hospital service upon the willingness of doctors and dentists to use their private cars upon the business of the hospital authorities, the medical and dental professions greatly regret that their current efforts to negotiate a fair rate of reimbursement for the use of private cars on N.H.S. business (which began with the submission of their first memorandum on 17 March 1966) are not yet within sight of a conclusion."

B.M.A. Nuffield Library

The Library service is available to all members of the Association resident in Great Britain and Northern Ireland (and by special arrangement to members of the Irish Medical Association). A copy of the library rules will be forwarded on application to the Librarian at B.M.A. House.

The following books have been added to the Library:

Myerson, R. M. and Pastor, B. H.: Congestive Heart Failure. 1967.
Nelson, R. S.: Gastroscopic Photography. 1966.
Ravin, A.: Auscultation of the Heart, 2nd edition. 1967.
Rowe, J. W. and Wheble, V. H.: A Concise Textbook of Anatomy and Physiology, 2nd edition. 1967.
Schulenburg, C. A. R.: Operative Cholangiography. 1966.
Sears, W. G.: Medicine for Nurses, 10th edition. 1966.
Smith, J. L. (Editor): Neuro-ophthalmology, Volume III. 1967.
Smith, M. J. H. and Smith, P. K.: The Salicylates. 1966.
Stewart, W. D., Danto, J. L. and Maddin, S.: Synopsis of Dermatology. 1966.
Stott, F. D.: Instruments in Clinical Medicine. 1967.
Verville, E.: Behavior Problems of Children. 1967.
Warick, C. K.: Anatomy and Physiology for Radiographers. 1966.
Welch, C. E.: Surgery of the Stomach and Duodenum, 4th edition. 1966.
Wells, B. B. and Halsted, J. A.: Clinical Pathology, 4th edition. 1967.
Widdess, J. D. H.: The Royal College of Surgeons in Ireland and its Medical School, 1784–1966. 1967.
Wynn, R. M. (Editor): Cellular Biology of the Uterus. 1967.
Young, M. E. J.: Radiological Physics. 1967.

H.M. Forces

ROYAL NAVY

ROYAL NAVAL RESERVE

Surgeon Lieutenants S. J. McDonald, J. R. Newstead, and J. R. N. Curt to be Surgeon Lieutenant-Commanders.

ARMY

Colonels R. J. Niven, M.C., J. McGhie, Q.H.P., and N. G. G. Talbot, O.B.E., T.D., late R.A.M.C., to be Brigadiers.

ROYAL ARMY MEDICAL CORPS

Captain R. D. Whitla to be Major.

REGULAR ARMY RESERVE OF OFFICERS

ROYAL ARMY MEDICAL CORPS

Short Service Commission.—Major A. C. MacLean, from Active List, to be Major.

TERRITORIAL AND ARMY VOLUNTEER RESERVE

ROYAL ARMY MEDICAL CORPS

Colonels T. W. A. Glenister, T.D., and I. C. Seymour, T.D., from T.A., to be Lieutenant-Colonels, relinquishing the rank of Colonel.

Lieutenant-Colonel J. P. W. Hughes, T.D., from T.A., to be Lieutenant-Colonel.

Lieutenant-Colonel B. K. Scott, from T.A., to be Major, relinquishing the rank of Lieutenant-Colonel at his own request.

Lieutenant-Colonels R. M. Stewart and A. R. Foster, from T.A., to be Majors, relinquishing the rank of Lieutenant-Colonel.

Major (Acting Lieutenant-Colonel) A. G. Hutchison, from T.A., to be Major, relinquishing the acting rank of Lieutenant-Colonel.

Majors J. C. Hewitt, S. R. T. Headley, T. Bird, R. A. Goodhead, T.D., D. J. B. Ashley, D. C. Provan, and R. E. D. Simpson, T.D., have been granted the acting rank of Lieutenant-Colonel.

Majors R. M. Gibson, N. E. Shaw, D. W. Sumner, L. Symon, B. R. Stead, and R. S. Kocen, from A.E.R.O., to be Majors.

Majors P. J. Daly, T.D., J. D. C. Turner, K. Boheimer, K. T. Burke, G. B. Smith, J. C. Denmark, R. H. Ramsay, T.D., P. W. Ross, J. P. V. Rigby, W. A. L. Thompson, and I. C. Balfour, from T.A., to be Majors.

Major A. R. Foster has resigned his commission and has been restored to the rank of Lieutenant-Colonel.

Major J. A. Ward, T.D., has resigned his commission, retaining the rank of Major.

Captains (Acting Majors) G. J. H. Everard and B. F. Reeves, from T.A., to be Captains, retaining the acting rank of Major.

Captain G. T. Haysey to be Major.

Captain H. T. Thompson has been granted the acting rank of Major.

TERRITORIAL ARMY

ROYAL ARMY MEDICAL CORPS

Lieutenant-Colonel S. Mattingly, T.D., has resigned his commission, retaining the rank of Lieutenant-Colonel.

Major J. F. K. Grieve, T.D., has retired, and has been restored to the rank of Colonel.

Major J. A. Stanton, T.D., has resigned his commission and has been restored to the rank of Lieutenant-Colonel.

Majors K. J. Zilkha and A. W. Howel-Evans have resigned their commissions, retaining the rank of Major.

Majors F. R. Wright and K. F. Kyle have resigned their commissions.

Captain J. Piggot to be Major.

TERRITORIAL ARMY RESERVE OF OFFICERS

ROYAL ARMY MEDICAL CORPS

Major J. Bleakley, M.B.E., having exceeded the age limit, has retired, retaining the rank of Major.

Major G. Savill has resigned his commission, retaining the rank of Major.

Major J. Davenport has resigned his commission.

Captain (Honorary Major) R. C. Connolly has resigned his commission, retaining the honorary rank of Major.

ROYAL AIR FORCE

Flight Lieutenants B. N. M. Oliver and A. Andrew to be Squadron Leaders.

Association Notices

Diary of Central Meetings

AUGUST

23	Wed.	Hospital Junior Staffs Group Executive Committee, 2 p.m.

SEPTEMBER

13	Wed.	Joint Formulary Committee, 10.30 a.m.
21	Thurs.	General Medical Services Committee (Scotland) (at 7 Drumsheugh Gardens, Edinburgh), 2.15 p.m.
22	Fri.	Hospital Junior Staffs Group Council, 11 a.m.
22	Fri.	Planning Unit, 4.30 p.m.
29	Fri.	Joint Committee of B.M.A. and Magistrates' Association, 11 a.m.

Branch and Division Meetings to be Held

Members proposing to attend meetings marked ● are asked to notify in advance the honorary secretary concerned.

DARTFORD DIVISION.—At "Little Mote," Eynsford, Thursday, 24 August, 8.30 p.m., meeting to receive report on Annual Representative Meeting.

GLASGOW DIVISION.—Tuesday, 22 August, 2.15 p.m., visit to John Brown's shipyard (men only).●

Branch and Division Officers Elected

ABERDEEN BRANCH.—President, Dr. F. Rae. President-elect, Dr. J. W. Taylor. Vice-president, Dr. W. Burgess. Honorary Secretary, Dr. D. E. Fraser.

ABERDEEN AND KINCARDINE COUNTIES DIVISION.—Chairman, Dr. J. L. T. Dickie. Vice-chairman, Dr. J. M. Gill. Honorary Secretary and Treasurer, Dr. J. W. Taylor. Assistant Honorary Secretary, Dr. F. L. P. Fouin.

BURTON-ON-TRENT DIVISION.—Chairman, Dr. L. Rose. Vice-chairman, Dr. P. Allebone. Honorary Secretary, Dr. N. F. Stewart. Honorary Treasurer, Dr. R. J. Mountain.

SWANSEA DIVISION.—Chairman, Mr. C. H. Tanner. Chairman-elect and Vice-chairman, Mr. E. M. Evans. Honorary Secretary and Treasurer, Dr. J. R. Ivey. Assistant Honorary Secretary, Mr. H. J. Hambury.

TEES-SIDE BRANCH.—President, Dr. T. E. Moody. President-elect, Dr. J. V. Walker. Honorary Secretary, Dr. G. Blair. Assistant Honorary Secretary, Dr. A. Fraser.

TORQUAY DIVISION.—Chairman, Dr. J. B. Taylor. Chairman-elect, Dr. J. Lyons. Vice-chairman, Mr. P. J. W. Monks. Honorary Secretary and Treasurer, Dr. A. Young. Assistant Honorary Secretary, Dr. J. Clunie.

Correction.—It was Dr. D. L. Williams, not, as reported (*Supplement*, 12 August, p. 114), Dr. G. P. Williams, who spoke in the General Medical Services Committee's recent debate on general practice. Dr. D. L. Williams this year succeeded Dr. G. P. Williams as a representative of Wales on the G.M.S. Committee.

British Medical Journal Supplement

LONDON SATURDAY 26 AUGUST 1967

CONTENTS

Security of Tenure of Consultant Appointment - - 123
Public Health Service Dispute - - - - - - 124
"Mediflash" - - - - - - - - - - 124
H.M. Forces - - - - - - - - - 124
Diary of Central Meetings - - - - - - 124
Branch and Division Officers Elected - - - - 124

Security of Tenure of Consultant Appointment

This account is based on an article submitted by Dr. P. H. A. Willcox.

A recent appeal to the Minister of Health by a consultant physician concerned the question of a consultant's security of tenure of a hospital appointment when the staff and functions of the hospital are transferred to a new hospital.

The appeal, by Dr. P. H. A. Willcox, was under paragraph 190 of the "Terms and Conditions of Service of Hospital Medical and Dental Staff (England and Wales), 1967." Paragraph 190 of the Terms and Conditions of Service states: "Where a consultant . . . considers that his appointment is being unfairly terminated, he shall be entitled to send a full statement of the facts to the Minister, who will obtain the written views of the Board concerned and place the case before a professional committee . . . for their advice. . . . This procedure shall be completed before the Board's decision to terminate the appointment is carried into effect. . . . " Paragraph 191 states, "It is understood that where a local change of organization in the hospital and specialist services involves displacement or serious disturbance of the services of a consultant . . . the Board recognizes that it has a moral obligation to render the greatest possible assistance to the practitioner with a view to his obtaining comparable work in another hospital."

Transfer Recommended

Dr. Willcox, senior physician to the Windsor group of hospitals, had a maximum part-time contract which included two sessions at Upton Hospital, Slough. When a new hospital was built at Wexham Park to serve Slough and to replace Upton Hospital physicians of the Windsor Group discussed the staffing arrangements at the new hospital, and they recommended that Dr. Willcox's two sessions at Upton Hospital should be transferred to Wexham Park. This was approved by the hospital management committee, and the recommendation was forwarded to the North-west Metropolitan Regional Hospital Board during the summer of 1965.

In November 1965 the Board's Secretary proposed transferring Dr. Willcox's two sessions at Slough to King Edward VII Hospital, Windsor, instead of to Wexham Park Hospital. Dr. Willcox protested on the grounds that (*a*) there was no more work in general medicine available at Windsor where he was already employed for two sessions, so that he would be underemployed by this amount of work; (*b*) it would debar his patients resident in Slough from the benefits of the most modern hospital in the group; and (*c*) it would damage his professional status and consulting practice. His request for an interview with the Board was not granted until 27 May 1966. The Board did not alter its policy after this interview.

On 19 March 1966 the Board advertised a new post of consultant physician at the new hospital. At the end of March the Board invited Dr. Willcox to agree to transfer his two sessions from Slough to Windsor. Dr. Willcox refused, giving notice that he would appeal to the Minister of Health. This he did on 22 April 1966.

On 19 April the Board informed Dr. Willcox that it had decided he would not be offered any appointment at the new hospital, and on 25 April Wexham Park Hospital was opened and all the patients, including 10 under the care of Dr. Willcox, all the consultants in charge of beds except Dr. Willcox, and all the resident medical staff were transferred to it from Upton Hospital.

Minister's Decision

Dr. Willcox's appeal to the Minister was heard on 15 September 1966. The professional committee was under the chairmanship of the Chief Medical Officer, Ministry of Health. The Minister of Health conveyed his decision to the Board on 3 November 1966 in the following terms:

> "The Professional Committee have expressed the view that Dr. Willcox had good grounds for anticipating that his work would be transferred to the new Wexham Park Hospital when Upton Hospital was closed, so that he might continue treating patients in the Slough area. At the same time the committee have recognized that it was reasonable and opportune for the Board to make changes in the organization of consultant staffing in accordance with the general principles recommended in the (Platt) Report on Medical Staffing Structure in the Hospital Service. In the opinion of the Committee, the Board was at fault in not discussing in sufficient detail the plans for reorganization with the medical staff concerned, which would have allowed them to come to an agreed solution; as a corollary, adjustments at Windsor and at the other hospitals in the Group should have been considered before the opening of Wexham Park. The Minister agrees with these views.
>
> "The Professional Committee recommends that the transfer of 4½ hours of Dr. Willcox's time to the Wexham Park Hospital would not be the most effective way of organizing the services at that hospital and that the proposal to concentrate Dr. Willcox's services in the Windsor area by increasing his sessions at King Edward VII Hospital from 2 to 4 is reasonable, provided that a proper and immediate redistribution of work amongst the physicians there takes place to ensure that these additional sessions are effectively employed and Dr. Willcox's grievance is removed. In reaching these conclusions the committee has been influenced by the fact that there is to be considerable development in the area served by the King Edward VII Hospital, Windsor, and Heatherwood Hospital, and suggests that Dr. Willcox be asked to devote some time to assisting in the planning of Heatherwood and the hospital service for Bracknell New Town. The Minister accepts these recommendations."

Dr. Willcox states that since the opening of the new hospital no further work has been made available to him at Windsor other than the two sessions he has had there for many years. In January 1967 the Regional Board granted him the privilege of admitting cases arising in his practice to the new hospital under his own care.

Public Health Service Dispute

After representatives of the local authorities associations had met representatives of the B.M.A. on 17 August it was stated that they had had a "useful discussion" towards "reaching a settlement on the public health medical officers' pay claim." A further meeting of the two sides is to be held on 13 September with a view to settling the differences between them.

In May the Council of the Association asked the British Medical Guild to recommend doctors not to apply for public health appointments until "a firm acceptable offer" of an increase in the pay of all public health medical officers had been made (*Supplement*, 27 May, p. 132). In June 1966, after the Review Body had recommended increases in pay for general practitioners and hospital doctors, the Staff Side of Whitley Committee C lodged a claim for all public health service doctors. The Management Side did not admit to any commitment to review the pay of public health medical offcers with effect from the date of the Review Body recommendations, and up to the present it had refused to make a firm offer in response to the Staff Side's claim.

"Mediflash"

The B.M.A. states that the reaction of police authorities to the Mediflash emergency light for doctors' cars (*Supplement*, 8 July, p. 23) has not been generally favourable. The Home Office has advised that, pending further consultations with chief constables, the issue of these lamps should be held up.

It is expected that the difficulty will be resolved, but there will be delay. When the necessary arrangements have been made through the Home Office lamps will be dispatched immediately to B.M.A. members who have paid for them. Members who ask for a refund will be notified when the lamps are ready for dispatch and asked to send in their remittance. Their orders will then be dispatched.

H.M. Forces

ROYAL NAVY

Surgeon Captain R. M. Latta, R.N., has been appointed honorary surgeon to the Queen, in succession to Surgeon Captain W. Wilson, R.N.

Surgeon Captains M. F. Sheehan and K. J. O'Connor have been placed on the Retired List.

ROYAL ARMY MEDICAL CORPS

Lieutenant-Colonel J. D. Beavan has retired on retired pay.

Major P. P. Leddy to be Lieutenant-Colonel.

Short Service Commission.—Captain D. M. Callum to be Major.

REGULAR ARMY RESERVE OF OFFICERS

ROYAL ARMY MEDICAL CORPS

The notification concerning Colonel N. T. Nicol, T.D., published in a *Supplement* to the *London Gazette* dated 9 May 1967, and in the *Supplement* to the *Journal*, 20 May, p. 121, has been cancelled.

TERRITORIAL AND ARMY VOLUNTEER RESERVE

ROYAL ARMY MEDICAL CORPS

Colonel N. T. Nicol, T.D., from T.A., to be Lieutenant and has been granted the acting rank of Captain.

Association Notices

Armed Forces Committee

Nomination of Members for Co-option

The constitution of the Armed Forces Committee was amended at the Annual Representative Meeting of the Association in Bristol in July 1967 to allow greater representation of serving medical officers, especially younger members, by means of co-option to the Committee. It is now open to the Committee to co-opt two representatives, of the rank of major or equivalent (lieutenant-commander or squadron leader) or below, one of whom should preferably be of specialist status, from the medical branch of each of the Services.

Serving medical officers are therefore invited to nominate members of the Association in the armed Forces in these ranks for co-option to the Committee.

Nominations should be sent to the Secretary of the Association by 30 September 1967. The first meeting of the Armed Forces Committee, at which co-opted members will be appointed, will be held in the autumn, and after it nominees will be informed of the appointments made.

DEREK STEVENSON,
Secretary.

Diary of Central Meetings

SEPTEMBER

1	Fri.	Staff Side, Committee C, Medical Whitley Council, 10 a.m.
13	Wed.	Public Health Committee, 10 a.m.
13	Wed.	Joint Formulary Committee, 10.30 a.m.
13	Wed.	Staff Side, Committee C, Medical Whitley Council, (at 41 Belgrave Square, London S.W.), 2 p.m. (followed by meeting with Management Side, 3.30 p.m.).
19	Tues.	Medical Science, Education, and Research Committee, 10.30 a.m.
21	Thurs.	General Medical Services Committee (Scotland) (at 7 Drumsheugh Gardens, Edinburgh), 2.15 p.m.
22	Fri.	Hospital Junior Staffs Group Council, 11 a.m.
22	Fri.	Planning Unit, 4.30 p.m.
25	Mon.	Scottish Committee for Hospital Medical Srvices (at 7 Drumsheugh Gardens, Edinburgh), 11 a.m.
28	Thurs.	General Purposes Committee, 10 a.m.
29	Fri.	Joint Committee of B.M.A. and Magistrates' Association, 11 a.m.

OCTOBER

3	Tues.	Scottish Council (at 7 Drumsheugh Gardens, Edinburgh),
11	Wed.	Journal Committee, 10.30 a.m.

Branch and Division Officers Elected

BANFF, MORAY, AND NAIRN DIVISION.—Chairman, Dr. D. MacLennan. Chairman-elect and Vice-chairman, Dr. J. M. Livingston. Honorary Secretary and Treasurer, Dr. W. G. MacDonald.

BATH, BRISTOL, AND SOMERSET BRANCH.—President, Dr. C. R. Gibson. President-elect, Mr. J. Angell James. Vice-presidents, Dr. W. H. Hylton, Dr. Beryl Corner. Honorary Secretary, Dr. A. L. T. Beddoe.

BELFAST DIVISION.—Chairman, Dr. P. Steen. Chairman-elect and Vice-chairman, Dr. D. L. W. Chapman. Honorary Secretary, Dr. Charlotte C. Arnold. Assistant Honorary Secretary, Dr. H. W. Dunn. Honorary Treasurer, Dr. G. T. C. Hamilton.

BISHOP AUCKLAND DIVISION.—Chairman, Dr. J. A. Anderson. Chairman-elect, Mr. J. H. Wrigley. Honorary Secretary and Treasurer, Dr. D. T. Prescott.

CARDIFF DIVISION.—Chairman, Dr. H. A. Thomas. Chairman-elect Dr. A. T. Jones. Honorary Secretary, Dr. M. L. Cattell. Assistant Honorary Secretary, Dr. A. C. Williams. Honorary Treasurer, Dr. A. Griffiths.

CORNWALL DIVISION.—Chairman, Dr. A. K. Thould. Vice-chairman, Dr. P. O'Fee Boyle. Honorary Secretary, Dr. E. Townsend. Honorary Treasurer, Dr. D. Hooker.

CROYDON DIVISION.—Chairman, Dr. Maureen B. Adams. Chairman-elect, Mr. J. C. Miller. Vice-chairman, Dr. P. O'Flynn. Honorary Secretary, Dr. G. Hirst. Assistant Honorary Secretary and Honorary Treasurer, Dr. B. R. T. Carroll.

CYPRUS BRANCH.—President, Dr. S. H. Nicolaides. President-elect, Dr. C. Angeli. Honorary Secretary and Treasurer, Dr. V. V. Kalbian.

DORSET DIVISION.—Chairman, Dr. A. N. Blades. Honorary Secretary and Treasurer, Dr. T. H. Barrie.

EASTBOURNE DIVISION.—Chairman, Dr. I. Brown. Chairman-elect and Vice-chairman, Dr. W. D. G. Troup. Honorary Secretary, Dr. M. F. P. Marshall. Assistant Honorary Secretary, Dr. R. A. Forster. Honorary Treasurer, Dr. H. Clarke.

EDINBURGH AND S.E. SCOTLAND BRANCH.—President, Dr. A. D. Mitchell. President-elect, Dr. Joan K. Sutherland. Vice-presidents, Professor N. M. Dott, Dr. J. E. Margaret Munro. Honorary Secretary, Dr. H. P. Dinwoodie.

GLASGOW AND WEST OF SCOTLAND BRANCH.—President, Major-General J. M. Macfie. President-elect, Dr. A. R. Miller. Vice-presidents, Mr. D. McKay Hart. Dr. Kennedy Campbell. Honorary Secretary and Treasurer, Dr. W. W. Fulton.

JERSEY DIVISION.—Chairman, Dr. I. H. Maine. Vice-chairman, Dr. D. N. Scott Warren. Honorary Secretary and Treasurer, Dr. D. S. Fullerton.

MIDLAND BRANCH.—President, Dr. B. T. Davis. President-elect, Dr. D. F. Croft. Honorary Secretary, Dr. E. I. Garratt. Assistant Honorary Secretary, Dr. G. A. Readett. Honorary Treasurer, Dr. W. R. Martine. Assistant Honorary Treasurer, Dr. Dorothy Sanderson.

TOWER HAMLETS DIVISION.—Chairman, Dr. M. Shalet. Vice-chairman, Dr. F. Morton-Gore. Honorary Secretary and Treasurer, Dr. B. Taylor. Assistant Honorary Secretary, Dr. J. N. Docherty.

TYNESIDE DIVISION.—Chairman, Dr. D. V. Cashman. Vice-chairman, Dr. C. D. Jobling. Honorary Secretary, Dr. W. D. Elliott. Assistant Honorary Secretary and Honorary Treasurer, Dr. G. L. Hindson.

WALTHAM FOREST DIVISION.—Chairman, Dr. H. Franks. Vice-chairman, Dr. W. R. John. Honorary Secretary, Dr. F. G. Tomlins. Honorary Treasurer, Dr. A. R. Fox.

YORKSHIRE BRANCH.—President, Dr. D. L. S. Johnston. President-elect, Dr. G. W. J. Hawbrook. Vice-president, Dr. E. G. Rhind. Honorary Secretary, Dr. H. Fidler.

British Medical Journal Supplement

LONDON SATURDAY 2 SEPTEMBER 1967

CONTENTS

Medical Registration - - - - - - - - 125
Compulsory Attachment Scheme - - - - - - 126
B.M.A. Planning Unit - - - - - - - - 126
B.M.A. Nuffield Library - - - - - - - - 126
Diary of Central Meetings - - - - - - - 126
Branch and Division Meetings - - - - - - 126

Medical Registration

The *Medical Register*, published by the General Medical Council, contains the names of all persons who are fully or provisionally registered on 1 January of the year to which the *Medical Register* relates. It does not contain the names of temporarily registered persons. The names of medical practitioners who are fully or provisionally registered by virtue of Commonwealth qualifications or those of foreign countries are recorded in a Commonwealth or a foreign list respectively.

Unless a doctor is registered under the Medical Act, 1956, he is neither "legally qualified" nor "duly qualified." Only registered practitioners may sign certain statutory certificates (including death certificates), hold medical appointments in public services or hospitals, practise under the National Health Service Acts, possess dangerous drugs, or recover charges in the courts.

A doctor who has passed his qualifying examination in the British Isles may apply for provisional registration. He must supply evidence to the General Medical Council from the university or body concerned that he has gained his degree or diploma. He must also pay a fee of £9. A doctor who is provisionally registered will be deemed to be registered only so far as it is necessary for him to be employed in a resident medical capacity in hospitals which are approved for the purpose of house-officer service.

After obtaining the requisite experience, a doctor holding a registrable qualification granted by a university or other body in the United Kingdom or in the Republic of Ireland, and who is provisionally registered under the Medical Act 1956 of the United Kingdom, is entitled to apply to the General Medical Council to be a fully registered medical practitioner. He will be expected to provide as evidence for the Council a certificate of experience. Section 15 of the Medical Act 1956 states that . . . "(2) A person must, after passing a qualifying examination, have been engaged for the prescribed period in employment in a resident medical capacity in one or more approved hospitals or approved institutions and have obtained a certificate under this section. (3) A person who has been employed as aforesaid may apply to his examining body for a certificate under this section, and if that body are satisfied (*a*) that during the time he has been employed as aforesaid he has been engaged for the prescribed period or minimum period in medicine and for the prescribed period or minimum period in surgery, and (*b*) that his service while so employed has been satisfactory, they shall grant him a certificate in the prescribed form that they are satisfied as aforesaid." Time spent in midwifery may be counted as medicine or as surgery up to a maximum of six months. The fee for full registration is £12.

Registration of Overseas Doctors

Three kinds of registration are open to medical practitioners who have qualified overseas—full, provisional, and temporary registration. Overseas graduates are eligible for full registration only if they have qualified in a country which has reciprocal arrangements with the United Kingdom for the registration of medical qualifications. They must also hold Commonwealth or foreign qualifications which are recognized by the General Medical Council for full or provisional registration (certain qualifications are recognized only when granted to students of specified medical colleges and certain other qualifications are not recognized when they have been obtained before a specified date).

Overseas graduates must also complete 12 months of satisfactory service as a resident house officer (including six months in medicine and six months in surgery) in an approved hospital or have had other professional experience which the General Medical Council will accept as equivalent experience. A fully registered overseas graduate is entitled to engage in any form of professional employment, including hospital work and general practice. No time limit is attached to full registration, and it therefore does not require to be renewed annually or on change of employment.

Provisional

Provisional registration is available to a Commonwealth or foreign doctor if he has qualified in a country which has reciprocal arrangements with the United Kingdom for the registration of medical qualifications and if, as under full registration, he holds Commonwealth or foreign qualifications which are recognized by the General Medical Council for full or provisional registration.

Provisional registration entitles an overseas graduate to work in this country only in resident posts in hospitals approved for the purpose of house-officer service. This type of registration does not require to be renewed on change of employment and is not granted for any specified period.

Temporary

Temporary registration is granted only to Commonwealth and foreign doctors, who must satisfy the Council that they are in the United Kingdom temporarily as distinct from indefinitely or permanently. It may be granted in respect of work in a particular hospital appointment, irrespective of grade. Temporary registration cannot be given in respect of any work outside a hospital or similar institution approved by the Council for purposes of temporary registration.

This type of registration covers an appointment for which an applicant has already been selected, and it needs to be renewed if the appointment is extended or if the practitioner takes up employment in another hospital. "An applicant must also satisfy the Council that he holds a qualification which may properly be recognized by them 'as furnishing a sufficient guarantee of the possession of the requisite knowledge and skill for the efficient practice of medicine, surgery, and midwifery.'" (*The Medical Register*, 1967. p. viii).

Information on registration may be obtained from the Registrar, General Medical Council, 44 Hallam Street, London W.1.

Compulsory Attachment Scheme

Very shortly doctors from abroad coming independently to Britain to look for appointments as house-officers or senior house-officers, and who have not been previously employed in this country, will have to complete a period of clinical attachment (not exceeding one month) before they can be employed by hospital authorities in permanent or locum posts. The requirement will not apply to sponsored overseas doctors nor to those being offered posts in the registrar or higher grade.

The Health Departments introduced a voluntary attachment scheme in July 1966 but it has proved to be unsatisfactory. According to the Ministry of Health very few unsponsored overseas doctors have used the scheme, and this, together with some instances of misuse of the period of attachment, has caused disillusionment among consultants, on whose co-operation the success of the scheme equally depends.

The Medical Director of the B.M.A.'s Commonwealth and International Medical Advisory Bureaux, Dr. R. A. Pallister, thinks the compulsory scheme may add to the anxieties of overseas doctors, who already experience difficulties and delays in entering Britain because of the Commonwealth Immigrants Act. It could lead to Commonwealth doctors seeking postgraduate training elsewhere.

Doctors from overseas whose experience has been recognized as fulfilling the requirements of the General Medical Council for full registration may ask, Dr. Pallister points out, why a further assessment of their ability is required. The freedom of hospital authorities to make appointments will also be restricted.

Doctors during their period of attachment will be paid at the rate of £550 a year and accommodation will be provided free. Meals will be charged for.

B.M.A. Planning Unit

The B.M.A.'s Planning Unit, the functions of which were described in the Annual Report of Council (*Supplement,* 6 May, p. 33), has set up small working parties of experts to advise it on subjects under investigation.

Among the first subjects to be selected for study are the application of mechanical aids for disabled persons and the problems of setting up intensive-care units. Britain is thought to have fallen behind other advanced countries in the provision and utilization of mechanical aids for the disabled, since their existence is unknown to many most likely to benefit from them. Mr. Duncan Guthrie, Director of the National Fund for Research into Crippling Diseases, is chairman of the working party on mechanical aids, and it is hoped that its report will be ready by the spring of 1968.

Dr. E. J. Moran Campbell heads the working party considering general measures for improving the care of acutely ill patients needing continuous supervision and attention. It is making a critical examination of intensive therapy units.

Other subjects being considered by the Planning Unit include computer science in relation to medicine and primary medical care. Suggestions have been received for matters for consideration in the future.

B.M.A. Nuffield Library

The Library service is available to all members of the Association resident in Great Britain and Northern Ireland (and by special arrangement to members of the Irish Medical Association). A copy of the library rules will be forwarded on application to the Librarian at B.M.A. House.

The following books have been added to the Library:

Amelar, R. D.: Infertility in Men. 1966.
Andrew, W.: Microfabric of Man. 1966.
Aronson, S. M., and Volk, B. W. (editors): Inborn Disorders of Sphingolipid Metabolism. 1967.
Artz, C. P., and Hardy, J. D. (editors): Complications in Surgery and their Management, 2nd edition. 1967.
Astrup, C., and Noreik, K.: Functional Psychoses. 1966.
Bass, B. H.: Lung Function Tests. 3rd edition. 1966.
Bennington, J. L., and Kradjian, R. M.: Renal Carcinoma. 1967.
Berkowitz, S. B.; Differential Diagnosis. 1967.
Biddle, W. E.: Hypnosis in the Psychoses. 1967.
Brainerd, H., *et al.*: Current Diagnosis and Treatment. 1966.
Burrows, R. B.: Microscopic Diagnosis of the Parasites of Man. 1965.
Calman, C. H.: Atlas of Hernia Repair. 1966.
Cutting, W. C.: Handbook of Pharmacology, 3rd edition. 1967.
Dale, D. M. C.: Deaf Children at Home and at School. 1967.
Dargeon, H. W. K.: Reticuloendothelioses in Childhood. 1966.
Day, E. D.: Foundations of Immunochemistry. 1966.
Dejours, P.: Respiration. 1966.
De Lange, S. A.: Surgical Treatment of Progressive Hydrocephalus. 1966.
Donizetti, P.: Shadow and Substance. 1967.
Duffy, J. C., and Litin, E. M.: The Emotional Health of Physicians. 1967.
Dummer, G. W. A., and Robertson, J. M. (editors): Medical Electronics Equipment, 1966–67. 1966.

Association Notices

Diary of Central Meetings

SEPTEMBER

1	Fri.	Staff Side, Committee C, Medical Whitley Council, 10 a.m.
7	Thurs.	G.M.S. Committee, 10.30 a.m.
13	Wed.	Public Health Committee, 10 a.m.
13	Wed.	Joint Formulary Committee, 10.30 a.m.
13	Wed.	Staff Side, Committee C, Medical Whitley Council, (at 41 Belgrave Square, London S.W.), 2 p.m. (followed by meeting with Management Side, 3.30 p.m.).
14	Thurs.	Grants Subcommittee (Organization Committee), 10 a.m.
14	Thurs.	Organization Committee, 11.30 a.m.
15	Fri.	Hospital Junior Staffs Group Council, 11 a.m.
19	Tues.	Medical Science, Education, and Research Committee, 10.30 a.m.
21	Thurs.	General Medical Services Committee (Scotland) (at 7 Drumsheugh Gardens, Edinburgh), 2.15 p.m.
22	Fri.	Planning Unit, 4.30 p.m.
25	Mon.	Scottish Committee for Hospital Medical Services (at 7 Drumsheugh Gardens, Edinburgh), 11 a.m.
27	Wed.	Annual Meetings Committee, 2 p.m.
28	Thurs.	General Purposes Committee, 10.30 a.m.
29	Fri.	Joint Committee of B.M.A. and Magistrates' Association, 11 a.m.

OCTOBER

3	Tues.	Scottish Council (at 7 Drumsheugh Gardens, Edinburgh),
11	Wed.	Journal Committee, 10.30 a.m.
12	Thurs.	G.M.S. Committee (at B.M.A. Scottish House, 7 Drumsheugh Gardens, Edinburgh), 10.30 a.m.

Branch and Division Meetings to be Held

Members proposing to attend meetings marked ● are asked to notify in advance the honorary secretary concerned.

GLASGOW DIVISION.—Tuesday, 5 September, 3 p.m., visit and tour of factory of Messrs. J. Robertson and Sons, Paisley.●

MID-ESSEX DIVISION.—At Medical Academic Unit, Chelmsford, Thursday, 7 September, 8 for 8.30 p.m., meeting to consider questionary submitted by Committee on Functions of the District General Hospital.

NORTH-EAST ESSEX DIVISION.—At Senior Common Room, Essex County Hospital, Wednesday, 6 September, 8.15 p.m., annual general meeting.

HOSPITAL JUNIOR STAFFS GROUP: NORTH-EAST METROPOLITAN REGION.—At B.M.A. House, London W.C., Tuesday, 5 September, 7 p.m., general meeting to discuss evidence for Review Body, and to elect officers.

JUNIOR STAFFS GROUP: SOUTH-EAST METROPOLITAN REGION.—At B.M.A. House, Tavistock Square, London W.C., Tuesday, 12 September, 7 p.m., general meeting to discuss evidence for Review Body, and to elect officers.

Branch and Division Officers Elected

GATESHEAD DIVISION.—Chairman, Dr. J. C. Arthur. Chairman-elect and Vice-chairman, Dr. P. Shadwick. Honorary Secretary and Treasurer, Dr. W. G. A. Riddle. Assistant Honorary Secretary, Dr. M. Spark.

HANNOVER BRANCH.—President, Colonel T. P. H. McKelvey. Honorary Secretary, Captain R. W. Bowman.

HARROGATE DIVISION.—Chairman, Mr. E. J. Somerset. Chairman-elect, Dr. L. H. Moss. Honorary Secretary and Treasurer, Dr. G. N. Tyler.

HARTLEPOOLS DIVISION.—Chairman, Dr. A. Fraser. Vice-chairman, Dr. W. M. Lowry. Honorary Secretary and Treasurer, Dr. R. L. Simpson. Assistant Honorary Secretary, Dr. D. J. Brewer.

British Medical Journal Supplement

LONDON SATURDAY 9 SEPTEMBER 1967

CONTENTS

Was it a Drug? - 127
"Alphabet of Opportunity" - 128
Medical Assistants in Scotland - 128
Association Notices - 128

Was it a Drug?

Regulation 16 of the National Health Service (Service Committees and Tribunal) Regulations, 1956, provides that when a practitioner prescribes under the National Health Service preparations which are not drugs or medicines, and therefore outside the scope of the Act, the executive council may recover their cost from him. If he challenges the council's action the matter may be referred to the local medical committee. Either party or the Minister can appeal to a referee or referees against the local medical committee's decision.

The referees on each occasion are appointed by the Minister of Health. They must not exceed three in number and they must not be officers of the Ministry of Health. At least one must be a general medical practitioner. In practice the number of referees appointed has usually been three. The chairman has been a layman with legal training, and his two colleagues have been general practitioners selected from a panel chosen by the General Medical Services Committee of the B.M.A.

The findings* of the referees in some recent appeals under the regulations are reported below. The decisions in these, as in all cases, are related only to the circumstances of the particular cases and are not binding on referees who may hear other cases.

Drox Shampoo

The referees considered three cases in which Drox shampoo had been prescribed. On a reference from the executive council the local medical committee in each case had decided that the shampoo was a drug that the executive council was bound to provide. The referees supported this decision in two of the cases.

In the first case the doctor had prescribed Drox shampoo for a patient suffering from psoriasis of the scalp. In reporting their decision that in this case the shampoo was a drug which the executive council was bound to provide, the referees stated that a consultant had advised treatment with an ointment and Drox shampoo. Drox shampoo contained propylene glycol 5%, solution of coal tar 1%, hexachlorophane 1%, and cresol 0.05%. The rest was soap.

The referees said they were referred to the following extract from the "Macgregor Report" [report of the Standing Committee on Classification of Proprietary Preparations (Macgregor Committee)]: "Shampoos . . . normally used for toilet purposes . . . should not be ordered on Form E.C.10. . . . The fact that a drug is present does not of necessity convert the preparation as a whole into a drug." The referees thought that the doctor had not prescribed the shampoo to help the patient wash his hair but as treatment for the psoriasis. The question was whether he had any reason to believe that the treatment would be less effective if the patient had washed his hair with his own soap and then applied propylene, coal tar, hexachlorophane, and cresol.

The doctor had said that Drox was specially apt for removing the scales, which was a necessary preliminary to the administration of the ointment recommended by the consultant, and it acted as a disinfectant. The Minister's representative thought that soap was the best keratolytic and that 1% of hexachlorophane would not be enough to be effective as a disinfectant.

"We do not know," the report concluded, "how Drox shampoo is normally used. The manufacturers say it has not been advertised to the public for some years. Our medical members think it is the word 'shampoo' which disturbed the Minister, but there are many shampoos in the *British Pharmacopoeia.* Soap is often the best vehicle for administering a medicament to the skin. Hexachlorophane is a powerful disinfectant, and 1% should have been sufficient for this case, and the doctor might well believe that the other ingredients would help in removing the scales. We decide that this Drox shampoo was a drug which the executive council was bound to provide."

No Defence

In another case Drox shampoo had been prescribed for a patient suffering from seborrhoea of the scalp. The doctor who prescribed it said his only defence was that it had been recommended by a consultant dermatologist. The referees said that that was no defence at all. In their report to the Minister they wrote: "It is for the doctor, not the consultant, to decide what can be ordered at the expense of the executive council. If this patient had seborrhoea of the scalp there would be scales on his head which would have to be removed before the application of any remedial preparation. Some disinfectant would also be needed. Our medical members think that both these purposes would be served by the special composition of Drox shampoo, and this is what the consultant had in mind. The doctor should pay more attention to the Standing Joint Committee on the Classification of Proprietary Preparations."

The referees decided that this was a drug that the executive council was bound to provide.

In the third case, in which Drox shampoo had been prescribed for dandruff and alopecia, the referees decided that it was not a drug the executive council was bound to provide. They commented: "We have before us the composition of Drox shampoo. Our medical members are unable to find in it anything which would be of any value in the treatment of either dandruff or alopecia except, of course, that cleanliness is always conducive to health. The local medical committee seem to have based their decision on the advice of the consultant, but consultants often advise treatment which executive councils are not bound to provide. It is for the doctor to decide what his terms of service authorize him to order at the expense of the executive council. A doctor who disregards the advice of the Macgregor Committee must be prepared to give much more information than we have in this case."

Ethisan

The referees, disagreeing with the local medical committee's opinion, decided that Ethisan shampoo was not a drug which the executive council should provide in a case of psoriasis of the scalp.

In their report the referees stated that Ethisan shampoo contained 0.938% of lanette wax and 6.56% of sodium lauryl sulphate, and was recommended by the makers for use in the treatment of the scalp as a cleaning agent. The referees did not know what local application was intended. Sodium lauryl sulphate was a detergent and their medical members knew of no treatment for psoriasis for which a detergent would be an essential requirement. The referees concluded: "If the doctor had read the report of the Standing Committee on the Classification of Proprietary Preparations he might have been more cautious about ordering shampoos at the expense of the executive council and told the patient to buy it himself."

---

* These findings are normally sent only to the interested parties. They are sent by the Ministry of Health to the *B.M.J.* with all names deleted.

Johnson's Baby Cream

A decision by a local medical committee that one tube of Johnson's Baby Cream for a patient with inflammation of the groins and buttocks was in that particular case a drug bound to be provided by the executive council was affirmed by the referees.

In their report the referees said that the mother had tried several preparations but found the cream more effective than other remedies. It contained 35% white oil, 5.6% anhydrous lanolin, and 0.2% hexachlorophane. The Minister's representative said the inflammation had probably been caused by infrequent changing of the napkin or by the napkin being covered by a waterproof material. He maintained that the mother was responsible for the inflammation and that she should have paid for the remedy.

The doctor had taken no part in the choice of the remedy. She had given the prescription only because the mother asked for it. The representative of the local medical committee said that its decision had been based on a passage in Sheldon's textbook on diseases of children which said that the affected parts should be freely smeared with a protective layer of grease to avoid further contact between the urine and the skin and so prevent the continuance of the inflammation.

"On the balance of probability," the referees concluded, "it seems to us that we should accept the Minister's representative's version of what really happened between the mother and the doctor, but there is one person who has so far been overlooked. The baby, through no fault of his own, suffered from a painful inflammation which he was entitled to have treated by the National Health Service whether by way of prevention or alleviation. Our decision will make no difference to this baby, but there is a principle involved which might affect other babies. The doctor may not have acted strictly in accordance with the traditions of her profession, but we do not think we ought to make her pay for this prescription just because she followed the advice of the mother, who, in this case, was in a better position to judge the efficacy of the remedy. We affirm the decision of the local medical committee."

"Alphabet of Opportunity"

The B.M.A. Career Service's "alphabet of opportunity" gives a list of the various specialties in the field of medicine open to a newly qualified doctor. This new service, under the direction of Dr. R. A. Pallister and Dr. A. Gilmour, aims to supply the Association's younger members with any factual information they may need when planning their future career.

The medical directors point out that a young doctor may ask about, for example, terms and conditions of service or about opportunities for vocational training in one or another branch of medicine. He may want to know the best way of entering a particular specialty, and the number of future vacancies there are likely to be in it. The Association's Career Service will provide the answers, and will if required interview the inquirer and put him in touch with senior colleagues in his region who will give individual advice on a career and on the right training for it. The advisers will normally be associated with medical schools or colleges, with whom the Association will closely co-operate.

For doctors seeking information about postgraduate diplomas, there are separate information sheets for each specialty listing the postgraduate diplomas obtainable and giving details of the licensing bodies, regulations for the examinations, and places providing courses of instruction, together with details of fees.

The service is open to inquiries on any matter related to a medical career. It is hoped to extend the service in due course to schools, for the benefit of school-leavers who are considering medicine as a career.

Particulars about the service may be obtained from the Medical Directors, B.M.A. Career Service, B.M.A. House, Tavistock Square, London W.C.1.

Medical Assistants in Scotland

The Scottish Home and Health Department has stated that all medical assistants in Scotland who have been transferred from posts of unlimited tenure in the junior hospital medical officer grade will be regarded as having been appointed to the medical assistant grade as from 1 November 1964.

Any doctor who held an appointment of limited tenure immediately before becoming a medical assistant will be assimilated to the medical assistant grade as from the day after the date of expiry of his last completed year in his previous grade.

The Scottish Home and Health Department has authorized regional hospital boards to make the necessary retrospective adjustment and to pay the arrears of salary to those concerned.

Association Notices

Diary of Central Meetings

SEPTEMBER

13	Wed.	Public Health Committee, 10 a.m.
13	Wed.	Joint Formulary Committee, 10.30 a.m.
13	Wed.	Staff Side, Committee C, Medical Whitley Council (at 41 Belgrave Square, London S.W.), 2 p.m. (followed by meeting with Management Side, 3.30 p.m.).
14	Thurs.	Grants Subcommittee (Organization Committee), 10 a.m.
14	Thurs.	Organization Committee, 11.30 a.m.
15	Fri.	Hospital Junior Staffs Group Council, 11 a.m.
19	Tues.	Medical Science, Education, and Research Committee, 10.30 a.m.
21	Thurs.	General Medical Services Committee (Scotland) (at 7 Drumsheugh Gardens, Edinburgh), 2.15 p.m.
22	Fri.	Planning Unit, 4.30 p.m.
25	Mon.	Scottish Committee for Hospital Medical Services (at 7 Drumsheugh Gardens, Edinburgh), 11 a.m.
27	Wed.	Annual Meetings Committee, 2 p.m.
28	Thurs.	General Purposes Committee, 10.30 a.m.
29	Fri.	Joint Committee of B.M.A. and Magistrates' Association, 11 a.m.
29	Fri.	Film Committee, 2 p.m.

OCTOBER

3	Tues.	Scottish Council (at 7 Drumsheugh Gardens, Edinburgh),
11	Wed.	Journal Committee, 10.30 a.m.
12	Thurs.	G.M.S. Committee (at B.M.A. Scottish House, 7 Drumsheugh Gardens, Edinburgh), 10.30 a.m.

Branch and Division Meetings to be Held

Members proposing to attend meetings marked ● are asked to notify in advance the honorary secretary concerned.

BUCKINGHAMSHIRE DIVISION.—At Clinical Lecture Room, Stoke Mandeville Hospital, Friday, 15 September, 8.30 p.m., general meeting.

NOTTINGHAM DIVISION.—At Refectory, Portland Building, Nottingham University, Wednesday, 13 September, 8.30 p.m., wine and cheese party.

JUNIOR STAFFS GROUP: SOUTH-EAST METROPOLITAN REGIONAL HOSPITALS.—At B.M.A. House, Tavistock Square, London W.C., Tuesday, 12 September, 7 p.m., general meeting to discuss evidence for Review Body, and elect officers

Branch and Division Officers Elected

HAVERING DIVISION.—Chairman, Dr. L. G. R. Wand. Vice-chairman, Dr. Jean Cuthbert. Honorary Secretary and Treasurer, Dr. R. G. Troup. Assistant Honorary Secretary, Dr. J. H. L. Lloyd-Thomas.

HEREFORD DIVISION.—Chairman, Dr. D. A. Chandler. Vice-chairman, Dr. W. H. J. Baker. Honorary Secretary and Treasurer, Dr. G. B. Chamberlain.

HERTFORDSHIRE BRANCH.—President, Dr. J. S. Ross. Honorary Secretary and Treasurer, Dr. E. H. J. Cotter.

NORWICH DIVISION.—Chairman, Mr. A. B. Birt. Chairman-elect Dr. N. J. Pratt. Honorary Secretary, Dr. R. H. Scott. Honorary Treasurer, Dr. J. F. Bennett.

British Medical Journal Supplement

LONDON SATURDAY 16 SEPTEMBER 1967

CONTENTS

Vocational Training for General Practice - - - - - 129
Better Medical Care - - - - - - - - - - 130
Hospitality - - - - - - - - - - - 130
B.M.A. Nuffield Library - - - - - - - 130
H.M. Forces - - - - - - - - - - 130
Association Notices - - - - - - - - - 130

Vocational Training for General Practice

At its meeting on 7 September the General Medical Services Committee debated a report on vocational training for general practice by its Advisory Committee on Vocational Training and Continuing Education for General Practice.[*] *The Advisory Committee was asked to reconsider some parts of the report in the light of the debate, but it was decided that in the meantime a copy of the report, as representing in general the G.M.S. Committee's views, should be sent to the Royal Commission on Medical Education and to the Central Committee on Postgraduate Education.*

A summary of the Advisory Committee's conclusions is printed below. A report of the G.M.S. Committee's debate on vocational training and on the other items on its agenda will be printed next week.

Summary of Committee's Conclusions

The report stated that, in order to fulfil his role of general physician to the community, the general practitioner of the future must have adequate vocational training after full registration and before becoming a principal. The vocational training must differ fundamentally from the present Trainee General Practitioner Scheme, and it must be adaptable to rapidly changing needs.

The Advisory Committee believed that vocational training should be a part of modern medical education, regardless of specialty or discipline, and that a planned programme of career training could provide a strong inducement to graduates of the right calibre to enter general practice. It thought the responsibility for vocational training should be vested in the Central Committee of Great Britain for Postgraduate Medical Education, which "will no doubt wish to conduct its operations through regional organizations."

Hospital Training

The Committee advocated a minimum of three years spent in whole-time hospital appointments, or their part-time equivalent, after qualification. Appointments should provide clinical experience in those subjects of particular importance to general practice, and a system of rotating appointments was proposed.

Hospital experience gained outside the United Kingdom, paid part-time hospital appointments, and further experience in greater depth should constitute an acceptable part of vocational training for general practice, it was thought.

General Practice Training

In the Committee's opinion whole-time in-service training in general practice for at least one year was essential. In-service general practice training posts should be known as "general practitioner registrarships," and the title "general practitioner teacher" was suggested to replace "trainer."

A general practitioner teacher should be entitled to a substantial increase in remuneration. Before a teacher is appointed his practice as a whole must be approved. Partners must "be prepared to collaborate in training programmes and they and the candidate [teacher] must be of good professional repute."

Approval of appointment as a teacher, the Committee thought, should be provisional for the first year. Substantive appointment should then be for a period of five years, and renewable thereafter on a five-yearly basis, subject to approval. Teachers should be required to study teaching methods and to undertake special commitments in continuing education.

Registrarships

The Committee regarded one year as the minimum term for a registrar's appointment to a teaching general practice. The registrar "should have clinical responsibility for patients as soon as possible." He should be afforded the opportunity of visiting different types of practice.

Registrars should learn about the administration of general practice, of local health authority services, of Government departments, and of voluntary services and the occupational health service. The Committee also thought there was a need for close integration of the hospital and the general practice components of vocational training.

University Departments and Postgraduate Centres

The Committee thought the development of university departments of general practice should be encouraged, and they should be intimately involved in vocational training.

Registrars should have close contacts with postgraduate medical centres. The Central Committee of Great Britain for Postgraduate Medical Education should be responsible for the administration of vocational training for general practice in the same way as for other types of postgraduate medical education.

A general practice subcommittee of a regional postgraduate committee should be formed to oversee, in conjunction with all interested bodies, vocational training for general practice. Its members should be drawn largely from local medical committees in the region and from the Royal College of General Practitioners. The Committee stated that the regional general practice subcommittee would require the services of a regional adviser in general practice to act in conjunction with the postgraduate dean. In some cases a district executive officer would be required.

Pay During Training

A doctor's remuneration, the Committee held, should increase in accordance with his expanding general professional experience within a vocational training programme.

The rate of the existing vocational training allowance was inadequate and must be increased.

A standing advisory body, whom the Minister would consult about individual cases relating to the assessment of the criteria for the vocational training allowance, should be set up immediately. In future, however, that function should be the responsibility of the regional subcommittee, and appeals from its decisions should be decided by the standing advisory body.

---

[*] The members of the Advisory Committee are: Mr. D. C. Bowie (chairman), and Drs. J. C. Cameron, P. W. R. M. Alberti, P. S. Byrne, Joan Chappell, A. Elliott, D. G. Emery, W. W. Fulton, J. P. Horder, R. A. Keable-Elliott, G. Murray Jones, G. Swift, D. B. Wallis, M. A. Wilson, and H. S. Howie Wood. Previous members of the Committee at the time when the report was being prepared were: Drs. J. R. Bennett, A. B. Gilmour, and J. S. Noble.

Better Medical Care

The Edinburgh and South-east Scotland Branch of the B.M.A. is arranging a conference on "Better Medical Care—Which Road?" The conference will be held on 7 October in the David Hume Tower, University of Edinburgh (George Square). Any doctor may attend, and a programme and registration form (registration fee 5s.) may be obtained from Dr. H. P. Dinwoodie, B.M.A. Scottish House, 7 Drumsheugh Gardens, Edinburgh 3.

Dr. A. D. Mitchell will take the chair at the morning session, which is to be on "The Present Position—Advantages and Disadvantages." The theme of the afternoon session (chairman, Dr. John Riddell) will be "The Future Organization of Medical Care," and that of the evening session, at which Dr. S. J. Hadfield will preside, will be "The Financing and Administration of Medical Care."

Hospitality

A French doctor living in Marseilles would be pleased to receive an *au pair* from 1 October for 10 to 12 months. The doctor has two sons, aged 17 and 16, and a daughter aged 10 years.

A French doctor living in Nice would like his daughter aged 19 years to stay *au pair* with a British medical family from December 1968 for six to eight months.

Would anyone who is interested please get in touch with Dr. R. A. Pallister, Medical Director, International Medical Advisory Bureau, B.M.A. House, Tavistock Square, London W.C.1.

B.M.A. Nuffield Library

The Library service is available to all members of the Association resident in Great Britain and Northern Ireland (and by special arrangement to members of the Irish Medical Association). A copy of the library rules will be forwarded on application to the Librarian at B.M.A. House.

The following books have been added to the Library:

Eisenstein, A. B. (editor): The Adrenal Cortex. 1967.
Ellis, P. P., and Smith, D. L.: Handbook of Ocular Therapeutics and Pharmacology, 2nd edition. 1966.
Farber, E., and Magee, P. N. (editors): Biochemical Pathology. 1966.
Foucault, M.: Madness and Civilization. 1967.
Fox, D. J., and Kelly, R. L.: The Research Process in Nursing. 1967.
Framkel, M. G., *et al.*: Functional Teaching of the Mentally Retarded. 1966.
Harrison, S. I., and Carek, D. J.: A Guide to Psychotherapy. 1966.
Illingworth, R. S.: Common Symptoms of Disease in Children. 1967.
Jarry, D. M.: Human Parasitology. 1967.
Jones, H. W., and Heller, R. H.: Pediatric and Adolescent Gynecology. 1966.
King, M. (editor): Medical Care in Developing Countries. 1966.
Koegler, R. R., and Brill, N. Q.: Treatment of Psychiatric Outpatients. 1967.
Millon, T. (editor): Theories of Psychopathology. 1967.
Moberg, E.: Emergency Surgery of the Hand. 1967.
Muntner, S. (editor): Treatise on Poisons and the Antidotes. 1966.
National Council of Social Service: Caring for People. 1967.
Ney, C., and Friedenberg, R. M.: Radiographic Atlas of the Genitourinary System. 1966.
Potts, W. J.: Your Wonderful Baby. 1967.
Ramsay, A. M., and Emond, R. T. D.: Infectious Diseases. 1967.
Rendle-Short, M. and J.: The Father of Child Care: Life of William Cadogan (1711–1797). 1966.
Roodyn, D. B. (editor): Enzyme Cytology. 1967.
Rose, A. H. (editor): Thermobiology. 1967.
Rose, G.: School for Young Offienders. 1967.
Schachtel, E. G.: Experimental Foundations of Rorschach's Test. 1967.
Sohier, R.: Kinesitherapy of the Shoulder. 1967.
Starr, I., and Noordergraaf, A.: Ballistocardiography in Cardiovascular Research. 1967.
Usdin, G. L. (editor): Psychoneurosis and Schizophrenia. 1966.

H.M. Forces

Appointments.—Group Captain H. A. N. Hamersley (deputy principal medical officer (H), Headquarters Air Support Command); Group Captain I. M. O'Connor (ophthalmic duties, R.A.F. Hospital, Wegberg, Germany); Wing Commander B. K. Wharton (neuropsychiatry duties, R.A.F. Hospital, Wegberg, Germany); Wing Commander J. I. Cromarty (exchange posting, Royal Australian Air Force).

ARMY

Colonel G. F. Valentine, late R.A.M.C., has retired on retired pay.

ROYAL ARMY MEDICAL CORPS

Lieutenant-Colonel R. J. C. Hart has retired on retired pay.

Majors O. M. P. Tobias and D. S. Hutton to be Lieutenant-Colonels.

TERRITORIAL AND ARMY VOLUNTEER RESERVE

ROYAL ARMY MEDICAL CORPS

Major C. Dulake, from T.A., to be Major.

Association Notices

Armed Forces Committee
Nomination of Members for Co-option

The constitution of the Armed Forces Committee was amended at the Annual Representative Meeting of the Association in Bristol in July 1967 to allow greater representation of serving medical officers, especially younger members, by means of co-option to the Committee. It is now open to the Committee to co-opt two representatives, of the rank of major or equivalent (lieutenant-commander or squadron leader) or below, one of whom should preferably be of specialist status, from the medical branch of each of the Services.

Serving medical officers are therefore invited to nominate members of the Association in the armed Forces in these ranks for co-option to the Committee.

Nominations should be sent to the Secretary of the Association by 30 September 1967. The first meeting of the Armed Forces Committee, at which co-opted members will be appointed, will be held in the autumn, and after it nominees will be informed of the appointments made.

DEREK STEVENSON,
Secretary.

Diary of Central Meetings

SEPTEMBER

19	Tues.	Medical Science, Education, and Research Committee, 10.30 a.m.
21	Thurs.	General Medical Services Committee (Scotland) (at 7 Drumsheugh Gardens, Edinburgh), 2.15 p.m.
22	Fri.	Planning Unit, 4.30 p.m.
25	Mon.	Scottish Committee for Hospital Medical Services (at 7 Drumsheugh Gardens, Edinburgh), 11 a.m.
27	Wed.	Private Practice Committee, 10 a.m.
27	Wed.	Annual Meetings Committee, 2 p.m.
28	Thurs.	General Purposes Committee, 10.30 a.m.
29	Fri.	Joint Committee of B.M.A. and Magistrates' Association, 11 a.m.
29	Fri.	Film Committee, 2 p.m.

OCTOBER

3	Tues.	Scottish Council (at 7 Drumsheugh Gardens, Edinburgh),
4	Wed.	Occupational Health Committee, 10.30 a.m.
6	Fri.	Committee on Overseas Affairs, 1.30 p.m.
9	Mon.	Armed Forces Committee, 2 p.m.
11	Wed.	Journal Committee, 10.30 a.m.
12	Thurs.	G.M.S. Committee (at B.M.A. Scottish House, 7 Drumsheugh Gardens, Edinburgh), 10.30 a.m.
24	Tues.	Joint Consultants Committee (at Royal College of Physicians and Surgeons of Glasgow, 242 St. Vincent Street, Glasgow), 10 a.m.

DECEMBER

13	Wed.	Journal Committee, 2 p.m.

Branch and Division Meetings to be Held

Members proposing to attend meetings marked ● are asked to notify in advance the honorary secretary concerned.

MID-HERTS DIVISION.—At Medical Centre, St. Albans City Hospital, Friday, 22 September, 8.45 p.m., annual general meeting.

NORTH MIDDLESEX DIVISION.—Staff Room, Outpatients Department, North Middlesex Hospital, Tuesday, 19 September, 8 for 8.30 p.m., Dr. J. Q. Matthias: "Modern Advances in Haematology." A business meeting will follow.

SALISBURY DIVISION.—At Medical Centre, Salisbury General Infirmary, Friday, 22 September, 8 p.m., meeting to consider document on "The Functions of a District General Hospital." Speaker, Dr. A. E. P. Twort.

SOUTHAMPTON DIVISION.—At Postgraduate Medical Centre, Wednesday, 20 September, 8.30 p.m., ordinary general meeting. Dr. Angus McGregor will show slides on India.

SOUTH WALES AND MONMOUTHSHIRE BRANCH.—At Ysgyborwen Country Club, Aberdare, Thursday, 21 September, 3 p.m., annual meeting.

SUTTON DIVISION.—At Atkinson Morley's Hospital, Copse Hill, Wimbledon, S.W., Tuesday, 19 September, 8.15 p.m., clinical meeting.

SWINDON DIVISION.—At Senior Staff Room, Princess Margaret Hospital, Swindon, Saturday, 23 September, 6.30 to 8.30 p.m., sherry party.

British Medical Journal Supplement

LONDON SATURDAY 23 SEPTEMBER 1967

CONTENTS

General Medical Services Committee - - - - - 132
Public Health Medical Officers' Salary Claim - - - 136
H.M. Forces - - - - - - - - - - - 136
Was it a Drug? - - - - - - - - - - 137
Diary of Central Meetings - - - - - - - 138
Branch and Division Meetings - - - - - - 138

General Medical Services Committee

Vocational Training for General Practice

The G.M.S. Committee discussed at length vocational training for general practice. Its advisory committee's report on the subject was presented by Mr. D. C. Bowie, the advisory committee's chairman. A summary of the conclusions in the report was printed last week (Supplement, 16 September, p. 129). The G.M.S. Committee approved the report in general and decided to send it to the Royal Commission on Medical Education and to the Central Committee on Postgraduate Medical Education. The advisory committee is to amend its report in the light of the G.M.S. Committee's debate, and particular attention is to be drawn to the G.M.S. Committee's concern that doctors who receive a vocational training for general practice should have available to them when they enter practice the necessary facilities to make effective use of their skills. See leading article at page 754.

The general practitioner's case at the next review of doctors' pay by the Review Body is to be presented by counsel. The memorandum of evidence is to be published but not the oral evidence.

A meeting of the General Medical Services Committee was held on 7 September, with Dr. J. C. CAMERON in the chair.

Advisory Committee's Report

Mr. D. C. BOWIE, chairman of the G.M.S. Committee's Advisory Committee on Vocational Training and Continuing Education for General Practice, introduced its report on vocational training for general practice.

Mr. Bowie referred to three current events of importance in medical education. The first was the setting up of the Royal Commission on Medical Education, which was due to report within the next six months. It would probably set the stage for medical education for the next 20 to 25 years. The second was the formation, by the joint action of the universities with medical schools and the medical colleges in England and Wales and in Scotland, of the Central Committee on Postgraduate Medical Education. The third was the publication of the General Medical Council's Recommendations on Basic Medical Education.

The General Medical Council had divided medical education for all doctors into four periods. These were (1) premedical education; (2) basic medical education (up to and including the pre-registration year); (3) vocational training; (4) continuing education.

Mr. Bowie quoted from the G.M.C.'s report: "The time is approaching when it will be necessary to identify programmes of training for each of the vocational branches of medicine, including general practice, and to arrange by an extension of the Medical Act for some form of official recognition to become available, such as the inclusion of names in a vocational register, for individual doctors for their selected careers in medicine." The sort of vocational register the G.M.C. had in mind was to be informative and not restrictive. On educational grounds, the G.M.C. had stated it would welcome the introduction of vocational training schedules.

Sources of Vocational Training

Mr. Bowie said that his committee's report was couched in general terms. The details would have to be worked out later. Contributions to vocational training could come from four sources. The first was from the hospital services, because it was there that concentrated experience in a reasonably short space of time could be had. The second was from university departments, and these included departments of general practice. The report advised that departments of general practice should be set up in all medical schools—the aim being to present the general-practitioner point of view in clinical situations to undergraduates at their impressionable periods, and to present them with a picture of good general practice, so that they would think of general practice as a career.

The third source of vocational training was general practice itself, by a modification of the existing trainee scheme. Mr. Bowie said he was glad that the trainee scheme, with all its imperfections, had survived, because it was now available for modification. The fourth source of vocational training was the local health authority services.

That these four sources of vocational training came under independent and separate authorities could create difficulties. The administration of vocational training for general practice should, like vocational training for other careers in medicine, be vested in the Central Committee on Postgraduate Medical Education. In this way general practitioners would be ranked with their colleagues and would have equal rights and equal claims on such a body. Such a national organization had to be sensitive to local needs and problems, and the report suggested various ways in which general practitioners could exercise their influence on regional bodies. There was a suggestion for general practice second-year registrarships, and that they should be elective.

As regards remuneration during training, a scheme was proposed whereby increasing general experience would be rewarded by increasing pay, even when the trainee moved to a department to which he could bring no particular previous experience.

Mr. Bowie concluded: "Even the improved rates of pay during training which are advocated [in the Committee's report] will fall below what doctors can currently expect to earn as assistants or as principals in general practice after little, if any, true vocational training. The rate of vocational training allowance now payable is far below what is needed even to make up the deficit for a doctor who has prepared himself conscientiously for his career. . . . Vocational training is, in effect, obligatory for doctors before they can secure appointments in specialist hospital practice. The general pattern is determined by the training requirements of the colleges for their specialist diplomas and by advisory appointments committees when electing applicants to consultant posts. If inducement payments, in the form of vocational training allowances, are to be the only incentives to vocational training for general practice the rates will have to be multiplied many times before these are effective. We suggest that standing advisory bodies should be formed to help to determine whether a scheme of vocational training measures up to what is desirable.

"Lastly, the report says that there is ample room for research and evaluation of different methods. We have not come forward with any single method [of vocational training], but we advise that if a scheme is accepted there will be variations throughout the country, and it will be desirable to evaluate them in order to progress"

General Debate

Dr. H. S. Howie Wood said that everybody was "having a go" at legislating for the doctor's first year or two after qualification, and it was fitting that the G.M.S. Committee should produce its own valuable contribution. As a trainer himself he was glad to see the proposal for co-operation between the hospitals and the local medical committees. He welcomed the role which the regional committee would play. Local medical committees should see to it that the training scheme did not become so educational that it lost touch with reality.

Dr. J. S. Happel thought it important that the responsibility for vocational training should be vested in an educational rather than a service authority. This was particularly the case in general practice, where the authority would have to co-ordinate contributions to vocational training from a number of independent bodies. The G.M.S. Committee would undoubtedly wish to be represented on the new committee. The advisory committee believed that a teacher must be appointed for long enough to encourage him to prepare himself seriously for his duties. It proposed that approval of the teacher should be provisional for the first year during which a registrar was attached to the practice, and it should then be reviewed. If the regional subcommittee was satisfied, and the teacher was prepared to continue, he would be reappointed for five years, and thereafter his appointment would be renewable on a five-yearly basis.

Dr. Happel said that five years was too long. The paragraph in the report as it stood was too weak. So many things could happen in respect of the personal commitments of the trainer and of his health, and Dr. Happel believed that the appointing committee should require some annual statement on these matters from the trainer. Mr. Bowie had mentioned the General Medical Council's recommendation of a vocational register. Did that mean, asked Dr. Happel, that only those general practitioners who had undergone vocational training would be principals on the register? Would those who had not undergone training become "medical assistants?

Local Control

Dr. A. Reeves commented on another report before the Committee entitled "A Future Trainee General Practitioner Scheme," which resulted from two separate two-day studies of the general practitioner trainee scheme organized by the British Postgraduate Medical Federation. The studies were directed to the community aspects of the work of general practitioners and the medical content was omitted. One of the conclusions was that organization should be in the hands of regional bodies engaged in postgraduate education in the other branches of medicine. Dr. Reeves thought there was a danger of general practitioners losing local control of their own affairs as a result of that suggestion. The scheme in his area, the West Riding, was proving effective, because the committee knew the trainers and knew the background. He hoped that the local element would be retained.

Dr. W. W. Fulton spoke as a member of the advisory committee, and he said that one of the difficulties facing it had been to decide on what the general practitioner of the future would be like. The committee's ideas had been vague. General practice was changing so rapidly, and therefore to try to say how general practitioners should be trained in future was a more difficult task than it would be for other specialties.

When it came to what the doctor should learn there had been more agreement, and in particular Dr. Fulton commented on the agreement between the representatives of the different bodies on the committee—the Royal College of General Practitioners, the B.M.A., the G.M.S. Committee, and the G.M.S. Committee (Scotland). The main point on which agreement had to be reached was the administration of a training scheme. In the other specialties the appropriate college set the standards. In general practice that had only just begun, and there was a long way to go. The standards were being set by the Royal College of General Practitioners, but there were very few university departments of general practice and there were practically no facilities for postgraduate vocational training for general practice.

Educational Responsibility

The advisory committee thought that the administration of the training scheme must be of an educational rather than a Health Service character, said Dr. Fulton, because there was inherent in the situation the dilemma that the needs of the Service, to provide medical care for patients, tended in the eyes of the Ministry of Health to be paramount. The Ministry must recognize that the N.H.S. had an obligation to provide vocational training for general practitioners as it had for hospital doctors. The committees responsible for this—nationally, regionally, and locally—must be educational committees, but Health Service administrative bodies must be represented on them, particularly regionally and locally. One of the difficulties would be to ensure that the hospital service would accept responsibility for the hospital part of the vocational training of general practitioners. Responsibility for training specialists was easily acceptable to hospitals, but it was more difficult for them to accept responsibility for others. Hospital authorities must be represented on the committees. Responsibility for the scheme should not be handed over to university departments.

The Health Departments, Dr. Fulton continued, would have to allocate money for educational purposes in the hospital service as well as in general practice. The Ministry must encourage experiments, and it was the G.M.S. Committee's job to push the Ministry to start doing something somewhere.

It was perhaps not for the advisory committee to say that there should be obligatory training for general practice, or to say that a doctor could not practise as an independent principal until he was recognized as a specialist in general practice. The time for that might be coming. The responsibility of the G.M.S. Committee was to say to the Ministry, "If there is to be an interim phase you must ensure that people who go through this vocational training are adequately recompensed for having done so." It was up to the G.M.S. Committee to ensure that.

New Concepts

Dr. A. Elliott said it seemed that the advisory committee and the General Medical Council and other bodies were thinking along the same lines. The G.M.C.'s recommendations were forward-looking. The concept of training was different from what it used to be. The idea used to be that a man became a "doctor" the day he got his diploma. It was interesting that mathematics were now part of medical training, because a knowledge of statistics was essential, and there was also training in psychology and sociology. Before a full vocational training scheme could be implemented there was a need to educate teachers, and that could not be done overnight. There were traditions in medicine which had been current for 150 years. It was up to the G.M.S. Committee and local medical committees to fight for the new concepts.

Dr. M. Goodman said that so long as general practice was the only subject to be left out of the undergraduate curriculum it would not command respect from prospective entrants. However, if university departments in general practice were created they must not be treated in the same way as other departments in the university sometimes were, with professors arguing over how many hours their specialty should be allocated.

General practitioners who were teachers would not have time to attend so many patients as before, and their lists would be smaller. Any payment to teachers would have to be commensurate not only with their skill but also compensatory for their smaller list. The committee selecting the teachers would have to learn by experience who made good trainers, and perhaps at the end of a certain period it would have to look at their work.

Lengthier Training

Dr. A. Speakman believed that every doctor should spend a period in general practice. Another aspect of a vocational training scheme was that it lengthened a doctor's period of training. The age of maturity was falling, and more and more undergraduates wanted to get married. They were not going to wait another four years before starting to earn their living. It was important that the social effects of a vocational training scheme should be considered. People must not be discouraged from entering general practice by the prospect of a prolonged course of training before they could settle in the job they wanted to do and in the circumstances in which they wanted to do it, with a wife and family. A trainee's pay should increase during his training so that he could live a normal social life.

Nobody but a general practitioner of experience should teach general practice, continued Dr. Speakman. One of the paragraphs in the report read:

> General practitioner teachers must be experienced principals who can combine their skill in domiciliary care with high standards of scientific medicine in the treatment of patients in the community they serve. Those who hold clinical appointments in other parts of the Health Service should be well placed for approval. Originality not amounting to eccentricity and enterprise are valuable qualities. Some general practitioners may have had experience of teaching medical students or junior doctors holding hospital appointments, and others may be teaching in some related field—for example, in health education. Evidence of original work and thought, the possession of certain higher qualifications, and participation in research projects should all be considered in the case of a doctor aspiring to become a general practitioner teacher.

These, said Dr. Speakman, might be called the criteria for those who wished to become general practitioner teachers. However, teaching was an art, and not everyone had that gift. "We must find a method whereby we can detect the good general practitioner who will be able to give to his trainee the results of his own experience and be able to put it across in the proper manner. None of these criteria necessarily imply this. On the other hand, we must be careful not to eschew those people who have none of these qualifications. There are many general practitioners who get on with their work quietly, and do the job excellently, but they do not get their names in print or get letters after their names. Yet they would be excellent teachers, because they are basically sympathetic to human problems, and training is a human problem."

Teachers' Pay

The teacher was entitled to "a substantial increase in remuneration." Dr. Speakman said he was not yet convinced as to the justification for the words "substantial increase in remuneration." Obviously the teachers would have to be subsidized, because they would have a smaller list. But he was not convinced that somebody who did less work should receive a substantial increase in remuneration *per se*.

Dr. Speakman agreed a teacher should get extra pay for an onerous and responsible task. But where should the money come from? If the "substantial increase in remuneration" was based on the existing method of payment Dr. Speakman said he foresaw trouble. If the Review Body was asked for extra money to pay doctors who were going to be teachers, and whose qualifications fulfilled certain criteria, the Review Body might say that these payments were merit awards "coming in by the back door." Dr. Speakman suggested that the extra remuneration for general practitioner teachers should come from the funds of the educational authority, and must be unrelated to the payments for general medical services which were negotiated with the Review Body. Then there could be no quibble, and nobody could say that these doctors were taking money which other doctors might have got.

Some Questions

Dr. Speakmen asked for an assurance that, if the suggested vocational register became mandatory, qualification for admission to the register would not be made retrospective—that was, that doctors who had been qualified for years should have to become trainees before they could be put on the register. Secondly, he wanted to know what a department of general practice was going to do. Was it going to be purely administrative? Was it going to be educational, and, if so, what could be taught in a department of general practice that could not be taught in a surgery? One could not learn in a university how to cope with personal problems.

Dr. Speakman also wanted to know what would be the function of the Royal College of General Practitioners. He was not implying any criticism of the College. It was said that it would be on an equal basis with local medical committees in forming the regional bodies. However, he did not consider it wise for a body which did not represent all general practitioners to be on an equal basis with local medical committees on the regional subcommittees. There had to be a happy marriage between the service departments and the educational departments, but the college was primarily an educational body, and he hoped that it would not have *carte blanche* to run the subcommittees. It was the local medical committee, the service side, that should have the final say.

Finally, the remuneration of the trainee would have to be increased during the long period of training, but that would mean that he was a salaried general practitioner. His pay would be laid down on a scale. If a doctor was salaried at the beginning of his career there was a danger that the Ministry would try to carry that over into his eventual method of payment.

Access to Hospitals

Dr. D. L. WILLIAMS believed that the worst corrosive influence on the morale of general practitioners was their inability to practise the skills which they had been taught in a training which had been mainly orientated to the hospital service. Yet here was a proposal for another two years of hospital training. Therefore the policy put forward in the report could be justified only if it was believed that general practitioners in the future were going to have direct access to the district general hospital, that they were to have hospital privileges commensurate with their training, and that they were going to be able to look after their own patients in hospital with full clinical responsibility, subject to the availability of specialist advice.

Dr. Williams went on: "If we believe that, then this report is right. But if we believe that, then we are proposing a hospital revolution, and if we are proposing a hospital revolution then the younger doctors will want to know that that revolution is going to be successful before they put two years of their lives in pawn. It would be irresponsible for this Committee to approve a further two years' training unless we clearly put in this document the changes which we think ought to take place in the hospital service before those extra two years are put into force. When we trained as doctors we had in mind what we were going to get when we finished. A general practitioner undertaking vocational training will want to know what he will get as a result of that vocational training in the way of extra rights and privileges."

Paragraph 5 of the report, said Dr. Williams, read as follows: "Vocational training is thus an essential part of the preparation for a career in any branch of medicine, and doctors who wish to enter general practice will have to undergo an acceptable programme of training after full registration. The Committee supports this principle."

Dr. Williams put forward an amendment, to add the words:

> "It is equally essential that doctors who complete a programme of training should have ample opportunity to use the additional skills they have acquired. In particular, they should enjoy hospital privileges commensurate with their training, including the right to attend their own patients in National Health Service hospitals, exercising full clinical responsibility and calling for the advice and help of specialist colleagues when necessary. Agreement on the detailed application of this principle should be reached before any formal scheme is introduced, in order to clothe vocational training with suitable academic and clinical incentives."

Probationary Assistant

Dr. Williams said he thought there was too quick a move from too little vocational training to too much. He believed there ought to be a method of combining the "assistantship with a view" with the trainee year as an alternative to the trainee scheme as such. For that reason he suggested a new paragraph headed "Alternative Arrangements for First Trainee Year." Some doctors might not wish, for family or other personal reasons, to postpone too long their final entry into practice and might wish to combine the first trainee year with a probationary assistantship with a view. That arrangement would be approved only where the practice concerned would have been eligible for appointment as a teaching practice. The assistant would receive the training normally given in a teaching practice, and, in addition, would be released on one day in each week to attend an organized vocational training course at a regional centre. He would be paid and employed by the practice as an assistant with a view, but the executive council would refund the proportion of his salary and expenses attributable to attendance at the training course.

Dr. Williams thought that, with the shortage of doctors and with emigration, any mention of compulsion for vocational training was farcical. Furthermore, he did not believe that it was right to compel the majority to do what a minority at the moment were doing—he was referring to the trainee practitioner scheme, where the numbers had been falling.

Dr. Williams thought that in places there was a "whiff of paternalism" in the advisory committee's report. One paragraph he would like to see deleted read: "While a doctor who had held a satisfactory series of hospital posts outside the vocational training scheme might be accepted for the general practice component of vocational training, the regional subcommittee should be satisfied that his application was genuine, and not, for example, merely to obtain finance and time to study for examinations for some other career." The regional subcommittee would have to be satisfied about his motives, and if officialdom did not approve of the method by which a doctor had gone about things then his motives must be questioned. Dr. Williams believed that that was a wrong approach.

There was another paragraph which read: "The Committee advises that when a doctor is accepted into a vocational training programme for general practice his remuneration should increase in accordance with his expanding general professional experience, irrespective of where, or under which employing authority, he may be working. This should provide an inducement for young doctors to prepare themselves properly for careers in general practice." That meant, said Dr. Williams, that experience in breadth and not in depth should entitle a trainee to an increase in salary—but again only when officialdom had approved the method by which he had gone about things. That would differentiate between those who were approved and those who were not, though the posts held might be comparable. That was nonsense. The words "when a doctor is accepted into a vocational training programme for general practice" should be deleted, and all doctors should have an increase in salary according to the breadth as well as the depth of their experience.

Approval of Conference

Dr. R. B. L. **Ridge** said that the reason why most reports on general practice gathered dust on shelves was because they were a step removed from reality, and the gap between what was proposed and what obtained was too wide. The reason why he particularly welcomed the advisory committee's report was because the gap between what was proposed and what obtained today was not too wide. However, before it could become policy it would have to receive the approval of the Conference of Representatives of Local Medical Committees.

Dr. Ridge referred to a proposal in the report that the regional general practice subcommittee "should be charged to procure, in conjunction with all interested bodies, a system of vocational training for general practice within the hospital region. The chairman of the regional committee and the postgraduate dean should be members *ex officio*, and the majority of members should be drawn from local medical committees and the Royal College of General Practitioners. University departments of general practice, the regional hospital board, and the executive council should also be represented." The scheme was to replace the existing trainee practitioner scheme. Local medical committees should continue to have a place in the new scheme, and therefore Dr. Ridge suggested that the paragraph should read, in the second sentence: "The chairman of the regional committee and the postgraduate dean should be members *ex officio*, and the majority of members should be drawn from local medical committees. The Royal College of General Practitioners, university departments of general practice, the regional hospital board, and the executive council should also be represented." Dr. Ridge said that if that alteration was not made he could see little prospect of the scheme receiving the support of the Conference.

To some extent the success of the scheme depended on the existence of departments of general practice in teaching hospitals. There were already one or two, but before they were established in every teaching hospital there had to be a great change in the climate of opinion. That would take a longer time than could be afforded to get the scheme started. Therefore Dr. Ridge hoped that the advisory committee would look at its report again to see to what extent the scheme could be brought into effect without necessarily having to rely on departments of general practice in teaching hospitals.

Dr. Ridge thought that there should be reconsideration of the proposal that there should be no appeal open to a doctor whose application to become a general practitioner teacher failed. Since the appointing committees would have the power of appointment they would also have the power of approving extra remuneration. In every other aspect of remuneration the G.M.S. Committee had always insisted that there must be an appeal machinery. It was noteworthy that in another paragraph of the report it was suggested that there should be appeals from the decisions of the regional subcommittees' assessments of the criteria for a vocational training allowance.

If the concept embodied in the report could be brought to fruition, concluded Dr. Ridge, it would do as much as, if not more than, anything else which the G.M.S. Committee had attempted to enhance the status of general practice.

Diploma in General Practice

Dr. G. **Murray Jones**, a member of the advisory committee, said that one of the reasons why newly qualified doctors suspected general practice was because of the ease with which they could go into it, and earn a fairly substantial income, compared with the difficulty in specializing.

He believed that a man who really believed that general practice was a specialty should be prepared to take a diploma in it. There was no reason why general practice, if it was a specialty, should not have a diploma or a higher qualification, when every other specialty had one. In answer to the question on what departments of general practice did, Dr. Jones said that they did the same as departments in other specialties—the professors organized the undergraduate and postgraduate education of students, and that was a gigantic task.

Dr. B. D. **Morgan Williams** commented on posts in hospitals for trainee general practitioners. The G.M.S. Committee should beware of what used to be called supernumerary posts, in which doctors had no clinical responsibility. Without responsibility there was little learning. He also commented on whether the teacher should be appointed for five years or less, and he thought it should be for, say, three years. Trainees should be asked to report each year to the local medical committee on what they had learnt.

The report proposed that when regional subcommittees appointed registrars to teaching practices the teachers concerned must be invited to take part. Dr. Williams wondered how any principal could be expected to take a trainee without appointing him personally or at least having some veto over the prospective appointment. If a principal was legally responsible for what a trainee did he must have the power to dismiss him. Dr. Williams thought that three years in hospital posts after qualification was too long. One preregistration year and a second year, perhaps in rotating appointments, was right, but not a third year. One of the attractions of general practice was that a man could be his own boss before he was 30 years of age. The age of responsibility should not be postponed further and further.

Training Course

Dr. D. B. **Wallis** drew attention to the need for training teachers, and mentioned the course that the Department of Adult Education in the University of Liverpool was running for a group of doctors who wanted to be trainers. They were shown the different teaching methods such as tutorials, one-to-one teaching, formal lectures, and the use of visual aids.

Dr. T. J. **Carter** suggested that a report on the report was needed to find out how many of its proposals were practicable. Would it be possible to find sufficient trainers of the calibre suggested? Would it be possible for doctors to find appropriate posts in hospitals over the three years in which they would be engaged in their training? What would be the time lag before these things were available? There should also be some way for young doctors to be put in touch with trainers, and an attempt should be made to help doctors to plan their training period.

Dr. H. N. **Rose** said that the report envisaged the upgrading of general practice and it told people how to become good general practitioners. There was an inference that in the future those who had not had a vocational training would not be good general practitioners. If a register was kept of doctors who had had this training there would be two classes of general practitioner.

Dr. Rose continued: "We are faced with the problem of whether in the future this should be mandatory or not. Can we expect people to undergo a course of training which is going to last eight or nine years before they can be recognized as good general practitioners? I think at the moment that this is pie in the sky." The scheme was a good scheme, but the realities of the situation had to be considered. There were too few doctors. If newly qualified doctors were asked to undertake this prolonged period of vocational training the general-practice work load would increase and the number of general practitioners would decrease. Was it possible to have perhaps a temporary scheme until there were more doctors? Dr. Rose suggested that, in addition to the preregistration period, there should be a period of perhaps three to six months in which doctors could learn the attractions of general practice. There could then be rotating clinical assistantships in hospitals, which would be mandatory, and they would attract a vocational training allowance. In that way they would continue to work in general practice and there would be no depletion of medical manpower.

Dr. Rose also pointed out that between 600 and 1,000 trainers would be needed for the proposed scheme, and if it was put into operation a crash training scheme for teachers would be required.

Idealistic Scheme

Dr. G. Cormack thought that the scheme was an idealistic one put forward by idealists. It was good to have idealists, but he was worried about one of the fundamental assumptions in the report: "The effectiveness of the contribution of new general practitioners will depend upon the adequacy of their training, while this in turn will increase the attractiveness of general practice and so improve recruitment."

Dr. Cormack said that the truth of that statement should be looked at in relation to what general practice consisted of for so many doctors today. A highly intelligent man or woman who trained for six years and then did three years' compulsory vocational training would turn out an exceptional member of the community. Were they to be expected to go to an industrial practice where they would spend most of the day signing certificates for people to stay off work? That was the anomaly of the scheme. It could not be considered in isolation from the nature and structure of general practice as it existed now in the N.H.S.

Dr. Cormack thought that the recommendation that a trainee should attend outpatient sessions in psychiatry for a year or hold a three months' house appointment was stretching it too far. The report stated that many general practitioners did not wish to practise obstetrics, in the sense of undertaking responsibility for confinements, but they would have an important function in shared antenatal and postnatal care and must "have had sufficient training to enable them to act appropriately in an obstetric emergency." Dr. Cormack submitted that any doctor who did not practise obstetrics should not do antenatal or postnatal care, because he was incompetent to do it.

Dr. B. E. P. Wookey agreed that obstetrics was an integral part of general practice, and every general practitioner should do it. A minimum of six months in obstetrics should be fundamental to the vocational training scheme.

Much depended on whether the scheme was going to be obligatory. He did not believe that a vocational training allowance would be an incentive, because those who were keen to be general practitioners would in any event take a course of training. To increase the attractiveness of general practice it was necessary to raise the bottom as well as to encourage the top.

Dr. Joan Chappell, a member of the advisory committee, said that medical teachers and the representatives of the colleges would have to be persuaded that a medical school could not function properly without a department of general practice. A department of general practice would make a contribution to the teaching of undergraduates, giving them some idea of general practice and of its administration. It would undertake research; it would also teach teachers; and one of its more subtle functions would be to teach the teachers in the other departments of the medical school. It was necessary to go ahead swiftly with a scheme for vocational training in general practice, and thus make a positive contribution to medicine.

Essentials for General Practice

Dr. E. Townsend welcomed the report for the very reason that it was an idealistic report. It was something to aim at. In 1962 Cornwall had put forward a motion to the Representative Body asking that all the necessary facilities for diagnosis and treatment should be provided for general practitioners. The motion had been lost. General practitioners now had ancillary help, and the next thing they must get was hospital beds and full diagnostic facilities. They were essential if general practice was to survive.

Dr. Townsend suggested that the postgraduate education committee should be represented on the regional general practice subcommittee. The postgraduate education committee was composed of a tutor, who was appointed to administer the postgraduate education in the hospital, and representatives of the local medical committee. Dr. Townsend hoped that the paragraph would be reworded as suggested by Dr. Ridge, to get the support of the Conference. The existing trainee scheme had come into disrepute because the local medical committees had failed to choose the right trainers. It was a task which they could not do, because, though the majority of members knew their colleagues socially, they did not go into their practices. Consultants often knew a great deal more about general practitioners.

Reply to Debate

Mr. Bowie, in replying to the debate, said that he had sensed a general approval for the report. It had sought to avoid details but to deal with principles. What the committee had had in mind in the question of the duration of appointment of trainers was that if quality among trainers was to be obtained the job must have some security of tenure and teachers an incentive to pursue their subjects. Careful assessment of the trainer and the trainees, and a feed back, would be necessary.

In answer to Dr. Speakman, Mr. Bowie said there was an objection to doing a general practice period soon after the preregistration year. The young doctor might not then have much experience of those specialties which would be of particular importance to him in general practice. On the question of additional income for teachers Mr. Bowie said that in the hospital service there was a system of clinical tutors all over the country, and the money came from the Treasury through the regional hospital boards and not through the University Grants Committee.

Mr. Bowie thought that a department of general practice would present the general practitioner's point of view in all clinical situations in the teaching hospitals. In addition to discussing the clinical condition and the social and other conditions which the general practitioner came up against it was valuable for these situations to be presented to the undergraduate, so that he was introduced to the concepts of general practice.

There was no doubt, Mr. Bowie continued, that Dr. D. L. Williams was right. If young men and women were trained in scientific medicine it would be a waste and a failure if they could not practise that kind of medicine. Therefore it was very important that conditions should be created in general practice in which young graduates could continue in the way they had been trained. It was a dilemma whether to make vocational training compulsory. Preliminary training in hospital practice had become obligatory by custom. What the advisory committee was seeking to do was to provide incentives for vocational training in general practice until custom had time to take over. He hoped that amendments to the report would not be accepted at this stage, but he would take the suggestions to his committee for its further consideration.

Mr. Bowie agreed that supernumerary hospital posts would be useless for training. Dr. Wallis had spoken of what Liverpool was doing, and it was hoped that such a course would become more general. The point about the number of posts available in hospitals and the number of teachers would have to be looked at again. Because of the competition for hospital jobs, there was bound to be complexity.

After a short discussion on the advisability of including Dr. Williams's amendments at this stage the Committee agreed that an expression of the general principle that it would be a waste if young men and women trained in scientific medicine could not apply it in general practice should be included in the report.

It was agreed that the report, as expressing in general the views of the G.M.S. Committee, should be sent to the Royal Commission on Medical Education and to the Central Committee on Postgraduate Medical Education.

It was also agreed that the advisory committee should be asked to revise its report in the light of the debate and to report back to the G.M.S. Committee in due course.

Other Items on Agenda

Review Body

The Chairman, in answer to a question on the forthcoming evidence to be presented to the Review Body, said that it would be presented in two parts—one on behalf of hospital doctors and the other for general practitioners. The hospital doctors had a complicated case, and they had instructed counsel to present it. The general practitioners' case would also be presented by counsel. As last time, the memorandum of evidence on behalf of general practitioners would be published, but not the oral evidence.

Dr. R. A. Keable-Elliott said that many doctors regretted that evidence for the hospital doctors should be given independently. The profession paid lip service to unity, but there would be no unity unless its members presented their case jointly.

The Chairman said that, through the Joint Evidence Committee, the hospital doctors and general practitioners would see each other's case. There would be a general case on behalf of the whole profession and a specific case for each of the two branches. It did not follow that professional unity would be disrupted, so long as one side did not present its case to the prejudice of the other.

Part-time Medical Assistants

Dr. C. J. Wells reported that there had been a meeting with the representatives of the Joint Consultants Committee, and then a tripartite meeting with representatives from the Ministry, to discuss the revised draft of a memorandum prepared by the Ministry on part-time appointments in intermediate medical and dental grades, together with proposals made by the Joint Consultants Committee and the General Medical Services Committee for the remuneration of general practitioners for on-call duties at hospitals.

The Ministry would not agree to any security of tenure for general practitioners now holding posts remunerated under section 94 of the terms and conditions of service. The profession's representatives had told the Ministry that they could not recommend general practitioners to take appointments in the medical assistant grade.

There had also been a discussion on the payments to be made for on-call duties. It had been suggested that payment should be made in two ways: either by a stand-by fee or by an item-of-service payment for each attendance at the hospital. The Ministry's reply, which was before the Committee, was: "The Department has considered the proposals for the remuneration of general practitioners for on-call duties and propose that each side submits evidence separately to the Review Body on this matter." Dr. Wells said his own view was that it would be quite wrong for the G.M.S. Committee to do that, because the Ministry had not yet accepted the principle that this was the method by which these duties should be remunerated. He suggested that no evidence should be given to the Review Body on this point until the Ministry had accepted the principle.

The Ministry now proposed to circulate regional hospital boards to suggest that they should offer part-time appointments in the medical assistant grade to general practitioners. The G.M.S. Committee had sent out about a year ago a recommendation to local medical committees that doctors should be advised not to take up these appointments. Dr. Wells said nothing in the negotiations or in the Ministry's letter had led him to suggest that the Committee should alter its attitude.

Dr. Ridge said that money would be got only from the Review Body. He did not think that the part-time employment of general practitioners in the hospital service should be linked with the fees for stand-by duties, which were an entirely separate matter. An unnecessary delay might be created if a claim for fees for stand-by and casualty work was not included in the next evidence to the Review Body.

The Committee decided that it would be premature to issue a reply to the Minister's letter until there had been further discussions on the whole arrangements for the employment of general practitioners in the hospital service.

Initial Practice Allowances

The Chairman reported that the Minister of Health had now agreed to introduce immediately a scheme for special allowances (to be known as "Type D" initial practice allowances) which would maintain (up to a specified amount) at their previous level the professional earnings of certain doctors who were willing to take up practice in new towns and redevelopment areas concurrently with the arrival of the new residents. These allowances would be offered in areas selected and approved by the Ministry in consultation with the Medical Practices Committee.

Type D allowances were considered appropriate for areas of rapid housing development where a considerable increase in population in comparatively few years was expected, and where it was desirable to have at the outset a doctor of experience and special qualities. The Type D allowance would take the form of a guarantee that the doctor's net annual professional income from all sources, after allowing for practice expenses actually incurred and accepted by the executive council as reasonable, would be made up if necessary to an amount agreed with the executive council as the amount of his previous net annual professional income from all sources subject to a maximum of £4,000 net per annum.

Dr. Goodman suggested that there should be a continuing practice allowance for doctors in redevelopment areas similar to that for the new development areas.

The Committee agreed that the case for a continuing practice allowance in redevelopment areas should be put to the Ministry.

The Chairman also reported that an investigation was being made into recruitment into general practice, and an attempt would be made to see how recruitment in the chronically underdoctored areas could be helped. The planning committee had decided it ought to get first-hand information from the doctors working in those areas, and a group would go to find out what doctors in those areas wanted. Did they want health centres? Did they want help in providing premises? Were the hospital arrangements satisfactory? Nine areas had been selected to begin with, and they were the ones that had been designated for a long time.

"Asset" Case

In reply to Dr. Speakman's request (*Supplement*, 12 August, p. 116) that the Association's solicitor should be consulted about the contract which general practitioners had, the solicitor had written stating that, for the purpose of answering Dr. Speakman's argument, it did not matter whether a general practitioner's contract was with the executive council, with the Minister, or with the executive council as agents for the Minister. It was the terms of the contract that mattered. In short, in the "Asset" case there had been a legally enforcible contract for payment of the new rate. In the case of general practitioners there was not.

Dr. Speakman said that in future when the Prime Minister accepted the Review Body's findings doctors should take no notice of it, because apparently it had no legal effect. They had made a mistake last time in accepting the Prime Minister's word. Another time they should keep the resignation letters until the money was produced. The solicitor had not answered his previous question about the legal basis on which doctors went to the Minister of Health to negotiate with him. The independence of the Review Body had been questioned time and time again. Its independence was built on the quicksands of political expediency, and the Review Body should be referred to as an arbitration tribunal. It was not the final arbiter.

The Chairman explained that there was always the danger that any body could be influenced by the Government. The relationship between the Review Body and the Prime Minister was the same as it had always been. It made recommendations to the Prime Minister. The Prime Minister was not bound to accept the advice of the Review Body any more than the profession was bound to accept its decision. General practitioners were independent contractors.

It was agreed that the matter should not be taken further, except that the exact nature of the general practitioner's contract should be clarified for future reference.

Public Health Medical Officers' Salary Claim

A meeting of Committee C of the Medical and (Hospital) Dental Whitley Council took place on 13 September, at which it was decided to remit the public health medical officers' salary claim to the Officers' Subcommittee of Committee C for further discussion. The position in relation to the claim, including the policy of the B.M.A. in refusing advertisements for public health appointments, will be considered further at a meeting of the Public Health Committee of the Association which will be held on 11 October.

H.M. Forces

A *Supplement* to the *London Gazette* has announced the following awards:

Royal Naval and Royal Marine Forces Reserve Decoration.—Surgeon Commanders C. W. R. Pyne, R. Woodside, Surgeon Lieutenant-Commanders R. A. J. Baily, H. J. S. Waldeck, G. S. Laird, P. W. O'Brien, I. H. Robinson, P. J. Roylance, and J. P. Williams, R.N.R.

Clasp to Royal Naval and Royal Marine Forces Volunteer Reserve Decoration.—Surgeon Lieutenant-Commander P. C. Collinson, V.R.D., R.N.R.

Royal Naval and Royal Marine Forces Volunteer Reserve Decoration.—Surgeon Lieutenant-Commanders R. Burtles, R.N.R., R. K. Newing, R.A.N.R., and N. Roydhouse, R.N.Z.N.V.R.

Territorial Efficiency Decoration.—Lieutenant-Colonel and Brevet Colonel J. Prentice, Lieutenant-Colonels W. Brabbin (now R.A.R.O.), A. G. Mackinnon, Major (Acting Lieutenant-Colonel) J. R. Watson, Majors N. L. Dallas, C. M. Scott, H. H. Sloan, H. Tubmen, and Captain J. R. Skene, R.A.M.C.

ROYAL NAVY

Surgeon Lieutenant-Commanders K. T. Hesketh and R. L. W. Cleave have been placed on the Retired List.

Surgeon Lieutenant-Commander J. R. P. White has been placed on the Emergency List.

Surgeon Lieutenant J. Gerwat to be Surgeon Lieutenant-Commander.

Group Committee: "That this meeting rejects the views stated by the Management Side of Whitley Committee B with reference to mileage allowances (*Supplement*, 19 August, p. 121) for the following reasons: (1) the expenditure properly attributable to motoring on official business is considerably more than the mileage allowance at present obtained as shown by the South-western Region Survey; (2) loan facilities for car hire purchase are not readily available to junior staff, more than 50% of whom already have substantial overdrafts; and asks that the special problems of junior staff on the use of their cars at night, in emergencies and under conditions of stress, be given consideration in the light of the facts now presented."

Dr. G. J. A. **Brown** said the resolution had arisen out of information received from a recent survey in the region. This had shown that consultants in the first two years claimed £180 a year, senior registrars claimed £65, registrars claimed £60, and senior house-officers claimed £35. There were many Commonwealth doctors who did not know what they were entitled to claim.

Dr. **Field** stressed the difficulties of the mileage negotiations and said that although a great deal of information and statistics had been obtained from both the Royal Automobile Club and the Automobile Association the Ministry would not accept the evidence.

Dr. **Pigott** moved: "That this Group Council should seek the support of the Central Committee for Hospital Medical Services in the use of the following limited action to bring pressure to bear on the Ministry—that is, in the area of certain selected hospital groups the use of private cars should cease for a limited period."

Another resolution from the South-western Region which the Group Council considered was: "That, in view of the success of the recent South-western Region survey on the costs of pursuing hospital careers, we propose that these facts be given urgent consideration, and that a similar study should be carried out by experts on a wider scale."

The Group Council supported this resolution.

Grading of Posts

The Group Council considered the following resolution from the South-east Metropolitan Region H.J.S. Committee: "That this meeting is of the opinion that candidates who are appointed to a particular post should be appointed to the grade at which the post was advertised, and not to a lower grade."

The Group Council agreed that the attention of the Central Committee for Hospital Medical Services should be drawn to the matter.

Organization Committee

The first meeting of the session of the Organization Committee was held on 14 September. Dr. J. S. **Noble** was unanimously re-elected Chairman and Dr. J. S. Ross was re-elected Deputy Chairman.

The **Chairman** said that during the year the Committee would be concerned with implementing the new constitution and preparing new standing orders for the Representative Body. Above all, the Committee must look to the membership of the Association.

Honorary Secretaries' Conference

Dr. C. C. **Lutton** strongly objected to the cancellation by the Council of the annual conference of honorary secretaries, and to the statement that medical politics were not within the purview of the conference. He contended that honorary secretaries had to deal with all current affairs, and medical politics were always current.

Dr. D. L. **Gullick**, Under Secretary, said that the conference was primarily to discuss the duties of honorary secretaries. It was impossible to draw a line between organization and medical politics. He suggested that a paper should be produced for the Committee about the future of the conference.

Membership

The **Chairman** said that the United Kingdom membership of the Association had increased by 1,200 in the past five months, but was still down by about 700 on the same time last year. The total membership was down by more than 3,000, but of this loss more than 2,000 was owing to the dissolution of the New Zealand Branch on 30 June. The latest recruiting circular had attracted so far more than 140 applications for membership or renewed membership.

Dr. A. B. **Gilmour**, Assistant Secretary, referring to the new B.M.A. career service, said that it was in many ways a concentration of what had for long been given as a personal service to members. The scope for giving advice on careers was enormous. The new service had been set up under Dr. R. A. Pallister and himself (*Supplement*, 9 September, p. 128). They were concentrating on newly qualified doctors and those interested in how best to prepare for their choice of career in medicine. The service gave individuals basic facts about prospects, and a series of information sheets on different specialties was available.

The **Chairman** hoped that the service would receive publicity and that it would expand. It was the sort of service that a modern professional association must give to its younger members. He congratulated Dr. Pallister and Dr. Gilmour on getting it going so quickly.

Recruitment

Dr. D. **Burrell** remarked that the Council had reduced its expenditure on propaganda, and he recommended that it should be suggested to the Council that if membership declined expenditure on propaganda should be increased.

Dr. **Joan Chappell** asked whether it was right for the Association to remain silent when accusations were made against it. It should advise editors and others what a great deal of work had been done.

Dr. **Ross** said that the feeling in the Association had been that if accusations were answered it led to correspondence, and a small matter could become inflated into something much greater than it really was. So the general policy had been to ignore such criticism. But he thought that policy had been taken too far. It needed to be reviewed, because the Association was, he thought, too cautious.

Dr. **Lutton** said that he encouraged young doctors to attend meetings to sign their applications for membership. He added that the importance of advertising must not be overlooked, and that at the Annual Representative Meeting he had suggested that *B.M.A. News* should be developed as a full-time medical newspaper. He believed that if criticism of the Association was fully answered there would be very little of it in future. Dr. J. M. **Dunlop** emphasized the importance of approaching students about becoming members of the Association as soon as they graduated. Dr. A. W. **Macara** urged the importance of recruitment among medical teachers, saying that students were not being encouraged because their teachers were often non-members.

Dr. R. A. A. R. **Lawrence** said that there was too great a gap between the medico-political functions of the Association and its scientific and academic functions. Many doctors looked upon the Association merely as a medico-political organization, believing that it had nothing to offer in the scientific and academic field. More ought also to be done in the field of postgraduate education. Dr. W. J. C. **Scott** thought that the Association should brush up its scientific image, possibly by joint scientific meetings with the Royal Colleges. He had been told that it was no part of a clinical teacher's job to sell the Association, and he had found teachers anti-Association and resistant to the suggestion that they might encourage young doctors to join it.

The **Chairman** said that the Committee must consider whether the trouble lay in the Association itself, whether it was doing what was right for the profession, whether it had not a more positive place to fill in the future, and whether the Association's relationship with the Royal Colleges and the General Medical Council should be looked at. He was sure that there was evidence of a change in the creation of the Planning Unit. This had benefited the Association, but that good would be maintained only if the Planning Unit produced results.

The Membership and Information Subcommittee, which would consider all these points, had an enormous problem on its hands, said the Chairman.

Dr. **Ross** said that it was by the image that the B.M.A. gave that it would be judged.

While the suggestions that had been made were of the greatest value, care must be taken to treat not only the symptoms but the underlying diseases.

A.R.M. Resolutions

The Committee considered a number of resolutions of the Annual Representative Meeting, 1967. Some were referred to other committees. In two cases it was agreed to ask the sponsoring Divisions to submit suggestions for implementing the resolutions.

The CHAIRMAN said that the memorandum by the East Yorkshire Branch, entitled "Proposals for Reform of the Constitution of the Association," was an important piece of work and that considerable time should be given to it. It was agreed that the matter should be placed on the agenda for the next meeting of the Committee, and that the East Yorkshire Branch should be invited to send representatives to the meeting.

Postgraduate Education

The Committee considered the following motion referred to it by the Council: "That a working party be set up as a matter of urgency to review the Association's policy and participation in the sphere of postgraduate education, and to consider what assistance the Association can give to the individual doctor and to postgraduate centres."

Dr. GILMOUR said that his concern was for the interests of the individual doctor and for the status of the B.M.A. in the world of medical education.

The CHAIRMAN said the subject was vitally important. The Association had an important function in relation to medical education in outlining the needs of the consumer. A planning unit in the field of medical education was needed. There were both short-term and long-term aspects, and the working party would be of value in regard to both.

The Committee agreed to report to the Council in favour of the proposal to set up a working party, and that its terms of reference should be: "To define B.M.A. policy with regard (1) to general principles and central organization in postgraduate activities; and (2) to the individual doctor undertaking postgraduate training; (3) to postgraduate centres."

Concessionary Subscription Rates

The Committee considered an A.R.M. resolution urging that the annual subscription of full-time lower grade university medical teachers should be reduced to 75% of the standard subscription. The Committee also considered a Junior Members Forum resolution advocating concessionary rates for subscriptions related not only to years since qualification but also to net annual income where that was below what might be expected.

The CHIEF ACCOUNTANT told the Committee that the Treasurer would be giving his views, and the CHAIRMAN suggested that the Committee should await the deliberations of the Finance Committee.

The Committee agreed.

Membership of Agenda Committee

The Committee discussed the question of eligibility for service on the Agenda Committee of the Representative Body, raised in a letter from Dr. B. L. Alexander. He pointed out that a member elected to serve on the Agenda Committee for the following year might arrive at the Representative Body meeting not having been re-elected as a representative.

The CHAIRMAN asked the Committee to express its view on whether a member elected to the Agenda Committee should serve until the end of the subsequent Representative Body meeting or subject to his re-election to the Representative Body for the following year.

The Committee decided by five votes to two in favour of the second alternative, and it was agreed to recommend it to the Council for submission to the A.R.M.

Junior Members Forum

The Committee considered the minutes of the Junior Members Forum 1967, and resolutions passed by the Forum about its future.

Dr. A. N. MATHIAS, Chairman of the Representative Body, said that the Forum at Manchester had been excellent and he had been greatly impressed by it. But it rested with the Council to confirm that the Forum should meet annually and on a two-day basis.

Dr. ROSS suggested that the Committee should strongly recommend that the Forum should meet annually for two days.

The Committee agreed.

Future of N.H.S.

The Committee had on its agenda the question of the method of obtaining the views of the profession on the development of the health services.

Dr. MATHIAS said that the subject was being cared for in the Planning Unit, and the General Medical Services Committee also had views about it. The Organization Committee was concerned with the organization of the Association and had a very full task until next year. He suggested that it should stick to its last, which it did with great skill and benefit to the Association, and "let those other people have a go."

The Committee agreed.

Community Services

Community services provided by local health authorities and family doctors are closely interrelated and developments in these services should not be planned in isolation.

This is emphasized in a circular issued by the Scottish Home and Health Department (H.&W.S. 29/1967), in which it is recognized that much has already been achieved in the development of closer co-operation between local health authorities and general practitioners, and between general practitioners and district nurses and midwives. In recent years many authorities have been experimenting in other directions, including the sharing of accommodation in clinic premises and the attachment of health visitors and other ancillary staff to general practitioners.

The circular suggests that to encourage the development of closer working relationships suitable accommodation in existing clinics which is not being fully utilized could be let to general practitioners on a full- or part-time basis. When a local authority is thinking of providing a new clinic local doctors should be consulted early about the possibility of sharing accommodation which would be used only intermittently by the local authority. If doctors want exclusive use of accommodation it is suggested that local authorities might consider building a health centre instead of a clinic. In appropriate cases the Secretary of State would consider delegating the necessary powers to local authorities to provide health centres.

Regional hospital boards should also be consulted when the joint use of premises and other forms of co-operation are being considered. The circular states that the boards might wish part-time use of consulting-rooms in the proposed buildings for out-patient consultations by visiting consultants.

Other suggestions put forward in the circular for consideration include the attachment of field workers to individual practices. The Department will in future tell local health authorities about proposals from general practitioners for new group practice premises, so that local authorities can take the initiative in co-ordinating services. It is also suggested that links through common membership of health service bodies would be further strengthened if local authorities co-opted family doctors to the health committee.

Police Tests in Hospital

The Ministry of Health has issued a circular (H.M.(67)64) commenting on the provisions of the Road Safety Act, 1967, which will affect hospital staff.

From 9 October it will become an offence to drive with more than 80 mg./100 ml. of alcohol in the blood. When a driver who has been in an accident is at hospital as a patient the Act enables the police to require him to provide specimens of breath, blood, or urine for the specified tests.

Under the Act a patient at a hospital is not liable to arrest without warrant, nor can he be required to go elsewhere to give the specimens of breath, blood, or urine.

Specimens may not be taken from a patient without his consent, and a specimen may not be taken from an unconscious patient or by catheterization.

The constable must notify the doctor in immediate charge of the case of the intention to require a patient to provide a specimen, and the doctor may object at any stage before a specimen has been provided if he considers that such action would be prejudicial to the proper examination, diagnosis, care, or treatment of the patient. He may also object to the patient being told of the requirement to provide a specimen or warned of the penalty.

Members of the hospital staff are not required to take part in the taking of specimens or in their evaluation, although the hospital is requested to arrange conditions of privacy under which patients may provide specimens. Hospital equipment will not be used in the tests.

The notification by the constable and any objection by the doctor will both normally be given orally.

The doctor may object on the above grounds at the beginning, or at a later stage, having first not objected. If he objects at any stage before the specimen has been provided the constable may not proceed.

H.M. Forces

Appointments.—Wing Commander J. L. M. Corbet (registrar, Princess Mary's R.A.F. Hospital, Halton); Wing Commander J. J. B. Hobbs (registrar, Princess Mary's R.A.F. Hospital, Akrotiri, Cyprus); Wing Commander A. W. Black (neuropsychiatry duties, R.A.F. Hospital, Wroughton); Wing Commander E. L. Gilbert (senior medical officer, R.A.F. Coltishall).

## ARMY

Brigadier R. T. Shipman, late R.A.M.C., has retired on retired pay.

Colonels J. J. Sullivan, O.B.E., C. C. Corfield, and M. G. Jackson-Smyth, late R.A.M.C., have retired on retired pay.

Lieutenant-Colonel C. D. Sanders, from R.A.M.C., to be Colonel.

ROYAL ARMY MEDICAL CORPS

Major T. H. E. Woods has resigned his commission.

Short Service Commission.—Captain B. Dennison to be Major.

REGULAR ARMY RESERVE OF OFFICERS

Royal Army Medical Corps

Majors D. J. C. Graff and J. A. Moncur, from T. and A.V.R., to be Majors.

TERRITORIAL AND ARMY VOLUNTEER RESERVE

Royal Army Medical Corps

Major J. A. Ward, E.R.D., has resigned his commission, retaining the rank of Major. (Substituted for the notification published in a *Supplement* to the *London Gazette* dated 25 July 1967, and in the *Supplement* to the *Journal*, 19 August, p. 122.)

Captain (Acting Major) J. C. D. Rawlins, from T.A., to be Captain, retaining the acting rank of Major.

Captain L. M. Honigsberger to be Major.

TERRITORIAL ARMY

Territorial Army Reserve of Officers:

Royal Army Medical Corps

Majors (Honorary Lieutenant-Colonels) W. S. Brown, T.D., W. C. Alford, O.B.E., A. V. Dickie, and B. Andrew have resigned their commission, retaining the honorary rank of Lieutenant-Colonel.

Major A. R. Currie has resigned his commission and has been granted the honorary rank of Lieutenant-Colonel.

Majors G. C. Chessor, A. Chambers, T.D., and J. D. Bruzaud have resigned their commissions, retaining the rank of Major.

Captains (Honorary Majors) A. S. Barling and S. H. B. Blaikie have resigned their commissions, retaining the honorary rank of Major.

Improvement Grants

Some changes have been made in the administration of the improvement grant scheme. The main change is that from 1 October executive councils will be responsible for approving grants for projects costing up to £500. When the estimated cost exceeds £500 the Minister's approval will be required, as at present. All doctors providing unrestricted general medical services will be eligible for grants provided their N.H.S. list contains 500 patients or 350 patients in the case of a rural practice.

Grants of one-third of the cost of the approved project, including professional fees and fees paid to the General Practice Advisory Service, will be paid, provided prior approval for the project has been obtained, and provided it is to improve existing practice premises for the provision of general medical services under the National Health Service. There must be adequate security of tenure of the premises, and when the premises are not used solely for N.H.S. practice purposes the grant will be only for that part of the work related to N.H.S. practice. Doctors will have to sign an undertaking that the approved premises will be used for N.H.S. medical practice for a minimum of three years in cases of grants up to £1,000 and four years in grants of over £1,000, and that if this undertaking is not observed they will repay the grant.

Expenses for which grants will not be paid are listed in paragraph 8 of a circular (E.C.N.621), and these include "any project where a contract has been entered into, or work commenced, without the prior approval of the executive council (for projects estimated to cost £500 or less), or the Department (for other projects)."

The Minister will consult representatives of the profession in individual cases of difficulty. Applications already made to executive councils will not be affected by the new arrangements.

B.M.A. Nuffield Library

The Library service is available to all members of the Association resident in Great Britain and Northern Ireland (and by special arrangement to members of the Irish Medical Association). A copy of the library rules will be forwarded on application to the Librarian at B.M.A. House.

The following books have been added to the Library:

Birch, C. A. (Editor): Emergencies in Medical Practice, 8th edition. 1967.

Brewer, J. I., and DeCosta, E. J.: Textbook of Gynecology, 4th edition. 1967.

Butt, W. R.: Hormone Chemistry. 1967.

Caceres, C. A., and Perry, L. W. (Editors): The Innocent Murmur. 1967.

Conley, J. (Editor): Cancer of the Head and Neck. 1967.

Crawford, T. (Editor): Modern Trends in Pathology—2. 1967.

Cunningham, E. R.: Classification for Medical Literature, 5th edition, revised by E. G. Steinke and M. L. Gladish. 1967.

Cunningham, P. J. (Editor): The Principles of Health Visiting. 1967.

Dawkins, J.: A Textbook of Sex Education. 1967.

Denson, K. W. E.: The Use of Antibodies in the Study of Blood Coagulation. 1967.

Freund, H. R.: Principles of Head and Neck Surgery. 1967.

Galdston, I.: Historic Derivations of Modern Psychiatry. 1967.

Gardner, E. K., and Shelton, B.: The Intensive Therapy Unit and the Nurse. 1967.

Hauschka, R.: Nutrition. 1967.

Hodson, M.: Doctors and Patients. 1967.

Hollander, E. P.: Principles and Methods of Social Psychology. 1967.

Hollander, E. P., and Hunt, R. G. (Editors): Current Perspectives in Social Psychology, 2nd edition. 1967.

Hoppenfeld, S.: Scoliosis. 1967.

Janeway, C. A., *et al.*: The Gamma Globulins. 1967.

Keddie, N. C.: Practical Management of the Acute Abdomen. 1967.

Lambertsen, C. J. (Editor): Underwater Physiology. 1967.

Laughlin, H. P.: The Neuroses. 1967.

Lenihan, J. M. A., Loutit, J. F., and Martin, J. H. (Editors): Strontium Metabolism. 1967.

Meltzer, D.: The Psycho-Analytical Process. 1967.

McCort, J. J.: Radiographic Examination in Blunt Abdominal Trauma. 1966.

Mitchell, G. A. G.: The Essentials of Neuroanatomy. 1966.

Moir, J. C.: The Vesico-Vaginal Fistula, 2nd edition. 1967.

Moroney, J.: Surgery for Nurses, 11th edition. 1967.

Oliver, L.: Parkinson's Disease. 1967.

Parry, C. B. Wynn: Rehabilitation of the Hand, 2nd edition. 1966.

Pirenne, M. H.: Vision and the Eye, 2nd edition. 1967.

Pratt, R. T. C.: The Genetics of Neurological Disorders. 1967.

Pyke, M.: The Science Century. 1967.

Rheingold, J. C.: The Mother, Anxiety, and Death. 1967.

Richardson, S. A., and Guttmacher, A. F. (Editors): Childbearing. 1967.

Roaf, R.: Scoliosis. 1966.

Sargant, W.: The Unquiet Mind. 1967.

Schouten, J.: The Rod and Serpent of Asklepios. 1967.

Schreiber, M. H., Wolma, F. J., and Hendrick, C. K.: Intravenous Abdominal Aortography and Placentography. 1967.

Turnbull, R. B., and Weakley, F. L.: Atlas of Intestinal Stomas. 1967.

Valdman, A. V. (Editor): Pharmacology and Physiology of the Reticular Formation. 1967.

Vulliamy, D. G.: The Newborn Child, 2nd edition. 1967.

Ward, F. A.: A Primer of Pathology, 2nd edition. 1967.

Wilson, G. S.: The Hazards of Immunization. 1967.

Wolfgang, M. E., and Ferracuti, F.: The Subculture of Violence. 1967.

Association Notices

Guyana Branch

Notice is hereby given by the Council to all concerned that the British Guiana Branch will henceforth be known as the Guyana Branch and will continue to function as a Branch of the British Medical Association.

DEREK STEVENSON,
Secretary.

Diary of Central Meetings

OCTOBER

3	Tues.	Scottish Council (at 7 Drumsheugh Gardens, Edinburgh).
4	Wed.	Constitution Subcommittee (Joint Consultants Committee), 10 a.m.
4	Wed.	Occupational Health Committee, 10.30 a.m.
5	Thurs.	Central Ethical Committee, 10.30 a.m.
6	Fri.	Committee on Overseas Affairs, 1.30 p.m.
6	Fri.	Full-time Medical Teachers and Research Workers Committee, 2 p.m.
6	Fri.	Hospital Junior Staffs Group Executive Committee, 2 p.m.
9	Mon.	Armed Forces Committee, 2 p.m.
10	Tues.	G.M.S. Advisory Committee on Vocational Training and Continuing Education, 2 p.m.
11	Wed.	Public Health Committee, 10 a.m.
11	Wed.	Journal Committee, 10.30 a.m.
11	Wed.	Film Committee, 2 p.m.
12	Thurs.	G.M.S. Committee (at B.M.A. Scottish House, 7 Drumsheugh Gardens, Edinburgh), 10.30 a.m.
13	Fri.	Public Health Committee (Scotland) (at 7 Drumsheugh Gardens, Edinburgh), 2.15 p.m.
19	Thurs.	Joint Consultants Committee (Scotland) (at 7 Drumsheugh Gardens, Edinburgh), 10.15 a.m., followed by meeting with Scottish Home and Health Department at St. Andrew's House, 2.30 p.m.
20	Fri.	Central Committee for Hospital Medical Services, 10.30 a.m.
21	Sat.	Central Committee for Hospital Medical Services, 10 a.m.
24	Tues.	Joint Consultants Committee (at Royal College of Physicians and Surgeons of Glasgow, 242 St. Vincent Street, Glasgow), 10 a.m.
25	Wed.	**Council**, 10 a.m.
26	Thurs.	S.H.M.O. Group Council, 2 p.m.

DECEMBER

13	Wed.	Journal Committee, 2 p.m.

Branch and Division Meetings to be Held

Members proposing to attend meetings marked ● are asked to notify in advance the honorary secretary concerned.

Birmingham Division.—At 36 Harborne Road, Edgbaston, Monday, 2 October, 8.15 p.m., meeting to consider revised constitution and elections to Representative Body.

Blackpool and Fylde Division.—At Savoy Hotel, Blackpool, Wednesday, 4 October, 7.30 p.m., dinner; 8.45 p.m., Dr. D. Longson: "More and Less—the Suprarenals in Health and Disease."●

Bournemouth Division.—At East Cliff Court Hotel, Friday, 6 October, 7.30 for 8 p.m., supper meeting, Mr. H. A. Cowan: "Sir Morell Mackenzie, Founder of British Laryngology." Guests are invited.●

Burnley Division.—At Swan and Royal Hotel, Clitheroe, Tuesday, 3 October, 7.30 for 8 p.m., annual dinner. Principal guest, Dr. Ronald Gibson (Chairman of Council, B.M.A.).

Bury and Rochdale Divisions.—At Royal Hotel, Silver Street, Bury, Friday, 6 October, 8.45 p.m., cocktail party for members and wives.

Darlington Division.—At White Horse Hotel, Friday, 6 October, 9 p.m., B.M.A. lecture by Dr. A. G. Leatham: "Modern Auscultation of the Heart."

Derbyshire Branch.—At Temple Hotel, Matlock, Sunday, 8 October, 3 p.m., annual general meeting.

Dewsbury Division.—At Board Room, Dewsbury General Hospital, Friday, 6 October, 8.30 p.m., B.M.A. lecture by Dr. Andrew Smith: "General Practice Extinction or Evolution?" (Preceded by short meeting in small committee room.)

Dunbartonshire Division.—At 9 Lynedoch Crescent, Glasgow, Friday, 6 October, 8 p.m., B.M.A. lecture by Dr. G. H. Day: "A Flop."

Edinburgh and South-east of Scotland Branch.—At David Hume Tower (Lecture Hall "A"), University of Edinburgh, Saturday, 7 October, 10 a.m., all-day conference on "Better Medical Care—Which Road?"

Harrow and Hillingdon Division.—At Whittington Hotel, Cannon Lane, Pinner, Tuesday, 3 October, 8.45 p.m., annual general meeting.

Havering Division.—At Nurses' Lecture Theatre, Oldchurch Hospital, Friday, 6 October, 8.30 p.m., Dr. W. W. Sargant: "Mechanisms of Brain Washing and Conversion" (illustrated by slides, film, and tape). Ladies are invited.

Lewisham Division.—At Medical Centre, Lewisham Hospital, Friday, 6 October, 8 p.m., Chairman's reception for doctors and wives.

Morpeth Division.—At Queen's Head Hotel, Wednesday, 4 October, 7.45 for 8 p.m., dinner followed by address by Professor H. G. Miller: "Future of Medicine and the National Health Service."

North Bedfordshire Division.—At Bedford Medical Institute, Thursday, 5 October, 8.30 p.m., B.M.A. lecture by Mr. F. G. St. Clair Strange: "Backache."

Renfrewshire Division.—Saturday, 7 October, visit to Polaris base. Wives are invited.●

Rotherham Division.—At Crown Hotel, Bawtry, Thursday, 5 October, 8 for 8.30 p.m., installation of chairman and dinner dance.

Sheffield Division.—At Arundel Room, Royal Victoria Hotel, Friday, 6 October, 8.30 p.m., annual general meeting.

South-west Wales Division.—At Ivy Bush Royal Hotel, Carmarthen, Saturday, 7 October, 7.15 p.m., annual general meeting and chairman's address by Mr. S. Morgan: "Travelling Clubs." Followed by buffet supper. Guests are invited.●

Swansea Division.—At Dragon Hotel, Thursday, 5 October, Chairman's address.

Torquay Division.—At Torre Abbey, Thursday, 5 October, 6.30 p.m., presentation to Dr. Agnes T. Kennie followed by wine and salami tasting.●

Wakefield, Pontefract, and Castleford Division.—At Rogerthorpe Country Club, Friday, 6 October, 7.30 for 8 p.m., annual dinner dance.

West Bromwich and Smethwick Division.—At Austin Showrooms, Lawhill Lane, Longbridge, Thursday, 5 October, 2.30 p.m., visit to Austin Motor Works.●

Winchester Division.—At Polygon Hotel, Southampton, Saturday, 7 October, 7.30 p.m., dinner dance.●

Branch and Division Officers Elected

Durham Division.—Chairman, Dr. P. Tattersall. Chairman-elect, Dr. J. S. Law. Honorary Secretary and Treasurer, Dr. J. S. Munro.

Mansfield Division.—Chairman, Dr. E. D. Cloughely. Chairman-elect and Vice-chairman, Mr. A. McEwen Smith. Honorary Secretary and Treasurer, Dr. D. C. Kilbride. Assistant Honorary Secretary, Dr. J. H. Beatty.

Norfolk Branch.—President, Dr. E. F. Claridge. President-elect Dr. P. G. E. Jolley. Vice-presidents, Dr. C. S. Hall-Smith, Dr. D. Vaughan. Honorary Secretary, Mr. N. A. Green.

North Wales Branch.—President, Mr. D. B. B. Whitehouse, Vice-president, Dr. L. W. Jones. President-elect, Dr. R. R. Prytherch. Honorary Secretary and Treasurer, Mr. A. H. Holmes.

Nottinghamshire Branch.—President, Dr. A. P. M. Page. President-elect, Dr. W. Dodd. Honorary Secretary, Dr. A. Murphy.

Oldham Division.—Chairman, Dr. A. Pool. Vice-chairman, Mr. A. F. Williams. Honorary Secretary, Dr. K. S. Mackenzie. Honorary Treasurer, Dr. W. K. Willan.

Orkney Division.—Dr. J. S. Walker has been appointed Honorary Secretary of the Division.

Scunthorpe Division.—Chairman, Dr. J. H. Willis. Chairman-elect, Mr. J. Eyton-Jones. Honorary Secretary and Treasurer, Dr. R. H. Foxton. Assistant Honorary Secretary, Dr. G. T. Birtwhistle.

Shetland Division.—Chairman, Dr. J. A. Hunter. Vice-chairman, Dr. I. M. Brooker. Honorary Secretary and Treasurer, Dr. W. M Prentice.

South Lancashire and East Cheshire Branch.—President, Dr. S. Freeman. Vice-president, Dr. T. D. Culbert. Honorary Secretary and Treasurer, Dr. C. Shiers.

Southport Division.—Chairman, Mr. C. R. Porteous. Chairman-elect and Vice-chairman, Dr. E. F. B Cadman. Honorary Secretary and Treasurer, Dr. N. S. Walls.

Stockport Division.—Chairman, Dr. D. M. Coates. Chairman-elect, and Vice-chairman, Dr. A. Lilker. Honorary Secretary and Treasurer, Dr. G. Beaumont. Assistant Honorary Secretary, Dr. J. L. Wilkinson.

Stockton Division.—Chairman, Dr. K. Chalmers. Vice-chairman, Dr. J. L. Merson. Honorary Secretary and Treasurer, Dr. D. J. Anderson. Assistant Honorary Secretary, Dr. A. M. Brown.

Sussex Branch.—President, Surgeon Captain C. B. Nicholson. President-elect, Dr. R. G. May. Vice-presidents, Dr. H. C. C. Taylor, Dr. S. P. Hall-Smith. Honorary Secretary, Mr. C. N. d'E. Eastes. Honorary Treasurer, Dr. D. Archdale-Smith.

Wessex Branch.—President, Dr. C. C. Thomas. President-elect, Mr. R. W. Knowlton. Vice-president, Dr. C. M. Norman, Dr. R. K. Machell. Honorary Secretary, Dr. R. G. Nicholson.

Woolwich Division.—Chairman, Dr. L. R. Sausman. Vice-chairman, Dr. D. Boomla. Honorary Secretary and Treasurer, Dr. P. F. Stebbing.